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Dossier zur Nutzenbewertung gemäß § 35a SGB V

Fruquintinib (FRUZAQLA®)

Takeda GmbH

Modul 4 A, Anhang 4-G

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

Zusatzanalysen

Stand: 03.06.2024

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Studie FRESCO-2, Zusatzanalysen

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Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	15 (4.5)
Number of Subjects Censored, n (%)	151 (97.4)	320 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.360 (0.570)
95% CI		(0.445, 4.158)
Log-rank p-value		0.620

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	95.3 (92.9, 97.7)
6 months	92.8 (83.2, 100.0)	94.4 (91.4, 97.4)
9 months	NE (NE, NE)	94.4 (91.4, 97.4)
12 months	NE (NE, NE)	94.4 (91.4, 97.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	154 (99.4)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.345 (1.050)
95% CI		(0.555, 34.013)
Log-rank p-value		0.128

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.0, 100.0)	96.7 (94.7, 98.7)
6 months	99.3 (98.0, 100.0)	96.7 (94.7, 98.7)
9 months	NE (NE, NE)	96.7 (94.7, 98.7)
12 months	NE (NE, NE)	96.7 (94.7, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	10 (3.0)
Number of Subjects Censored, n (%)	153 (98.7)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.153 (0.776)
95% CI		(0.471, 9.841)
Log-rank p-value		0.309

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	96.7 (94.7, 98.7)
6 months	98.7 (96.8, 100.0)	96.7 (94.7, 98.7)
9 months	NE (NE, NE)	96.7 (94.7, 98.7)
12 months	NE (NE, NE)	96.7 (94.7, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	33 (21.3)	121 (36.1)
Number of Subjects Censored, n (%)	122 (78.7)	214 (63.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	1.12 (0.69, 1.84)
Median (95% CI)	NE (NE, NE)	NE (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.652 (0.199)
95% CI		(1.118, 2.441)
Log-rank p-value		0.011

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (68.7, 83.5)	67.4 (62.3, 72.5)
6 months	76.1 (68.7, 83.5)	60.6 (54.4, 66.7)
9 months	NE (NE, NE)	58.3 (51.7, 65.0)
12 months	NE (NE, NE)	51.6 (40.9, 62.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	6 (3.9)	51 (15.2)
Number of Subjects Censored, n (%)	149 (96.1)	284 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.093 (0.433)
95% CI		(1.754, 9.555)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.1, 99.2)	84.8 (80.9, 88.7)
6 months	95.6 (92.1, 99.2)	84.3 (80.3, 88.3)
9 months	NE (NE, NE)	84.3 (80.3, 88.3)
12 months	NE (NE, NE)	84.3 (80.3, 88.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.06

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	13 (8.4)	29 (8.7)
Number of Subjects Censored, n (%)	142 (91.6)	306 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.772 (0.345)
95% CI		(0.393, 1.517)
Log-rank p-value		0.483

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (86.1, 95.7)	93.0 (90.1, 95.8)
6 months	90.9 (86.1, 95.7)	89.7 (85.7, 93.7)
9 months	NE (NE, NE)	87.6 (82.7, 92.4)
12 months	NE (NE, NE)	87.6 (82.7, 92.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.55

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	7 (4.5)	23 (6.9)
Number of Subjects Censored, n (%)	148 (95.5)	312 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.318 (0.437)
95% CI		(0.559, 3.106)
Log-rank p-value		0.524

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.9, 98.6)	93.4 (90.6, 96.1)
6 months	94.8 (90.9, 98.6)	92.1 (88.8, 95.3)
9 months	NE (NE, NE)	92.1 (88.8, 95.3)
12 months	NE (NE, NE)	92.1 (88.8, 95.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.48

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	15 (4.5)
Number of Subjects Censored, n (%)	152 (98.1)	320 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.200 (0.635)
95% CI		(0.634, 7.630)
Log-rank p-value		0.218

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.9, 100.0)	95.3 (93.0, 97.6)
6 months	98.0 (95.9, 100.0)	95.3 (93.0, 97.6)
9 months	NE (NE, NE)	95.3 (93.0, 97.6)
12 months	NE (NE, NE)	95.3 (93.0, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.52

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	154 (99.4)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.171 (1.068)
95% CI		(0.391, 25.712)
Log-rank p-value		0.269

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	97.9 (96.3, 99.4)
6 months	99.4 (98.1, 100.0)	97.0 (94.8, 99.3)
9 months	NE (NE, NE)	94.2 (89.6, 98.7)
12 months	NE (NE, NE)	94.2 (89.6, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	21 (13.5)	128 (38.2)
Number of Subjects Censored, n (%)	134 (86.5)	207 (61.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.028 (0.237)
95% CI		(1.903, 4.817)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (80.3, 91.8)	61.9 (56.5, 67.3)
6 months	80.3 (68.2, 92.4)	59.8 (54.0, 65.5)
9 months	NE (NE, NE)	53.4 (44.8, 62.0)
12 months	NE (NE, NE)	53.4 (44.8, 62.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.66

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	14 (9.0)	119 (35.5)
Number of Subjects Censored, n (%)	141 (91.0)	216 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.72, 1.64)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.223 (0.284)
95% CI		(2.421, 7.366)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (84.8, 95.1)	64.8 (59.5, 70.1)
6 months	89.9 (84.8, 95.1)	63.4 (57.9, 69.0)
9 months	NE (NE, NE)	55.1 (46.0, 64.1)
12 months	NE (NE, NE)	55.1 (46.0, 64.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.76

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	34 (21.9)	105 (31.3)
Number of Subjects Censored, n (%)	121 (78.1)	230 (68.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.15, NE)	1.84 (1.02, 2.69)
Median (95% CI)	NE (NE, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.326 (0.200)
95% CI		(0.896, 1.962)
Log-rank p-value		0.160

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (68.9, 83.4)	69.3 (64.1, 74.4)
6 months	76.1 (68.9, 83.4)	66.2 (60.4, 72.0)
9 months	NE (NE, NE)	58.4 (48.3, 68.5)
12 months	NE (NE, NE)	58.4 (48.3, 68.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	15 (9.7)	34 (10.1)
Number of Subjects Censored, n (%)	140 (90.3)	301 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.811 (0.317)
95% CI		(0.436, 1.510)
Log-rank p-value		0.494

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (84.9, 94.7)	90.7 (87.4, 94.0)
6 months	89.8 (84.9, 94.7)	87.4 (83.0, 91.7)
9 months	NE (NE, NE)	86.2 (81.4, 91.1)
12 months	NE (NE, NE)	86.2 (81.4, 91.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	3.35

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	6 (3.9)	30 (9.0)
Number of Subjects Censored, n (%)	149 (96.1)	305 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.966 (0.453)
95% CI		(0.809, 4.781)
Log-rank p-value		0.128

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (92.7, 99.1)	92.1 (89.1, 95.1)
6 months	95.9 (92.7, 99.1)	89.3 (85.2, 93.3)
9 months	NE (NE, NE)	87.3 (81.7, 92.8)
12 months	NE (NE, NE)	87.3 (81.7, 92.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.29

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	18 (5.4)
Number of Subjects Censored, n (%)	153 (98.7)	317 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.881 (0.748)
95% CI		(0.896, 16.816)
Log-rank p-value		0.047

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	94.7 (92.2, 97.1)
6 months	98.5 (96.4, 100.0)	93.7 (90.6, 96.8)
9 months	NE (NE, NE)	93.7 (90.6, 96.8)
12 months	NE (NE, NE)	93.7 (90.6, 96.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.48

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	5 (3.2)	8 (2.4)
Number of Subjects Censored, n (%)	150 (96.8)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.644 (0.578)
95% CI		(0.207, 2.000)
Log-rank p-value		0.417

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (93.7, 99.5)	97.5 (95.8, 99.2)
6 months	96.6 (93.7, 99.5)	97.5 (95.8, 99.2)
9 months	NE (NE, NE)	97.5 (95.8, 99.2)
12 months	NE (NE, NE)	97.5 (95.8, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	8 (2.4)
Number of Subjects Censored, n (%)	154 (99.4)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.650 (1.117)
95% CI		(0.185, 14.735)
Log-rank p-value		0.593

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.1, 100.0)	98.8 (97.6, 100.0)
6 months	99.3 (98.1, 100.0)	97.8 (95.6, 100.0)
9 months	NE (NE, NE)	91.0 (82.9, 99.1)
12 months	NE (NE, NE)	91.0 (82.9, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	8 (2.4)
Number of Subjects Censored, n (%)	155 (100.0)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.100

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.6, 99.2)
6 months	100.0 (100.0, 100.0)	97.4 (95.6, 99.2)
9 months	NE (NE, NE)	97.4 (95.6, 99.2)
12 months	NE (NE, NE)	97.4 (95.6, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	15 (9.7)	106 (31.6)
Number of Subjects Censored, n (%)	140 (90.3)	229 (68.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (1.05, 3.58)
Median (95% CI)	NE (NE, NE)	13.14 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.14 (NE, NE)
Min, Max	0.1, 6.8*	0.0, 13.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.420 (0.277)
95% CI		(1.985, 5.891)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (85.2, 94.8)	70.6 (65.6, 75.6)
6 months	90.0 (85.2, 94.8)	64.2 (58.0, 70.5)
9 months	NE (NE, NE)	62.9 (56.3, 69.6)
12 months	NE (NE, NE)	62.9 (56.3, 69.6)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.56	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	61 (18.2)
Number of Subjects Censored, n (%)	153 (98.7)	274 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		14.214 (0.720)
95% CI		(3.469, 58.242)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	83.1 (79.0, 87.2)
6 months	98.7 (96.9, 100.0)	78.4 (73.0, 83.8)
9 months	NE (NE, NE)	78.4 (73.0, 83.8)
12 months	NE (NE, NE)	78.4 (73.0, 83.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	11 (3.3)
Number of Subjects Censored, n (%)	151 (97.4)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.286 (0.585)
95% CI		(0.409, 4.047)
Log-rank p-value		0.678

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.8, 99.9)	96.6 (94.7, 98.6)
6 months	97.4 (94.8, 99.9)	96.6 (94.7, 98.6)
9 months	NE (NE, NE)	96.6 (94.7, 98.6)
12 months	NE (NE, NE)	96.6 (94.7, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	13 (3.9)
Number of Subjects Censored, n (%)	154 (99.4)	322 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.898 (1.040)
95% CI		(0.768, 45.314)
Log-rank p-value		0.054

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.0, 100.0)	96.2 (94.1, 98.3)
6 months	99.3 (98.0, 100.0)	95.6 (93.2, 98.0)
9 months	NE (NE, NE)	95.6 (93.2, 98.0)
12 months	NE (NE, NE)	95.6 (93.2, 98.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	21 (13.5)	83 (24.8)
Number of Subjects Censored, n (%)	134 (86.5)	252 (75.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.01 (2.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.685 (0.247)
95% CI		(1.039, 2.735)
Log-rank p-value		0.045

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (80.1, 91.5)	77.2 (72.5, 81.8)
6 months	85.8 (80.1, 91.5)	70.4 (64.4, 76.5)
9 months	NE (NE, NE)	70.4 (64.4, 76.5)
12 months	NE (NE, NE)	65.0 (53.4, 76.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	7 (4.5)	30 (9.0)
Number of Subjects Censored, n (%)	148 (95.5)	305 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.002 (0.421)
95% CI		(0.876, 4.571)
Log-rank p-value		0.102

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.7, 98.6)	91.2 (88.1, 94.2)
6 months	94.7 (90.7, 98.6)	90.4 (87.0, 93.8)
9 months	NE (NE, NE)	90.4 (87.0, 93.8)
12 months	NE (NE, NE)	90.4 (87.0, 93.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.22

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	6 (1.8)
Number of Subjects Censored, n (%)	151 (97.4)	329 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.562 (0.654)
95% CI		(0.156, 2.026)
Log-rank p-value		0.372

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.8, 99.9)	98.1 (96.5, 99.6)
6 months	97.3 (94.8, 99.9)	98.1 (96.5, 99.6)
9 months	NE (NE, NE)	98.1 (96.5, 99.6)
12 months	NE (NE, NE)	98.1 (96.5, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	8 (2.4)
Number of Subjects Censored, n (%)	152 (98.1)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.170 (0.681)
95% CI		(0.308, 4.447)
Log-rank p-value		0.882

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.4, 100.0)	97.5 (95.8, 99.2)
6 months	97.8 (95.4, 100.0)	97.5 (95.8, 99.2)
9 months	NE (NE, NE)	97.5 (95.8, 99.2)
12 months	NE (NE, NE)	97.5 (95.8, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	21 (13.5)	78 (23.3)
Number of Subjects Censored, n (%)	134 (86.5)	257 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (3.02, 6.54)
Median (95% CI)	NE (NE, NE)	13.60 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (NE, NE)
Min, Max	0.2, 6.5*	0.0, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.242 (0.252)
95% CI		(0.757, 2.036)
Log-rank p-value		0.392

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (78.8, 91.3)	80.4 (76.0, 84.9)
6 months	79.8 (68.1, 91.4)	71.0 (64.6, 77.4)
9 months	NE (NE, NE)	66.5 (58.6, 74.3)
12 months	NE (NE, NE)	66.5 (58.6, 74.3)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.46	2.86

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	5 (3.2)	55 (16.4)
Number of Subjects Censored, n (%)	150 (96.8)	280 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	13.60 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (NE, NE)
Min, Max	0.4*, 6.8*	0.2, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.939 (0.471)
95% CI		(1.565, 9.913)
Log-rank p-value		0.002

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.5, 99.5)	85.6 (81.6, 89.6)
6 months	96.5 (93.5, 99.5)	80.3 (75.0, 85.6)
9 months	NE (NE, NE)	75.9 (68.1, 83.8)
12 months	NE (NE, NE)	75.9 (68.1, 83.8)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.63	3.06

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	7 (2.1)
Number of Subjects Censored, n (%)	151 (97.4)	328 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.528 (0.656)
95% CI		(0.146, 1.910)
Log-rank p-value		0.333

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.5, 99.9)	98.1 (96.7, 99.6)
6 months	97.2 (94.5, 99.9)	97.5 (95.6, 99.4)
9 months	NE (NE, NE)	97.5 (95.6, 99.4)
12 months	NE (NE, NE)	97.5 (95.6, 99.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	12 (7.7)	67 (20.0)
Number of Subjects Censored, n (%)	143 (92.3)	268 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (4.60, 7.69)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.786 (0.321)
95% CI		(0.951, 3.352)
Log-rank p-value		0.057

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (88.2, 96.8)	85.0 (80.9, 89.0)
6 months	88.9 (80.9, 96.9)	73.2 (66.4, 80.0)
9 months	NE (NE, NE)	63.8 (54.1, 73.6)
12 months	NE (NE, NE)	63.8 (54.1, 73.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.06

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	11 (3.3)
Number of Subjects Censored, n (%)	151 (97.4)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.767 (0.622)
95% CI		(0.227, 2.593)
Log-rank p-value		0.775

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	97.5 (95.8, 99.2)
6 months	86.5 (69.2, 100.0)	95.4 (92.1, 98.7)
9 months	NE (NE, NE)	93.7 (89.1, 98.4)
12 months	NE (NE, NE)	93.7 (89.1, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.61

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	6 (1.8)
Number of Subjects Censored, n (%)	153 (98.7)	329 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.760 (0.870)
95% CI		(0.138, 4.179)
Log-rank p-value		0.764

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	99.0 (97.9, 100.0)
6 months	98.7 (96.9, 100.0)	96.6 (93.7, 99.5)
9 months	NE (NE, NE)	96.6 (93.7, 99.5)
12 months	NE (NE, NE)	96.6 (93.7, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	8 (2.4)
Number of Subjects Censored, n (%)	155 (100.0)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.112

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (95.9, 99.4)
6 months	100.0 (100.0, 100.0)	96.7 (94.1, 99.2)
9 months	NE (NE, NE)	96.7 (94.1, 99.2)
12 months	NE (NE, NE)	96.7 (94.1, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	25 (16.1)	51 (15.2)
Number of Subjects Censored, n (%)	130 (83.9)	284 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.753 (0.250)
95% CI		(0.461, 1.230)
Log-rank p-value		0.270

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.6, 89.0)	86.3 (82.5, 90.1)
6 months	82.8 (76.6, 89.0)	80.9 (75.5, 86.3)
9 months	NE (NE, NE)	79.7 (73.9, 85.5)
12 months	NE (NE, NE)	79.7 (73.9, 85.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	3.22

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	17 (11.0)	26 (7.8)
Number of Subjects Censored, n (%)	138 (89.0)	309 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.481 (0.327)
95% CI		(0.253, 0.913)
Log-rank p-value		0.025

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (82.1, 93.2)	94.1 (91.5, 96.8)
6 months	87.7 (82.1, 93.2)	88.6 (83.8, 93.4)
9 months	NE (NE, NE)	87.5 (82.2, 92.7)
12 months	NE (NE, NE)	87.5 (82.2, 92.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	24 (7.2)
Number of Subjects Censored, n (%)	153 (98.7)	311 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.304 (0.737)
95% CI		(1.252, 22.477)
Log-rank p-value		0.011

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	92.5 (89.5, 95.4)
6 months	98.6 (96.6, 100.0)	92.5 (89.5, 95.4)
9 months	NE (NE, NE)	92.5 (89.5, 95.4)
12 months	NE (NE, NE)	92.5 (89.5, 95.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.48

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	69 (20.6)
Number of Subjects Censored, n (%)	155 (100.0)	266 (79.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.1 (77.8, 86.4)
6 months	100.0 (100.0, 100.0)	73.2 (67.0, 79.5)
9 months	NE (NE, NE)	70.8 (63.9, 77.7)
12 months	NE (NE, NE)	70.8 (63.9, 77.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.86

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	63 (18.8)
Number of Subjects Censored, n (%)	155 (100.0)	272 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.01 (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.1 (80.0, 88.2)
6 months	100.0 (100.0, 100.0)	75.3 (69.2, 81.4)
9 months	NE (NE, NE)	72.9 (66.1, 79.6)
12 months	NE (NE, NE)	72.9 (66.1, 79.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.86

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	14 (9.0)	45 (13.4)
Number of Subjects Censored, n (%)	141 (91.0)	290 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.045 (0.315)
95% CI		(0.564, 1.939)
Log-rank p-value		0.849

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (85.6, 95.5)	87.8 (84.0, 91.6)
6 months	87.2 (79.2, 95.2)	81.7 (76.4, 87.0)
9 months	NE (NE, NE)	81.7 (76.4, 87.0)
12 months	NE (NE, NE)	81.7 (76.4, 87.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.22

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	9 (5.8)	21 (6.3)
Number of Subjects Censored, n (%)	146 (94.2)	314 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.620 (0.418)
95% CI		(0.273, 1.408)
Log-rank p-value		0.295

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.5 (89.3, 97.7)	94.2 (91.5, 97.0)
6 months	93.5 (89.3, 97.7)	91.0 (87.1, 94.9)
9 months	NE (NE, NE)	91.0 (87.1, 94.9)
12 months	NE (NE, NE)	91.0 (87.1, 94.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.42

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	154 (99.4)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.330 (1.062)
95% CI		(0.415, 26.712)
Log-rank p-value		0.262

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (94.7, 98.9)
6 months	96.4 (89.6, 100.0)	95.9 (93.3, 98.6)
9 months	NE (NE, NE)	95.9 (93.3, 98.6)
12 months	NE (NE, NE)	95.9 (93.3, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	6 (1.8)
Number of Subjects Censored, n (%)	153 (98.7)	329 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.128 (0.833)
95% CI		(0.221, 5.771)
Log-rank p-value		0.849

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.1, 100.0)	98.3 (96.9, 99.8)
6 months	98.4 (96.1, 100.0)	97.4 (95.0, 99.7)
9 months	NE (NE, NE)	97.4 (95.0, 99.7)
12 months	NE (NE, NE)	97.4 (95.0, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	24 (15.5)	44 (13.1)
Number of Subjects Censored, n (%)	131 (84.5)	291 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.601 (0.262)
95% CI		(0.359, 1.004)
Log-rank p-value		0.074

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.5 (78.6, 90.3)	88.3 (84.6, 91.9)
6 months	81.1 (72.5, 89.7)	83.6 (78.6, 88.7)
9 months	NE (NE, NE)	81.8 (75.7, 87.9)
12 months	NE (NE, NE)	78.1 (68.9, 87.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.32

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	16 (4.8)
Number of Subjects Censored, n (%)	152 (98.1)	319 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.713 (0.640)
95% CI		(0.489, 6.002)
Log-rank p-value		0.388

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	95.5 (93.1, 97.9)
6 months	97.7 (95.2, 100.0)	93.9 (90.7, 97.2)
9 months	NE (NE, NE)	93.9 (90.7, 97.2)
12 months	NE (NE, NE)	89.7 (80.9, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.58

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	13 (3.9)
Number of Subjects Censored, n (%)	153 (98.7)	322 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.991 (0.777)
95% CI		(0.435, 9.122)
Log-rank p-value		0.306

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	96.8 (94.9, 98.8)
6 months	98.7 (96.9, 100.0)	95.2 (92.3, 98.2)
9 months	NE (NE, NE)	93.3 (88.5, 98.0)
12 months	NE (NE, NE)	93.3 (88.5, 98.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	36 (48.0)	83 (68.6)
Number of Subjects Censored, n (%)	39 (52.0)	38 (31.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.30, 0.99)	0.66 (0.26, 0.69)
Median (95% CI)	3.71 (1.61, NE)	1.38 (0.72, 2.60)
75% percentile (95% CI)	NE (NE, NE)	7.29 (4.50, NE)
Min, Max	0.0, 13.0*	0.0, 11.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.408 (0.205)
95% CI		(0.942, 2.106)
Log-rank p-value		0.123

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.4 (41.9, 65.0)	40.1 (31.2, 48.9)
6 months	47.0 (33.8, 60.2)	28.0 (18.8, 37.1)
9 months	47.0 (33.8, 60.2)	22.6 (12.6, 32.6)
12 months	47.0 (33.8, 60.2)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	1.38

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	14 (18.7)	39 (32.2)
Number of Subjects Censored, n (%)	61 (81.3)	82 (67.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	1.54 (0.69, 4.76)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.660 (0.313)
95% CI		(0.898, 3.069)
Log-rank p-value		0.096

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (73.4, 91.0)	69.0 (60.6, 77.3)
6 months	79.0 (68.6, 89.4)	65.9 (56.8, 74.9)
9 months	79.0 (68.6, 89.4)	65.9 (56.8, 74.9)
12 months	79.0 (68.6, 89.4)	65.9 (56.8, 74.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.99

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	11 (14.7)	22 (18.2)
Number of Subjects Censored, n (%)	64 (85.3)	99 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.60, NE)	NE (6.97, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.227 (0.389)
95% CI		(0.572, 2.629)
Log-rank p-value		0.669

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.2 (75.5, 92.8)	83.2 (76.5, 89.9)
6 months	84.2 (75.5, 92.8)	83.2 (76.5, 89.9)
9 months	84.2 (75.5, 92.8)	77.6 (67.9, 87.4)
12 months	84.2 (75.5, 92.8)	77.6 (67.9, 87.4)
18 months	NE (NE, NE)	77.6 (67.9, 87.4)
Median Follow-up Time (months)	2.83	4.37

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	5 (6.7)	10 (8.3)
Number of Subjects Censored, n (%)	70 (93.3)	111 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.835 (0.566)
95% CI		(0.275, 2.534)
Log-rank p-value		0.687

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (87.6, 99.0)	94.9 (91.0, 98.9)
6 months	93.3 (87.6, 99.0)	92.5 (87.5, 97.6)
9 months	93.3 (87.6, 99.0)	90.5 (84.2, 96.8)
12 months	93.3 (87.6, 99.0)	80.5 (61.1, 99.9)
18 months	NE (NE, NE)	80.5 (61.1, 99.9)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	21 (17.4)
Number of Subjects Censored, n (%)	73 (97.3)	100 (82.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (4.50, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.063 (0.744)
95% CI		(1.411, 26.048)
Log-rank p-value		0.007

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.3, 100.0)	84.2 (77.6, 90.7)
6 months	97.2 (93.3, 100.0)	82.6 (75.5, 89.7)
9 months	97.2 (93.3, 100.0)	82.6 (75.5, 89.7)
12 months	97.2 (93.3, 100.0)	82.6 (75.5, 89.7)
18 months	NE (NE, NE)	41.3 (0.0, 98.7)
Median Follow-up Time (months)	2.83	3.98

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	4 (3.3)
Number of Subjects Censored, n (%)	72 (96.0)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.517 (0.792)
95% CI		(0.109, 2.442)
Log-rank p-value		0.436

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.7, 100.0)	98.2 (95.8, 100.0)
6 months	95.6 (90.7, 100.0)	95.4 (90.9, 99.9)
9 months	95.6 (90.7, 100.0)	95.4 (90.9, 99.9)
12 months	95.6 (90.7, 100.0)	95.4 (90.9, 99.9)
18 months	NE (NE, NE)	95.4 (90.9, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	5 (4.1)
Number of Subjects Censored, n (%)	72 (96.0)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.758 (0.755)
95% CI		(0.173, 3.326)
Log-rank p-value		0.655

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (91.4, 100.0)	96.6 (93.2, 99.9)
6 months	95.9 (91.4, 100.0)	96.6 (93.2, 99.9)
9 months	95.9 (91.4, 100.0)	96.6 (93.2, 99.9)
12 months	95.9 (91.4, 100.0)	90.1 (77.5, 100.0)
18 months	NE (NE, NE)	90.1 (77.5, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.399

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.7, 100.0)
9 months	100.0 (100.0, 100.0)	96.6 (92.7, 100.0)
12 months	100.0 (100.0, 100.0)	96.6 (92.7, 100.0)
18 months	NE (NE, NE)	96.6 (92.7, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.229

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (95.7, 100.0)
6 months	100.0 (100.0, 100.0)	96.8 (93.0, 100.0)
9 months	100.0 (100.0, 100.0)	96.8 (93.0, 100.0)
12 months	100.0 (100.0, 100.0)	96.8 (93.0, 100.0)
18 months	NE (NE, NE)	96.8 (93.0, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	2 (1.7)
Number of Subjects Censored, n (%)	75 (100.0)	119 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.358

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.0 (92.6, 100.0)
9 months	100.0 (100.0, 100.0)	97.0 (92.6, 100.0)
12 months	100.0 (100.0, 100.0)	97.0 (92.6, 100.0)
18 months	NE (NE, NE)	97.0 (92.6, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	35 (46.7)	85 (70.2)
Number of Subjects Censored, n (%)	40 (53.3)	36 (29.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.59, 1.84)	0.56 (0.39, 0.69)
Median (95% CI)	5.36 (1.87, NE)	1.45 (0.72, 2.27)
75% percentile (95% CI)	NE (5.36, NE)	6.47 (3.68, NE)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.668 (0.207)
95% CI		(1.112, 2.502)
Log-rank p-value		0.016

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.8 (43.0, 66.6)	36.7 (28.0, 45.4)
6 months	30.1 (7.0, 53.2)	25.7 (16.7, 34.8)
9 months	NE (NE, NE)	23.6 (14.3, 32.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.00	1.45

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	8 (10.7)	29 (24.0)
Number of Subjects Censored, n (%)	67 (89.3)	92 (76.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.95 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.899 (0.405)
95% CI		(0.859, 4.198)
Log-rank p-value		0.121

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (81.8, 96.2)	79.9 (72.7, 87.1)
6 months	89.0 (81.8, 96.2)	72.9 (63.5, 82.3)
9 months	89.0 (81.8, 96.2)	70.6 (60.5, 80.8)
12 months	89.0 (81.8, 96.2)	70.6 (60.5, 80.8)
18 months	NE (NE, NE)	70.6 (60.5, 80.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	10 (13.3)	22 (18.2)
Number of Subjects Censored, n (%)	65 (86.7)	99 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.44 (5.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.278 (0.424)
95% CI		(0.557, 2.932)
Log-rank p-value		0.630

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (77.7, 94.1)	87.0 (80.9, 93.2)
6 months	85.9 (77.7, 94.1)	78.8 (69.9, 87.8)
9 months	85.9 (77.7, 94.1)	74.4 (64.0, 84.7)
12 months	85.9 (77.7, 94.1)	74.4 (64.0, 84.7)
18 months	NE (NE, NE)	74.4 (64.0, 84.7)
Median Follow-up Time (months)	2.83	4.27

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	7 (9.3)	25 (20.7)
Number of Subjects Censored, n (%)	68 (90.7)	96 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.57, NE)	7.98 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.114 (0.467)
95% CI		(0.846, 5.284)
Log-rank p-value		0.081

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (84.5, 98.0)	85.1 (78.5, 91.7)
6 months	85.2 (72.0, 98.3)	76.7 (67.8, 85.5)
9 months	85.2 (72.0, 98.3)	73.6 (63.3, 83.9)
12 months	85.2 (72.0, 98.3)	73.6 (63.3, 83.9)
18 months	NE (NE, NE)	58.9 (31.8, 86.0)
Median Follow-up Time (months)	2.83	4.24

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	5 (6.7)	21 (17.4)
Number of Subjects Censored, n (%)	70 (93.3)	100 (82.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.81, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.064 (0.503)
95% CI		(0.770, 5.534)
Log-rank p-value		0.177

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (86.9, 98.9)	85.0 (78.4, 91.6)
6 months	92.9 (86.9, 98.9)	81.1 (73.5, 88.8)
9 months	92.9 (86.9, 98.9)	78.4 (69.4, 87.5)
12 months	92.9 (86.9, 98.9)	78.4 (69.4, 87.5)
18 months	NE (NE, NE)	78.4 (69.4, 87.5)
Median Follow-up Time (months)	2.83	4.21

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	19 (15.7)
Number of Subjects Censored, n (%)	72 (96.0)	102 (84.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	10.18 (6.21, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.443 (0.637)
95% CI		(0.701, 8.512)
Log-rank p-value		0.131

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.2, 100.0)	88.6 (82.8, 94.5)
6 months	88.3 (71.4, 100.0)	85.3 (78.0, 92.6)
9 months	88.3 (71.4, 100.0)	80.5 (71.0, 90.0)
12 months	88.3 (71.4, 100.0)	74.3 (59.7, 88.9)
18 months	NE (NE, NE)	74.3 (59.7, 88.9)
Median Follow-up Time (months)	2.86	4.57

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	16 (13.2)
Number of Subjects Censored, n (%)	71 (94.7)	105 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.788 (0.639)
95% CI		(0.797, 9.753)
Log-rank p-value		0.095

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (88.7, 99.7)	88.4 (82.7, 94.1)
6 months	94.2 (88.7, 99.7)	86.7 (80.2, 93.2)
9 months	94.2 (88.7, 99.7)	83.7 (75.2, 92.2)
12 months	94.2 (88.7, 99.7)	83.7 (75.2, 92.2)
18 months	NE (NE, NE)	83.7 (75.2, 92.2)
Median Follow-up Time (months)	2.83	4.57

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	4 (3.3)
Number of Subjects Censored, n (%)	73 (97.3)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.881 (0.899)
95% CI		(0.151, 5.126)
Log-rank p-value		0.725

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.4 (93.0, 99.9)
6 months	89.7 (72.7, 100.0)	96.4 (93.0, 99.9)
9 months	NE (NE, NE)	96.4 (93.0, 99.9)
12 months	NE (NE, NE)	96.4 (93.0, 99.9)
18 months	NE (NE, NE)	96.4 (93.0, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	5 (4.1)
Number of Subjects Censored, n (%)	74 (98.7)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.348 (1.112)
95% CI		(0.266, 20.756)
Log-rank p-value		0.422

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	96.7 (93.5, 99.9)
6 months	98.7 (96.1, 100.0)	95.2 (91.0, 99.5)
9 months	98.7 (96.1, 100.0)	95.2 (91.0, 99.5)
12 months	98.7 (96.1, 100.0)	95.2 (91.0, 99.5)
18 months	NE (NE, NE)	95.2 (91.0, 99.5)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	4 (3.3)
Number of Subjects Censored, n (%)	75 (100.0)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.160

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
6 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
9 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
12 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
18 months	NE (NE, NE)	96.6 (93.4, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.275

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (94.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (94.7, 100.0)
9 months	100.0 (100.0, 100.0)	97.5 (94.7, 100.0)
12 months	100.0 (100.0, 100.0)	97.5 (94.7, 100.0)
18 months	NE (NE, NE)	97.5 (94.7, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	17 (22.7)	51 (42.1)
Number of Subjects Censored, n (%)	58 (77.3)	70 (57.9)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (0.76, NE)	1.58 (0.69, 2.76)
Median (95% CI)	10.18 (NE, NE)	NE (4.60, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.813 (0.298)
95% CI		(1.011, 3.253)
Log-rank p-value		0.059

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (68.0, 87.4)	62.5 (53.6, 71.3)
6 months	77.7 (68.0, 87.4)	56.7 (46.9, 66.5)
9 months	77.7 (68.0, 87.4)	50.3 (39.2, 61.3)
12 months	0.0 (NE, NE)	50.3 (39.2, 61.3)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	10 (13.3)	30 (24.8)
Number of Subjects Censored, n (%)	65 (86.7)	91 (75.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.24 (1.94, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.985 (0.404)
95% CI		(0.899, 4.383)
Log-rank p-value		0.121

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (77.9, 94.1)	78.4 (70.8, 85.9)
6 months	86.0 (77.9, 94.1)	75.3 (66.9, 83.7)
9 months	86.0 (77.9, 94.1)	68.9 (58.4, 79.3)
12 months	86.0 (77.9, 94.1)	68.9 (58.4, 79.3)
18 months	NE (NE, NE)	68.9 (58.4, 79.3)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	5 (4.1)
Number of Subjects Censored, n (%)	74 (98.7)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.330 (1.103)
95% CI		(0.268, 20.246)
Log-rank p-value		0.441

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	95.7 (92.0, 99.4)
6 months	98.6 (96.0, 100.0)	95.7 (92.0, 99.4)
9 months	98.6 (96.0, 100.0)	95.7 (92.0, 99.4)
12 months	98.6 (96.0, 100.0)	95.7 (92.0, 99.4)
18 months	NE (NE, NE)	95.7 (92.0, 99.4)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	7 (5.8)
Number of Subjects Censored, n (%)	73 (97.3)	114 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.734 (0.807)
95% CI		(0.357, 8.435)
Log-rank p-value		0.509

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.5, 100.0)	94.0 (89.7, 98.3)
6 months	97.3 (93.5, 100.0)	94.0 (89.7, 98.3)
9 months	97.3 (93.5, 100.0)	94.0 (89.7, 98.3)
12 months	97.3 (93.5, 100.0)	94.0 (89.7, 98.3)
18 months	NE (NE, NE)	94.0 (89.7, 98.3)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	3 (2.5)
Number of Subjects Censored, n (%)	73 (97.3)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.562 (0.986)
95% CI		(0.081, 3.881)
Log-rank p-value		0.621

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (92.9, 100.0)	98.3 (96.1, 100.0)
6 months	97.0 (92.9, 100.0)	98.3 (96.1, 100.0)
9 months	97.0 (92.9, 100.0)	94.1 (85.6, 100.0)
12 months	97.0 (92.9, 100.0)	94.1 (85.6, 100.0)
18 months	NE (NE, NE)	94.1 (85.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	7 (5.8)
Number of Subjects Censored, n (%)	75 (100.0)	114 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.067

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.9 (91.0, 98.9)
6 months	100.0 (100.0, 100.0)	94.9 (91.0, 98.9)
9 months	100.0 (100.0, 100.0)	92.0 (85.1, 98.9)
12 months	100.0 (100.0, 100.0)	92.0 (85.1, 98.9)
18 months	NE (NE, NE)	92.0 (85.1, 98.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	7 (5.8)
Number of Subjects Censored, n (%)	75 (100.0)	114 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.104

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (92.2, 99.4)
6 months	100.0 (100.0, 100.0)	92.3 (86.4, 98.3)
9 months	100.0 (100.0, 100.0)	92.3 (86.4, 98.3)
12 months	100.0 (100.0, 100.0)	92.3 (86.4, 98.3)
18 months	NE (NE, NE)	92.3 (86.4, 98.3)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	5 (4.1)
Number of Subjects Censored, n (%)	75 (100.0)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.147

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
6 months	100.0 (100.0, 100.0)	96.6 (93.4, 99.9)
9 months	100.0 (100.0, 100.0)	94.4 (89.1, 99.7)
12 months	100.0 (100.0, 100.0)	94.4 (89.1, 99.7)
18 months	NE (NE, NE)	94.4 (89.1, 99.7)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	2 (1.7)
Number of Subjects Censored, n (%)	74 (98.7)	119 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.588 (1.347)
95% CI		(0.042, 8.234)
Log-rank p-value		0.763

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	99.2 (97.5, 100.0)
6 months	98.6 (96.0, 100.0)	99.2 (97.5, 100.0)
9 months	98.6 (96.0, 100.0)	94.9 (86.4, 100.0)
12 months	98.6 (96.0, 100.0)	94.9 (86.4, 100.0)
18 months	NE (NE, NE)	94.9 (86.4, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	4 (3.3)
Number of Subjects Censored, n (%)	73 (97.3)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.841 (0.905)
95% CI		(0.143, 4.956)
Log-rank p-value		0.905

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.6 (93.3, 99.9)
6 months	98.6 (96.0, 100.0)	96.6 (93.3, 99.9)
9 months	98.6 (96.0, 100.0)	96.6 (93.3, 99.9)
12 months	0.0 (NE, NE)	96.6 (93.3, 99.9)
18 months	0.0 (NE, NE)	96.6 (93.3, 99.9)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	1 (0.8)
Number of Subjects Censored, n (%)	75 (100.0)	120 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.655

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
6 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
9 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
12 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
18 months	NE (NE, NE)	99.2 (97.6, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	15 (20.0)	45 (37.2)
Number of Subjects Censored, n (%)	60 (80.0)	76 (62.8)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (1.58, NE)	1.91 (1.18, 4.67)
Median (95% CI)	NE (5.59, NE)	16.79 (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.2*, 6.8*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.585 (0.312)
95% CI		(0.860, 2.922)
Log-rank p-value		0.179

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (73.1, 90.9)	70.2 (61.9, 78.5)
6 months	68.2 (47.7, 88.7)	62.4 (52.5, 72.3)
9 months	NE (NE, NE)	53.2 (41.3, 65.2)
12 months	NE (NE, NE)	53.2 (41.3, 65.2)
18 months	NE (NE, NE)	35.5 (6.0, 65.0)
Median Follow-up Time (months)	2.83	3.38

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	6 (8.0)	10 (8.3)
Number of Subjects Censored, n (%)	69 (92.0)	111 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.756 (0.527)
95% CI		(0.269, 2.124)
Log-rank p-value		0.482

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (87.1, 98.9)	92.8 (87.9, 97.6)
6 months	84.5 (67.9, 100.0)	89.5 (82.9, 96.1)
9 months	NE (NE, NE)	89.5 (82.9, 96.1)
12 months	NE (NE, NE)	89.5 (82.9, 96.1)
18 months	NE (NE, NE)	89.5 (82.9, 96.1)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	9 (7.4)
Number of Subjects Censored, n (%)	73 (97.3)	112 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.451 (0.883)
95% CI		(0.435, 13.820)
Log-rank p-value		0.392

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	94.9 (91.0, 98.9)
6 months	89.7 (72.7, 100.0)	93.6 (88.9, 98.3)
9 months	NE (NE, NE)	88.1 (79.5, 96.7)
12 months	NE (NE, NE)	88.1 (79.5, 96.7)
18 months	NE (NE, NE)	88.1 (79.5, 96.7)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	8 (6.6)
Number of Subjects Censored, n (%)	73 (97.3)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.357 (0.836)
95% CI		(0.264, 6.986)
Log-rank p-value		0.744

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	95.8 (92.1, 99.4)
6 months	89.7 (72.7, 100.0)	93.8 (88.5, 99.0)
9 months	NE (NE, NE)	88.3 (79.4, 97.2)
12 months	NE (NE, NE)	88.3 (79.4, 97.2)
18 months	NE (NE, NE)	88.3 (79.4, 97.2)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	5 (4.1)
Number of Subjects Censored, n (%)	75 (100.0)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.186

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (93.3, 99.9)
6 months	100.0 (100.0, 100.0)	96.6 (93.3, 99.9)
9 months	100.0 (100.0, 100.0)	94.2 (88.5, 99.8)
12 months	100.0 (100.0, 100.0)	94.2 (88.5, 99.8)
18 months	NE (NE, NE)	94.2 (88.5, 99.8)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	8 (6.6)
Number of Subjects Censored, n (%)	74 (98.7)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.709 (1.076)
95% CI		(0.450, 30.563)
Log-rank p-value		0.201

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (90.8, 98.9)
6 months	95.8 (87.8, 100.0)	93.1 (88.0, 98.3)
9 months	95.8 (87.8, 100.0)	88.9 (79.4, 98.4)
12 months	95.8 (87.8, 100.0)	88.9 (79.4, 98.4)
18 months	NE (NE, NE)	88.9 (79.4, 98.4)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	3 (2.5)
Number of Subjects Censored, n (%)	73 (97.3)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.735 (0.915)
95% CI		(0.122, 4.413)
Log-rank p-value		0.725

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.0, 100.0)	97.5 (94.6, 100.0)
6 months	96.6 (92.0, 100.0)	97.5 (94.6, 100.0)
9 months	96.6 (92.0, 100.0)	97.5 (94.6, 100.0)
12 months	96.6 (92.0, 100.0)	97.5 (94.6, 100.0)
18 months	NE (NE, NE)	97.5 (94.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	9 (7.4)
Number of Subjects Censored, n (%)	74 (98.7)	112 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	NE (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.727 (1.065)
95% CI		(0.463, 30.041)
Log-rank p-value		0.204

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.0 (89.6, 98.3)
6 months	100.0 (100.0, 100.0)	91.4 (85.9, 96.9)
9 months	NE (NE, NE)	91.4 (85.9, 96.9)
12 months	NE (NE, NE)	91.4 (85.9, 96.9)
18 months	NE (NE, NE)	91.4 (85.9, 96.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	5 (4.1)
Number of Subjects Censored, n (%)	74 (98.7)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.857 (1.117)
95% CI		(0.208, 16.593)
Log-rank p-value		0.513

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.3, 100.0)	98.3 (96.1, 100.0)
6 months	98.4 (95.3, 100.0)	95.6 (91.1, 100.0)
9 months	98.4 (95.3, 100.0)	93.4 (87.3, 99.4)
12 months	98.4 (95.3, 100.0)	93.4 (87.3, 99.4)
18 months	NE (NE, NE)	93.4 (87.3, 99.4)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.451

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (96.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (93.7, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (88.7, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (88.7, 100.0)
18 months	NE (NE, NE)	94.8 (88.7, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	1 (0.8)
Number of Subjects Censored, n (%)	75 (100.0)	120 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
12 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	24 (32.0)	54 (44.6)
Number of Subjects Censored, n (%)	51 (68.0)	67 (55.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.33, NE)	0.69 (0.69, 0.95)
Median (95% CI)	NE (NE, NE)	11.53 (2.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.368 (0.255)
95% CI		(0.829, 2.256)
Log-rank p-value		0.293

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.4 (56.6, 78.1)	59.1 (50.2, 67.9)
6 months	67.4 (56.6, 78.1)	56.3 (47.0, 65.5)
9 months	67.4 (56.6, 78.1)	51.4 (40.6, 62.2)
12 months	67.4 (56.6, 78.1)	42.8 (25.1, 60.6)
18 months	NE (NE, NE)	42.8 (25.1, 60.6)
Median Follow-up Time (months)	2.76	2.79

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	6 (8.0)	23 (19.0)
Number of Subjects Censored, n (%)	69 (92.0)	98 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.618 (0.474)
95% CI		(1.034, 6.630)
Log-rank p-value		0.056

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (85.2, 98.0)	80.8 (73.8, 87.9)
6 months	91.6 (85.2, 98.0)	80.8 (73.8, 87.9)
9 months	91.6 (85.2, 98.0)	80.8 (73.8, 87.9)
12 months	91.6 (85.2, 98.0)	80.8 (73.8, 87.9)
18 months	NE (NE, NE)	80.8 (73.8, 87.9)
Median Follow-up Time (months)	2.83	3.94

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	9 (12.0)	14 (11.6)
Number of Subjects Censored, n (%)	66 (88.0)	107 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.809 (0.459)
95% CI		(0.329, 1.989)
Log-rank p-value		0.640

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (80.4, 95.3)	90.8 (85.6, 96.0)
6 months	87.8 (80.4, 95.3)	89.1 (83.1, 95.2)
9 months	87.8 (80.4, 95.3)	89.1 (83.1, 95.2)
12 months	87.8 (80.4, 95.3)	82.3 (68.2, 96.3)
18 months	NE (NE, NE)	61.7 (25.2, 98.2)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	14 (18.7)	15 (12.4)
Number of Subjects Censored, n (%)	61 (81.3)	106 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.576 (0.395)
95% CI		(0.265, 1.249)
Log-rank p-value		0.118

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.9 (71.8, 89.9)	89.2 (83.6, 94.7)
6 months	80.9 (71.8, 89.9)	89.2 (83.6, 94.7)
9 months	80.9 (71.8, 89.9)	87.2 (80.5, 93.9)
12 months	80.9 (71.8, 89.9)	77.5 (58.6, 96.3)
18 months	NE (NE, NE)	77.5 (58.6, 96.3)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.208

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (94.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (94.5, 100.0)
9 months	100.0 (100.0, 100.0)	97.4 (94.5, 100.0)
12 months	100.0 (100.0, 100.0)	97.4 (94.5, 100.0)
18 months	NE (NE, NE)	97.4 (94.5, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	0
Number of Subjects Censored, n (%)	74 (98.7)	121 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.239

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.6, 100.0)	100.0 (100.0, 100.0)
6 months	98.5 (95.6, 100.0)	100.0 (100.0, 100.0)
9 months	98.5 (95.6, 100.0)	100.0 (100.0, 100.0)
12 months	98.5 (95.6, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	13 (17.3)	51 (42.1)
Number of Subjects Censored, n (%)	62 (82.7)	70 (57.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	0.95 (0.62, 1.87)
Median (95% CI)	NE (NE, NE)	NE (4.47, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.693 (0.323)
95% CI		(1.429, 5.075)
Log-rank p-value		0.002

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (72.8, 90.8)	61.3 (52.5, 70.1)
6 months	81.8 (72.8, 90.8)	55.1 (45.3, 65.0)
9 months	NE (NE, NE)	53.0 (42.7, 63.3)
12 months	NE (NE, NE)	53.0 (42.7, 63.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	6 (8.0)	49 (40.5)
Number of Subjects Censored, n (%)	69 (92.0)	72 (59.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.12 (0.62, 1.87)
Median (95% CI)	NE (NE, NE)	NE (4.47, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.329 (0.435)
95% CI		(2.273, 12.493)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (85.1, 98.0)	62.0 (53.2, 70.8)
6 months	91.6 (85.1, 98.0)	57.7 (48.2, 67.2)
9 months	NE (NE, NE)	55.6 (45.6, 65.5)
12 months	NE (NE, NE)	55.6 (45.6, 65.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	14 (18.7)	48 (39.7)
Number of Subjects Censored, n (%)	61 (81.3)	73 (60.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (2.56, NE)	1.45 (0.82, 1.84)
Median (95% CI)	NE (5.59, NE)	9.76 (5.29, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.026 (0.320)
95% CI		(1.082, 3.792)
Log-rank p-value		0.030

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (75.8, 92.9)	65.5 (57.0, 74.1)
6 months	65.4 (42.7, 88.2)	57.6 (47.6, 67.7)
9 months	NE (NE, NE)	55.5 (45.0, 66.0)
12 months	NE (NE, NE)	49.3 (34.6, 64.1)
18 months	NE (NE, NE)	49.3 (34.6, 64.1)
Median Follow-up Time (months)	2.83	2.83

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	13 (10.7)
Number of Subjects Censored, n (%)	73 (97.3)	108 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.066 (1.041)
95% CI		(1.048, 62.077)
Log-rank p-value		0.017

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.5, 100.0)	90.0 (84.6, 95.4)
6 months	97.3 (93.5, 100.0)	88.3 (82.2, 94.5)
9 months	97.3 (93.5, 100.0)	88.3 (82.2, 94.5)
12 months	97.3 (93.5, 100.0)	88.3 (82.2, 94.5)
18 months	NE (NE, NE)	88.3 (82.2, 94.5)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	20 (16.5)
Number of Subjects Censored, n (%)	71 (94.7)	101 (83.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (5.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.348 (0.558)
95% CI		(0.787, 7.006)
Log-rank p-value		0.117

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (91.2, 100.0)	85.7 (79.4, 92.0)
6 months	87.1 (70.3, 100.0)	83.6 (76.3, 91.0)
9 months	NE (NE, NE)	78.3 (68.2, 88.3)
12 months	NE (NE, NE)	78.3 (68.2, 88.3)
18 months	NE (NE, NE)	78.3 (68.2, 88.3)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	8 (6.6)
Number of Subjects Censored, n (%)	72 (96.0)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.342 (0.703)
95% CI		(0.339, 5.321)
Log-rank p-value		0.723

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	94.1 (89.9, 98.4)
6 months	90.4 (79.3, 100.0)	92.4 (87.1, 97.7)
9 months	90.4 (79.3, 100.0)	92.4 (87.1, 97.7)
12 months	90.4 (79.3, 100.0)	92.4 (87.1, 97.7)
18 months	NE (NE, NE)	92.4 (87.1, 97.7)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	6 (5.0)
Number of Subjects Censored, n (%)	75 (100.0)	115 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.112

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.7 (92.0, 99.4)
6 months	100.0 (100.0, 100.0)	93.7 (88.4, 99.0)
9 months	100.0 (100.0, 100.0)	93.7 (88.4, 99.0)
12 months	100.0 (100.0, 100.0)	93.7 (88.4, 99.0)
18 months	NE (NE, NE)	93.7 (88.4, 99.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	4 (3.3)
Number of Subjects Censored, n (%)	74 (98.7)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.274 (1.119)
95% CI		(0.254, 20.387)
Log-rank p-value		0.442

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.6 (93.4, 99.9)
6 months	98.6 (96.0, 100.0)	96.6 (93.4, 99.9)
9 months	98.6 (96.0, 100.0)	96.6 (93.4, 99.9)
12 months	98.6 (96.0, 100.0)	96.6 (93.4, 99.9)
18 months	NE (NE, NE)	96.6 (93.4, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.191

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (94.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (94.4, 100.0)
9 months	100.0 (100.0, 100.0)	97.4 (94.4, 100.0)
12 months	100.0 (100.0, 100.0)	97.4 (94.4, 100.0)
18 months	NE (NE, NE)	97.4 (94.4, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	12 (16.0)	51 (42.1)
Number of Subjects Censored, n (%)	63 (84.0)	70 (57.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	1.15 (0.66, 1.71)
Median (95% CI)	NE (NE, NE)	NE (2.99, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.132 (0.342)
95% CI		(1.601, 6.127)
Log-rank p-value		0.002

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (76.6, 93.1)	59.0 (50.0, 68.0)
6 months	80.4 (68.8, 92.0)	56.4 (47.2, 65.7)
9 months	80.4 (68.8, 92.0)	53.1 (42.3, 63.9)
12 months	80.4 (68.8, 92.0)	53.1 (42.3, 63.9)
18 months	NE (NE, NE)	53.1 (42.3, 63.9)
Median Follow-up Time (months)	2.83	2.79

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	27 (22.3)
Number of Subjects Censored, n (%)	71 (94.7)	94 (77.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.635 (0.611)
95% CI		(1.399, 15.362)
Log-rank p-value		0.010

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (89.2, 99.7)	80.6 (73.4, 87.7)
6 months	94.5 (89.2, 99.7)	76.2 (67.9, 84.5)
9 months	94.5 (89.2, 99.7)	72.8 (62.4, 83.1)
12 months	94.5 (89.2, 99.7)	72.8 (62.4, 83.1)
18 months	NE (NE, NE)	72.8 (62.4, 83.1)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	7 (5.8)
Number of Subjects Censored, n (%)	71 (94.7)	114 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.448 (0.682)
95% CI		(0.380, 5.515)
Log-rank p-value		0.774

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (89.4, 99.7)	93.9 (89.5, 98.3)
6 months	94.6 (89.4, 99.7)	93.9 (89.5, 98.3)
9 months	94.6 (89.4, 99.7)	93.9 (89.5, 98.3)
12 months	94.6 (89.4, 99.7)	93.9 (89.5, 98.3)
18 months	NE (NE, NE)	93.9 (89.5, 98.3)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	2 (2.7)	0
Number of Subjects Censored, n (%)	73 (97.3)	121 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.015

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (95.7, 100.0)	100.0 (100.0, 100.0)
6 months	94.3 (85.6, 100.0)	100.0 (100.0, 100.0)
9 months	94.3 (85.6, 100.0)	100.0 (100.0, 100.0)
12 months	94.3 (85.6, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	16 (21.3)	32 (26.4)
Number of Subjects Censored, n (%)	59 (78.7)	89 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	5.49 (1.58, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.971 (0.319)
95% CI		(0.520, 1.814)
Log-rank p-value		0.783

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.1 (67.2, 87.1)	78.3 (70.9, 85.7)
6 months	77.1 (67.2, 87.1)	73.6 (64.9, 82.4)
9 months	77.1 (67.2, 87.1)	69.4 (59.5, 79.4)
12 months	77.1 (67.2, 87.1)	69.4 (59.5, 79.4)
18 months	NE (NE, NE)	69.4 (59.5, 79.4)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	11 (9.1)
Number of Subjects Censored, n (%)	71 (94.7)	110 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.096 (0.603)
95% CI		(0.336, 3.575)
Log-rank p-value		0.872

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (89.2, 99.7)	94.2 (90.0, 98.4)
6 months	94.5 (89.2, 99.7)	92.6 (87.6, 97.7)
9 months	94.5 (89.2, 99.7)	88.3 (80.7, 95.9)
12 months	94.5 (89.2, 99.7)	88.3 (80.7, 95.9)
18 months	NE (NE, NE)	88.3 (80.7, 95.9)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	4 (3.3)
Number of Subjects Censored, n (%)	72 (96.0)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.794)
95% CI		(0.189, 4.252)
Log-rank p-value		0.751

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (91.5, 100.0)	96.7 (93.5, 99.9)
6 months	96.0 (91.5, 100.0)	96.7 (93.5, 99.9)
9 months	96.0 (91.5, 100.0)	96.7 (93.5, 99.9)
12 months	96.0 (91.5, 100.0)	96.7 (93.5, 99.9)
18 months	NE (NE, NE)	96.7 (93.5, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	4 (3.3)
Number of Subjects Censored, n (%)	74 (98.7)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.292 (1.119)
95% CI		(0.256, 20.540)
Log-rank p-value		0.447

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.7 (93.5, 99.9)
6 months	98.6 (96.0, 100.0)	96.7 (93.5, 99.9)
9 months	98.6 (96.0, 100.0)	96.7 (93.5, 99.9)
12 months	98.6 (96.0, 100.0)	96.7 (93.5, 99.9)
18 months	NE (NE, NE)	96.7 (93.5, 99.9)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	9 (12.0)	34 (28.1)
Number of Subjects Censored, n (%)	66 (88.0)	87 (71.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.76 (1.02, NE)
Median (95% CI)	NE (NE, NE)	NE (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.045 (0.378)
95% CI		(0.975, 4.288)
Log-rank p-value		0.065

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (79.9, 95.2)	73.8 (65.9, 81.8)
6 months	87.5 (79.9, 95.2)	71.0 (62.4, 79.6)
9 months	87.5 (79.9, 95.2)	71.0 (62.4, 79.6)
12 months	87.5 (79.9, 95.2)	60.9 (41.0, 80.7)
18 months	NE (NE, NE)	60.9 (41.0, 80.7)
Median Follow-up Time (months)	2.83	3.68

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	7 (9.3)	24 (19.8)
Number of Subjects Censored, n (%)	68 (90.7)	97 (80.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.829 (0.433)
95% CI		(0.783, 4.271)
Log-rank p-value		0.180

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (83.4, 97.1)	81.3 (74.3, 88.4)
6 months	90.3 (83.4, 97.1)	78.4 (70.5, 86.3)
9 months	90.3 (83.4, 97.1)	78.4 (70.5, 86.3)
12 months	90.3 (83.4, 97.1)	78.4 (70.5, 86.3)
18 months	NE (NE, NE)	78.4 (70.5, 86.3)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	3 (2.5)
Number of Subjects Censored, n (%)	74 (98.7)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.710 (1.158)
95% CI		(0.177, 16.553)
Log-rank p-value		0.632

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	97.5 (94.7, 100.0)
6 months	98.6 (96.0, 100.0)	97.5 (94.7, 100.0)
9 months	98.6 (96.0, 100.0)	97.5 (94.7, 100.0)
12 months	98.6 (96.0, 100.0)	97.5 (94.7, 100.0)
18 months	NE (NE, NE)	97.5 (94.7, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	17 (22.7)	29 (24.0)
Number of Subjects Censored, n (%)	58 (77.3)	92 (76.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.58, NE)	6.37 (3.71, 11.53)
Median (95% CI)	NE (5.78, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.707 (0.326)
95% CI		(0.373, 1.340)
Log-rank p-value		0.340

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.3 (71.0, 89.6)	83.3 (76.5, 90.2)
6 months	56.2 (28.6, 83.8)	77.5 (69.0, 86.1)
9 months	56.2 (28.6, 83.8)	67.3 (55.1, 79.5)
12 months	56.2 (28.6, 83.8)	59.8 (42.3, 77.4)
18 months	NE (NE, NE)	39.9 (5.9, 73.9)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	8 (6.6)
Number of Subjects Censored, n (%)	71 (94.7)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.738 (0.658)
95% CI		(0.203, 2.683)
Log-rank p-value		0.847

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.6, 100.0)	95.7 (92.0, 99.4)
6 months	88.1 (75.3, 100.0)	94.4 (89.9, 98.8)
9 months	88.1 (75.3, 100.0)	90.1 (82.9, 97.3)
12 months	88.1 (75.3, 100.0)	90.1 (82.9, 97.3)
18 months	NE (NE, NE)	90.1 (82.9, 97.3)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	6 (5.0)
Number of Subjects Censored, n (%)	71 (94.7)	115 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.658 (0.695)
95% CI		(0.169, 2.567)
Log-rank p-value		0.486

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.7, 100.0)	98.1 (95.5, 100.0)
6 months	90.0 (78.3, 100.0)	95.7 (91.6, 99.9)
9 months	90.0 (78.3, 100.0)	93.4 (87.3, 99.4)
12 months	90.0 (78.3, 100.0)	84.0 (65.8, 100.0)
18 months	NE (NE, NE)	84.0 (65.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	3 (2.5)
Number of Subjects Censored, n (%)	74 (98.7)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.033 (1.164)
95% CI		(0.106, 10.109)
Log-rank p-value		0.994

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	97.2 (94.1, 100.0)
6 months	98.6 (96.0, 100.0)	97.2 (94.1, 100.0)
9 months	98.6 (96.0, 100.0)	97.2 (94.1, 100.0)
12 months	98.6 (96.0, 100.0)	97.2 (94.1, 100.0)
18 months	NE (NE, NE)	97.2 (94.1, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	12 (16.0)	16 (13.2)
Number of Subjects Censored, n (%)	63 (84.0)	105 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.701 (0.399)
95% CI		(0.320, 1.533)
Log-rank p-value		0.377

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (72.7, 91.4)	88.8 (83.1, 94.6)
6 months	82.1 (72.7, 91.4)	87.6 (81.4, 93.7)
9 months	82.1 (72.7, 91.4)	82.7 (73.8, 91.5)
12 months	82.1 (72.7, 91.4)	82.7 (73.8, 91.5)
18 months	NE (NE, NE)	82.7 (73.8, 91.5)
Median Follow-up Time (months)	2.83	4.24

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	11 (14.7)	10 (8.3)
Number of Subjects Censored, n (%)	64 (85.3)	111 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.384 (0.466)
95% CI		(0.154, 0.957)
Log-rank p-value		0.046

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.6 (74.7, 92.6)	93.9 (89.6, 98.3)
6 months	83.6 (74.7, 92.6)	92.7 (87.8, 97.6)
9 months	83.6 (74.7, 92.6)	90.6 (84.3, 96.9)
12 months	83.6 (74.7, 92.6)	90.6 (84.3, 96.9)
18 months	NE (NE, NE)	60.4 (11.9, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	6 (5.0)
Number of Subjects Censored, n (%)	74 (98.7)	115 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.582 (1.095)
95% CI		(0.536, 39.182)
Log-rank p-value		0.141

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	94.9 (90.9, 98.9)
6 months	98.6 (96.0, 100.0)	94.9 (90.9, 98.9)
9 months	98.6 (96.0, 100.0)	94.9 (90.9, 98.9)
12 months	98.6 (96.0, 100.0)	94.9 (90.9, 98.9)
18 months	NE (NE, NE)	94.9 (90.9, 98.9)
Median Follow-up Time (months)	2.86	4.57

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	31 (25.6)
Number of Subjects Censored, n (%)	74 (98.7)	90 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (2.53, 6.90)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		14.041 (1.019)
95% CI		(1.905, 103.513)
Log-rank p-value		0.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	81.8 (74.7, 88.9)
6 months	98.6 (96.0, 100.0)	66.8 (55.6, 78.1)
9 months	98.6 (96.0, 100.0)	63.8 (51.6, 76.0)
12 months	98.6 (96.0, 100.0)	57.4 (41.2, 73.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	31 (25.6)
Number of Subjects Censored, n (%)	74 (98.7)	90 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (2.53, 7.33)
Median (95% CI)	NE (NE, NE)	NE (7.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		13.813 (1.020)
95% CI		(1.872, 101.915)
Log-rank p-value		0.001

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	81.8 (74.7, 88.9)
6 months	98.6 (96.0, 100.0)	68.4 (57.5, 79.4)
9 months	98.6 (96.0, 100.0)	61.8 (48.6, 75.1)
12 months	98.6 (96.0, 100.0)	55.7 (39.1, 72.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	13 (10.7)
Number of Subjects Censored, n (%)	72 (96.0)	108 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.313 (0.769)
95% CI		(0.734, 14.958)
Log-rank p-value		0.098

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (91.3, 100.0)	91.5 (86.5, 96.6)
6 months	95.9 (91.3, 100.0)	88.4 (82.0, 94.9)
9 months	95.9 (91.3, 100.0)	86.2 (78.5, 93.9)
12 months	95.9 (91.3, 100.0)	86.2 (78.5, 93.9)
18 months	NE (NE, NE)	86.2 (78.5, 93.9)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	5 (4.1)
Number of Subjects Censored, n (%)	72 (96.0)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.225 (0.854)
95% CI		(0.230, 6.535)
Log-rank p-value		0.837

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (91.3, 100.0)	96.6 (93.3, 99.9)
6 months	95.9 (91.3, 100.0)	96.6 (93.3, 99.9)
9 months	95.9 (91.3, 100.0)	94.2 (88.5, 99.8)
12 months	95.9 (91.3, 100.0)	94.2 (88.5, 99.8)
18 months	NE (NE, NE)	94.2 (88.5, 99.8)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	1 (1.3)	1 (0.8)
Number of Subjects Censored, n (%)	74 (98.7)	120 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.401 (1.476)
95% CI		(0.022, 7.246)
Log-rank p-value		0.503

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (95.7, 100.0)	99.2 (97.5, 100.0)
6 months	98.6 (95.7, 100.0)	99.2 (97.5, 100.0)
9 months	98.6 (95.7, 100.0)	99.2 (97.5, 100.0)
12 months	98.6 (95.7, 100.0)	99.2 (97.5, 100.0)
18 months	NE (NE, NE)	99.2 (97.5, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	5 (4.1)
Number of Subjects Censored, n (%)	75 (100.0)	116 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.128

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (93.5, 99.9)
6 months	100.0 (100.0, 100.0)	95.5 (91.5, 99.4)
9 months	100.0 (100.0, 100.0)	95.5 (91.5, 99.4)
12 months	100.0 (100.0, 100.0)	95.5 (91.5, 99.4)
18 months	NE (NE, NE)	95.5 (91.5, 99.4)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	6 (5.0)
Number of Subjects Censored, n (%)	75 (100.0)	115 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.098

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.5 (91.7, 99.4)
6 months	100.0 (100.0, 100.0)	94.4 (90.0, 98.8)
9 months	100.0 (100.0, 100.0)	94.4 (90.0, 98.8)
12 months	100.0 (100.0, 100.0)	94.4 (90.0, 98.8)
18 months	NE (NE, NE)	94.4 (90.0, 98.8)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	3 (2.5)
Number of Subjects Censored, n (%)	75 (100.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.231

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (94.1, 100.0)
6 months	100.0 (100.0, 100.0)	97.2 (94.1, 100.0)
9 months	100.0 (100.0, 100.0)	97.2 (94.1, 100.0)
12 months	100.0 (100.0, 100.0)	97.2 (94.1, 100.0)
18 months	NE (NE, NE)	97.2 (94.1, 100.0)
Median Follow-up Time (months)	2.86	4.67

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

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	0	1 (0.8)
Number of Subjects Censored, n (%)	75 (100.0)	120 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.5, 100.0)
6 months	100.0 (100.0, 100.0)	99.2 (97.5, 100.0)
9 months	100.0 (100.0, 100.0)	99.2 (97.5, 100.0)
12 months	100.0 (100.0, 100.0)	99.2 (97.5, 100.0)
18 months	NE (NE, NE)	99.2 (97.5, 100.0)
Median Follow-up Time (months)	2.86	4.67

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	5 (45.5)	15 (71.4)
Number of Subjects Censored, n (%)	6 (54.5)	6 (28.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, NE)	0.46 (0.03, 0.99)
Median (95% CI)	NE (0.49, NE)	1.45 (0.46, NE)
75% percentile (95% CI)	NE (1.28, NE)	5.98 (1.51, NE)

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Min, Max	0.5, 2.9*	0.0, 6.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.569 (0.641)
95% CI		(0.162, 1.997)
Log-rank p-value		0.279

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	33.3 (13.2, 53.5)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.28	1.45

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	4 (19.0)
Number of Subjects Censored, n (%)	10 (90.9)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 2.9*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.236 (1.197)
95% CI		(0.118, 12.914)
Log-rank p-value		0.809

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	80.4 (63.0, 97.7)
6 months	NE (NE, NE)	80.4 (63.0, 97.7)
9 months	NE (NE, NE)	80.4 (63.0, 97.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	7 (33.3)
Number of Subjects Censored, n (%)	8 (72.7)	14 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.59, NE)	1.05 (0.03, NE)
Median (95% CI)	NE (0.62, NE)	NE (1.05, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.446 (0.907)
95% CI		(0.075, 2.635)
Log-rank p-value		0.455

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.7 (46.4, 99.0)	65.6 (44.9, 86.4)
6 months	72.7 (46.4, 99.0)	65.6 (44.9, 86.4)
9 months	NE (NE, NE)	65.6 (44.9, 86.4)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.79

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	5 (23.8)
Number of Subjects Censored, n (%)	10 (90.9)	16 (76.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	6.11 (0.30, NE)
Median (95% CI)	NE (NE, NE)	NE (4.37, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.11, NE)
Min, Max	0.5, 6.5*	0.3, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.139 (1.357)
95% CI		(0.219, 44.898)
Log-rank p-value		0.519

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	84.6 (68.5, 100.0)
6 months	90.9 (73.9, 100.0)	76.9 (56.4, 97.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.37

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.45, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	1 (4.8)
Number of Subjects Censored, n (%)	9 (81.8)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (0.99, NE)
Median (95% CI)	NE (1.28, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	1.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.016

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
6 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	1 (4.8)
Number of Subjects Censored, n (%)	10 (90.9)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.183 (1.416)
95% CI		(0.011, 2.927)
Log-rank p-value		0.177

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
6 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	1 (4.8)
Number of Subjects Censored, n (%)	10 (90.9)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.167 (1.414)
95% CI		(0.010, 2.665)
Log-rank p-value		0.149

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
6 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	1 (4.8)
Number of Subjects Censored, n (%)	10 (90.9)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	NE (5.98, NE)
Median (95% CI)	NE (NE, NE)	NE (5.98, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	1.0*, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.014

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	100.0 (100.0, 100.0)
6 months	90.9 (73.9, 100.0)	83.3 (53.5, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	9 (81.8)	16 (76.2)
Number of Subjects Censored, n (%)	2 (18.2)	5 (23.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.69)	0.69 (0.03, 1.31)
Median (95% CI)	0.69 (0.07, 1.71)	1.51 (0.69, 2.56)
75% percentile (95% CI)	1.71 (0.69, NE)	4.07 (1.51, NE)
Min, Max	0.0, 1.9*	0.0, 5.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.400 (0.635)
95% CI		(0.115, 1.388)
Log-rank p-value		0.085

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	25.8 (6.5, 45.1)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.69	1.45

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	8 (38.1)
Number of Subjects Censored, n (%)	9 (81.8)	13 (61.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	1.31 (0.07, NE)
Median (95% CI)	NE (1.77, NE)	NE (1.31, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.1, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.315 (0.897)
95% CI		(0.227, 7.628)
Log-rank p-value		0.598

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (54.0, 100.0)	66.0 (45.5, 86.6)
6 months	79.5 (54.0, 100.0)	58.7 (36.0, 81.4)
9 months	NE (NE, NE)	58.7 (36.0, 81.4)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	4 (36.4)	7 (33.3)
Number of Subjects Censored, n (%)	7 (63.6)	14 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.36 (0.07, NE)	3.48 (0.53, NE)
Median (95% CI)	NE (0.30, NE)	NE (3.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.157 (1.168)
95% CI		(0.016, 1.545)
Log-rank p-value		0.052

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.6 (35.2, 92.1)	79.8 (62.1, 97.6)
6 months	63.6 (35.2, 92.1)	56.4 (30.8, 82.1)
9 months	NE (NE, NE)	56.4 (30.8, 82.1)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.28	3.48

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	5 (45.5)	8 (38.1)
Number of Subjects Censored, n (%)	6 (54.5)	13 (61.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.41 (0.10, 2.53)	1.51 (0.03, 4.21)
Median (95% CI)	2.53 (0.72, NE)	NE (1.51, NE)
75% percentile (95% CI)	NE (1.45, NE)	NE (NE, NE)
Min, Max	0.1, 2.9*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.796 (0.801)
95% CI		(0.166, 3.828)
Log-rank p-value		0.957

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	69.4 (48.9, 89.9)
6 months	NE (NE, NE)	54.0 (29.3, 78.7)
9 months	NE (NE, NE)	54.0 (29.3, 78.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.45	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	1 (4.8)
Number of Subjects Censored, n (%)	8 (72.7)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.03, NE)	NE (1.02, NE)
Median (95% CI)	NE (0.69, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 2.9*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.047 (1.535)
95% CI		(0.002, 0.952)
Log-rank p-value		0.112

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	95.0 (85.4, 100.0)
6 months	NE (NE, NE)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.31	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	4 (19.0)
Number of Subjects Censored, n (%)	11 (100.0)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.21 (0.53, NE)
Median (95% CI)	NE (NE, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	69.3 (43.3, 95.2)
9 months	NE (NE, NE)	69.3 (43.3, 95.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	1 (4.8)
Number of Subjects Censored, n (%)	10 (90.9)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	94.7 (84.7, 100.0)
6 months	90.9 (73.9, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	5 (23.8)
Number of Subjects Censored, n (%)	10 (90.9)	16 (76.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.71, NE)	NE (0.39, NE)
Median (95% CI)	NE (1.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.4, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.171 (1.288)
95% CI		(0.174, 27.106)
Log-rank p-value		0.575

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	75.4 (56.6, 94.2)
6 months	87.5 (64.6, 100.0)	75.4 (56.6, 94.2)
9 months	NE (NE, NE)	75.4 (56.6, 94.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	0
Number of Subjects Censored, n (%)	8 (72.7)	21 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.66, NE)	NE (NE, NE)
Median (95% CI)	NE (0.72, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.008

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.1 (41.3, 99.0)	100.0 (100.0, 100.0)
6 months	70.1 (41.3, 99.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	4 (36.4)	9 (42.9)
Number of Subjects Censored, n (%)	7 (63.6)	12 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.85 (0.43, NE)	0.69 (0.03, 3.94)
Median (95% CI)	NE (0.76, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	0.0, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.496 (0.810)
95% CI		(0.101, 2.426)
Log-rank p-value		0.493

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.6 (29.8, 91.5)	59.9 (38.1, 81.8)
6 months	60.6 (29.8, 91.5)	51.4 (27.1, 75.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.54	2.76

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	7 (33.3)
Number of Subjects Censored, n (%)	8 (72.7)	14 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.54 (0.76, NE)	2.73 (0.03, NE)
Median (95% CI)	NE (0.85, NE)	NE (2.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.5*	0.0, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.945 (0.948)
95% CI		(0.147, 6.059)
Log-rank p-value		0.970

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.1 (41.3, 99.0)	70.7 (51.0, 90.5)
6 months	70.1 (41.3, 99.0)	59.0 (32.2, 85.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	86.6 (68.4, 100.0)
9 months	NE (NE, NE)	86.6 (68.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.94

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (83.9, 100.0)
6 months	100.0 (100.0, 100.0)	85.9 (67.2, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.07

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.43, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.240 (1.525)
95% CI		(0.012, 4.778)
Log-rank p-value		0.414

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	89.5 (75.7, 100.0)
6 months	90.9 (73.9, 100.0)	89.5 (75.7, 100.0)
9 months	NE (NE, NE)	89.5 (75.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	86.6 (68.4, 100.0)
9 months	NE (NE, NE)	86.6 (68.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	10 (47.6)
Number of Subjects Censored, n (%)	8 (72.7)	11 (52.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.10, NE)	0.95 (0.69, 1.91)
Median (95% CI)	NE (0.69, NE)	3.68 (0.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (3.68, NE)
Min, Max	0.1, 6.5*	0.7, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.310 (0.819)
95% CI		(0.062, 1.540)
Log-rank p-value		0.086

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.7 (46.4, 99.0)	54.9 (32.8, 77.0)
6 months	72.7 (46.4, 99.0)	47.1 (23.4, 70.8)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.91

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	4 (19.0)
Number of Subjects Censored, n (%)	10 (90.9)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	NE (0.92, NE)
Median (95% CI)	NE (1.64, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.9, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.027 (1.564)
95% CI		(0.048, 22.029)
Log-rank p-value		0.929

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	85.2 (69.6, 100.0)
6 months	87.5 (64.6, 100.0)	78.1 (58.5, 97.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	4 (19.0)
Number of Subjects Censored, n (%)	11 (100.0)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (3.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.445

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.2 (69.6, 100.0)
6 months	100.0 (100.0, 100.0)	77.4 (57.2, 97.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (4.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	88.9 (68.4, 100.0)
9 months	NE (NE, NE)	88.9 (68.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	87.3 (70.2, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.9, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (4.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	84.2 (62.8, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	4 (36.4)	8 (38.1)
Number of Subjects Censored, n (%)	7 (63.6)	13 (61.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.85 (0.20, NE)	1.54 (0.03, NE)
Median (95% CI)	NE (0.72, NE)	NE (1.54, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.673 (0.681)
95% CI		(0.177, 2.555)
Log-rank p-value		0.514

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.3 (32.9, 91.7)	71.1 (51.6, 90.6)
6 months	62.3 (32.9, 91.7)	57.5 (34.2, 80.7)
9 months	NE (NE, NE)	57.5 (34.2, 80.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.25

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	1 (4.8)
Number of Subjects Censored, n (%)	10 (90.9)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.163 (1.718)
95% CI		(0.006, 4.713)
Log-rank p-value		0.221

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	94.7 (84.7, 100.0)
6 months	90.9 (73.9, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	3 (14.3)
Number of Subjects Censored, n (%)	9 (81.8)	18 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.85, NE)	NE (0.69, NE)
Median (95% CI)	NE (1.64, NE)	NE (4.30, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.260 (1.112)
95% CI		(0.029, 2.298)
Log-rank p-value		0.223

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (54.0, 100.0)	95.2 (86.1, 100.0)
6 months	79.5 (54.0, 100.0)	79.9 (59.0, 100.0)
9 months	NE (NE, NE)	79.9 (59.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.30

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.20, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.096 (1.478)
95% CI		(0.060, 19.854)
Log-rank p-value		0.929

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	90.5 (77.9, 100.0)
6 months	90.9 (73.9, 100.0)	90.5 (77.9, 100.0)
9 months	NE (NE, NE)	90.5 (77.9, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.6, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.7, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	6 (28.6)
Number of Subjects Censored, n (%)	10 (90.9)	15 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	1.68 (0.20, NE)
Median (95% CI)	NE (1.61, NE)	NE (1.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 2.9*	0.2, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.324 (1.154)
95% CI		(0.138, 12.718)
Log-rank p-value		0.796

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	71.1 (51.6, 90.6)
6 months	NE (NE, NE)	71.1 (51.6, 90.6)
9 months	NE (NE, NE)	71.1 (51.6, 90.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	4 (19.0)
Number of Subjects Censored, n (%)	11 (100.0)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.23, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.2, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.316

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.0 (64.2, 97.7)
6 months	100.0 (100.0, 100.0)	81.0 (64.2, 97.7)
9 months	NE (NE, NE)	81.0 (64.2, 97.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	5 (45.5)	8 (38.1)
Number of Subjects Censored, n (%)	6 (54.5)	13 (61.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.03, NE)	0.36 (0.03, NE)
Median (95% CI)	NE (0.46, NE)	NE (0.36, NE)
75% percentile (95% CI)	NE (2.53, NE)	NE (NE, NE)
Min, Max	0.0, 2.9*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.539 (0.721)
95% CI		(0.131, 2.215)
Log-rank p-value		0.378

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	61.9 (41.1, 82.7)
6 months	NE (NE, NE)	61.9 (41.1, 82.7)
9 months	NE (NE, NE)	61.9 (41.1, 82.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.28	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	1 (4.8)
Number of Subjects Censored, n (%)	9 (81.8)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (0.20, NE)
Median (95% CI)	NE (0.69, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	0.2, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.014

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
6 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.36, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.4, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.9 (76.7, 100.0)
6 months	100.0 (100.0, 100.0)	89.9 (76.7, 100.0)
9 months	NE (NE, NE)	89.9 (76.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	6 (28.6)
Number of Subjects Censored, n (%)	9 (81.8)	15 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	1.35 (0.03, NE)
Median (95% CI)	NE (0.79, NE)	NE (1.35, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	0.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.830 (1.220)
95% CI		(0.168, 19.989)
Log-rank p-value		0.569

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	70.7 (51.0, 90.5)
6 months	81.8 (59.0, 100.0)	70.7 (51.0, 90.5)
9 months	NE (NE, NE)	70.7 (51.0, 90.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.02

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	3 (14.3)
Number of Subjects Censored, n (%)	10 (90.9)	18 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.79, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.274

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	85.7 (70.7, 100.0)
6 months	90.9 (73.9, 100.0)	85.7 (70.7, 100.0)
9 months	NE (NE, NE)	85.7 (70.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.13, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.1, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	4 (19.0)
Number of Subjects Censored, n (%)	10 (90.9)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	6.11 (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (6.11, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.0, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.280 (1.319)
95% CI		(0.021, 3.709)
Log-rank p-value		0.275

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	84.9 (69.1, 100.0)
6 months	90.9 (73.9, 100.0)	84.9 (69.1, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (6.11, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.11, NE)
Min, Max	0.6, 6.5*	0.0, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (1.426)
95% CI		(0.016, 4.289)
Log-rank p-value		0.275

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
6 months	90.9 (73.9, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.7, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.150 (1.594)
95% CI		(0.007, 3.406)
Log-rank p-value		0.351

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	89.9 (76.7, 100.0)
6 months	90.9 (73.9, 100.0)	89.9 (76.7, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.7, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.150 (1.594)
95% CI		(0.007, 3.406)
Log-rank p-value		0.351

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	89.9 (76.7, 100.0)
6 months	90.9 (73.9, 100.0)	89.9 (76.7, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	3 (14.3)
Number of Subjects Censored, n (%)	9 (81.8)	18 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.10, NE)	NE (0.66, NE)
Median (95% CI)	NE (1.41, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.7, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.519

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.9 (50.2, 100.0)	84.7 (68.6, 100.0)
6 months	77.9 (50.2, 100.0)	84.7 (68.6, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.21

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	0
Number of Subjects Censored, n (%)	9 (81.8)	21 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (1.61, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.194

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (54.0, 100.0)	100.0 (100.0, 100.0)
6 months	79.5 (54.0, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	0
Number of Subjects Censored, n (%)	9 (81.8)	21 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (2.10, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.194

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.8 (45.2, 100.0)	100.0 (100.0, 100.0)
6 months	75.8 (45.2, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.10	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	0
Number of Subjects Censored, n (%)	10 (90.9)	21 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (NE, NE)
Median (95% CI)	NE (1.61, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	100.0 (100.0, 100.0)
6 months	87.5 (64.6, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	5 (23.8)
Number of Subjects Censored, n (%)	11 (100.0)	16 (76.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.9, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.299

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	79.8 (62.1, 97.6)
6 months	100.0 (100.0, 100.0)	63.9 (32.5, 95.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	4 (19.0)
Number of Subjects Censored, n (%)	11 (100.0)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.9, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.388

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.2 (69.6, 100.0)
6 months	100.0 (100.0, 100.0)	68.1 (35.8, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	3 (14.3)
Number of Subjects Censored, n (%)	9 (81.8)	18 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (0.46, NE)
Median (95% CI)	NE (0.95, NE)	NE (4.80, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.5, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.443 (0.989)
95% CI		(0.064, 3.076)
Log-rank p-value		0.301

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	90.5 (77.9, 100.0)
6 months	81.8 (59.0, 100.0)	80.4 (58.8, 100.0)
9 months	NE (NE, NE)	80.4 (58.8, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	2 (9.5)
Number of Subjects Censored, n (%)	11 (100.0)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (4.80, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
6 months	100.0 (100.0, 100.0)	84.7 (63.5, 100.0)
9 months	NE (NE, NE)	84.7 (63.5, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	0
Number of Subjects Censored, n (%)	10 (90.9)	21 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	100.0 (100.0, 100.0)
6 months	90.9 (73.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	1 (9.1)	2 (9.5)
Number of Subjects Censored, n (%)	10 (90.9)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	NE (0.56, NE)
Median (95% CI)	NE (1.54, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	0.6, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.412 (2.119)
95% CI		(0.006, 26.218)
Log-rank p-value		0.564

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	90.2 (77.3, 100.0)
6 months	87.5 (64.6, 100.0)	90.2 (77.3, 100.0)
9 months	NE (NE, NE)	90.2 (77.3, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	0	1 (4.8)
Number of Subjects Censored, n (%)	11 (100.0)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 6.5*	1.0*, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	124 (56.6)	300 (69.0)
Number of Subjects Censored, n (%)	95 (43.4)	135 (31.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.69)	0.43 (0.30, 0.62)
Median (95% CI)	1.87 (1.35, 2.76)	1.25 (0.95, 1.61)
75% percentile (95% CI)	NE (NE, NE)	6.93 (4.50, NE)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.231 (0.108)
95% CI		(0.997, 1.520)
Log-rank p-value		0.072

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	43.2 (36.4, 50.0)	38.0 (33.4, 42.6)
6 months	35.0 (25.0, 45.0)	26.0 (21.1, 30.9)
9 months	35.0 (25.0, 45.0)	20.9 (15.2, 26.6)
12 months	35.0 (25.0, 45.0)	20.9 (15.2, 26.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.64	1.12

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	51 (23.3)	151 (34.7)
Number of Subjects Censored, n (%)	168 (76.7)	284 (65.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (1.35, NE)	1.18 (0.85, 1.61)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.438 (0.163)
95% CI		(1.045, 1.979)
Log-rank p-value		0.025

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.4 (70.5, 82.2)	67.1 (62.6, 71.6)
6 months	70.2 (59.8, 80.7)	63.0 (58.1, 67.9)
9 months	70.2 (59.8, 80.7)	60.4 (54.3, 66.5)
12 months	70.2 (59.8, 80.7)	60.4 (54.3, 66.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	34 (15.5)	84 (19.3)
Number of Subjects Censored, n (%)	185 (84.5)	351 (80.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.139 (0.205)
95% CI		(0.761, 1.703)
Log-rank p-value		0.579

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (78.1, 88.5)	82.2 (78.6, 85.9)
6 months	83.3 (78.1, 88.5)	79.1 (74.8, 83.3)
9 months	83.3 (78.1, 88.5)	76.9 (71.8, 82.0)
12 months	83.3 (78.1, 88.5)	76.9 (71.8, 82.0)
18 months	NE (NE, NE)	76.9 (71.8, 82.0)
Median Follow-up Time (months)	2.60	3.25

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	22 (10.0)	41 (9.4)
Number of Subjects Censored, n (%)	197 (90.0)	394 (90.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.800 (0.269)
95% CI		(0.472, 1.355)
Log-rank p-value		0.360

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (84.9, 93.7)	92.0 (89.4, 94.6)
6 months	84.4 (74.0, 94.7)	89.7 (86.4, 92.9)
9 months	84.4 (74.0, 94.7)	88.9 (85.3, 92.5)
12 months	84.4 (74.0, 94.7)	84.2 (74.7, 93.8)
18 months	NE (NE, NE)	84.2 (74.7, 93.8)
Median Follow-up Time (months)	2.79	3.71

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	6 (2.7)	61 (14.0)
Number of Subjects Censored, n (%)	213 (97.3)	374 (86.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	NE (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.905 (0.429)
95% CI		(2.114, 11.379)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.7, 99.4)	87.3 (84.1, 90.5)
6 months	97.1 (94.7, 99.4)	85.6 (82.0, 89.1)
9 months	97.1 (94.7, 99.4)	83.3 (78.6, 87.9)
12 months	97.1 (94.7, 99.4)	83.3 (78.6, 87.9)
18 months	NE (NE, NE)	55.5 (11.0, 100.0)
Median Follow-up Time (months)	2.83	3.42

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	26 (11.9)	26 (6.0)
Number of Subjects Censored, n (%)	193 (88.1)	409 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.349 (0.286)
95% CI		(0.199, 0.612)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (82.8, 92.3)	96.1 (94.2, 98.0)
6 months	83.9 (77.1, 90.7)	91.9 (88.6, 95.2)
9 months	83.9 (77.1, 90.7)	91.9 (88.6, 95.2)
12 months	83.9 (77.1, 90.7)	91.9 (88.6, 95.2)
18 months	NE (NE, NE)	85.8 (73.8, 97.8)
Median Follow-up Time (months)	2.83	3.94

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	16 (7.3)	21 (4.8)
Number of Subjects Censored, n (%)	203 (92.7)	414 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.574 (0.339)
95% CI		(0.295, 1.115)
Log-rank p-value		0.094

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (88.5, 95.9)	95.4 (93.4, 97.4)
6 months	92.2 (88.5, 95.9)	95.4 (93.4, 97.4)
9 months	92.2 (88.5, 95.9)	93.4 (89.0, 97.8)
12 months	92.2 (88.5, 95.9)	90.6 (83.6, 97.5)
18 months	NE (NE, NE)	90.6 (83.6, 97.5)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	15 (3.4)
Number of Subjects Censored, n (%)	215 (98.2)	420 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.011 (0.591)
95% CI		(0.318, 3.219)
Log-rank p-value		0.963

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.0, 100.0)	98.3 (97.1, 99.6)
6 months	98.0 (96.0, 100.0)	96.5 (94.3, 98.7)
9 months	98.0 (96.0, 100.0)	95.2 (91.9, 98.5)
12 months	98.0 (96.0, 100.0)	87.9 (79.4, 96.5)
18 months	NE (NE, NE)	87.9 (79.4, 96.5)
Median Follow-up Time (months)	2.83	3.94

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	11 (2.5)
Number of Subjects Censored, n (%)	215 (98.2)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.981 (0.598)
95% CI		(0.304, 3.167)
Log-rank p-value		0.918

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.3, 100.0)	98.0 (96.5, 99.4)
6 months	97.7 (95.3, 100.0)	97.0 (95.0, 98.9)
9 months	97.7 (95.3, 100.0)	95.7 (92.5, 98.8)
12 months	97.7 (95.3, 100.0)	95.7 (92.5, 98.8)
18 months	NE (NE, NE)	95.7 (92.5, 98.8)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.3)
Number of Subjects Censored, n (%)	218 (99.5)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.377 (1.056)
95% CI		(0.552, 34.693)
Log-rank p-value		0.127

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	98.1 (96.9, 99.4)
6 months	99.5 (98.6, 100.0)	97.7 (96.2, 99.2)
9 months	99.5 (98.6, 100.0)	95.9 (92.1, 99.7)
12 months	99.5 (98.6, 100.0)	95.9 (92.1, 99.7)
18 months	NE (NE, NE)	95.9 (92.1, 99.7)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	122 (55.7)	293 (67.4)
Number of Subjects Censored, n (%)	97 (44.3)	142 (32.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.59 (0.39, 0.69)	0.49 (0.43, 0.69)
Median (95% CI)	1.87 (1.38, 2.92)	1.45 (0.99, 1.87)
75% percentile (95% CI)	5.59 (4.34, NE)	6.70 (4.90, 10.12)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.098 (0.109)
95% CI		(0.886, 1.361)
Log-rank p-value		0.354

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	42.4 (35.1, 49.7)	39.3 (34.5, 44.0)
6 months	20.8 (4.8, 36.9)	25.8 (20.5, 31.2)
9 months	NE (NE, NE)	19.5 (13.5, 25.5)
12 months	NE (NE, NE)	16.7 (9.5, 23.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.35

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	22 (10.0)	102 (23.4)
Number of Subjects Censored, n (%)	197 (90.0)	333 (76.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (3.12, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.072 (0.237)
95% CI		(1.301, 3.299)
Log-rank p-value		0.002

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (85.6, 93.8)	79.8 (75.9, 83.6)
6 months	89.7 (85.6, 93.8)	72.9 (67.6, 78.2)
9 months	89.7 (85.6, 93.8)	69.0 (62.8, 75.3)
12 months	89.7 (85.6, 93.8)	63.7 (52.2, 75.2)
18 months	NE (NE, NE)	63.7 (52.2, 75.2)
Median Follow-up Time (months)	2.76	2.86

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	38 (17.4)	72 (16.6)
Number of Subjects Censored, n (%)	181 (82.6)	363 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	9.20 (6.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.730 (0.206)
95% CI		(0.487, 1.093)
Log-rank p-value		0.119

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (77.0, 87.5)	85.5 (82.0, 88.9)
6 months	78.6 (70.1, 87.1)	81.0 (76.5, 85.5)
9 months	78.6 (70.1, 87.1)	78.1 (72.5, 83.6)
12 months	78.6 (70.1, 87.1)	74.0 (66.5, 81.6)
18 months	NE (NE, NE)	74.0 (66.5, 81.6)
Median Follow-up Time (months)	2.76	3.38

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	32 (14.6)	75 (17.2)
Number of Subjects Censored, n (%)	187 (85.4)	360 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.57, NE)	9.23 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.889 (0.216)
95% CI		(0.582, 1.359)
Log-rank p-value		0.629

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (78.5, 89.5)	85.6 (82.1, 89.1)
6 months	80.8 (72.7, 89.0)	81.3 (77.0, 85.6)
9 months	80.8 (72.7, 89.0)	76.5 (70.6, 82.4)
12 months	80.8 (72.7, 89.0)	71.5 (62.9, 80.2)
18 months	NE (NE, NE)	63.6 (47.0, 80.2)
Median Follow-up Time (months)	2.79	3.35

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	19 (8.7)	77 (17.7)
Number of Subjects Censored, n (%)	200 (91.3)	358 (82.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.595 (0.260)
95% CI		(0.959, 2.654)
Log-rank p-value		0.075

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (85.5, 95.0)	84.8 (81.3, 88.4)
6 months	88.6 (83.0, 94.2)	79.0 (74.3, 83.7)
9 months	88.6 (83.0, 94.2)	75.9 (70.3, 81.6)
12 months	88.6 (83.0, 94.2)	73.8 (66.9, 80.7)
18 months	NE (NE, NE)	73.8 (66.9, 80.7)
Median Follow-up Time (months)	2.83	3.35

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	28 (12.8)	62 (14.3)
Number of Subjects Censored, n (%)	191 (87.2)	373 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (7.39, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.839 (0.235)
95% CI		(0.530, 1.330)
Log-rank p-value		0.454

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.2 (82.6, 91.8)	88.6 (85.5, 91.7)
6 months	80.2 (69.1, 91.3)	84.5 (80.3, 88.6)
9 months	80.2 (69.1, 91.3)	80.8 (75.5, 86.1)
12 months	80.2 (69.1, 91.3)	76.1 (68.1, 84.2)
18 months	NE (NE, NE)	76.1 (68.1, 84.2)
Median Follow-up Time (months)	2.83	3.65

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	7 (3.2)	66 (15.2)
Number of Subjects Censored, n (%)	212 (96.8)	369 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.572 (0.399)
95% CI		(2.092, 9.988)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.9, 99.1)	86.2 (82.9, 89.4)
6 months	96.5 (93.9, 99.1)	83.8 (80.0, 87.6)
9 months	96.5 (93.9, 99.1)	81.6 (76.7, 86.4)
12 months	96.5 (93.9, 99.1)	81.6 (76.7, 86.4)
18 months	NE (NE, NE)	81.6 (76.7, 86.4)
Median Follow-up Time (months)	2.83	3.38

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	7 (3.2)	29 (6.7)
Number of Subjects Censored, n (%)	212 (96.8)	406 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.650 (0.428)
95% CI		(0.713, 3.818)
Log-rank p-value		0.262

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (95.0, 99.4)	94.7 (92.6, 96.9)
6 months	90.7 (78.3, 100.0)	91.8 (88.7, 95.0)
9 months	NE (NE, NE)	90.5 (86.4, 94.5)
12 months	NE (NE, NE)	90.5 (86.4, 94.5)
18 months	NE (NE, NE)	90.5 (86.4, 94.5)
Median Follow-up Time (months)	2.83	3.71

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	15 (3.4)
Number of Subjects Censored, n (%)	215 (98.2)	420 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.628 (0.572)
95% CI		(0.531, 4.996)
Log-rank p-value		0.364

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.2, 99.9)	97.2 (95.7, 98.8)
6 months	98.1 (96.2, 99.9)	96.0 (93.8, 98.3)
9 months	98.1 (96.2, 99.9)	94.8 (91.5, 98.1)
12 months	98.1 (96.2, 99.9)	94.8 (91.5, 98.1)
18 months	NE (NE, NE)	94.8 (91.5, 98.1)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	11 (2.5)
Number of Subjects Censored, n (%)	215 (98.2)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.250 (0.586)
95% CI		(0.397, 3.938)
Log-rank p-value		0.676

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.9, 100.0)	97.3 (95.7, 98.9)
6 months	97.9 (95.9, 100.0)	97.3 (95.7, 98.9)
9 months	97.9 (95.9, 100.0)	97.3 (95.7, 98.9)
12 months	97.9 (95.9, 100.0)	97.3 (95.7, 98.9)
18 months	NE (NE, NE)	97.3 (95.7, 98.9)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	8 (3.7)	3 (0.7)
Number of Subjects Censored, n (%)	211 (96.3)	432 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.135 (0.715)
95% CI		(0.033, 0.547)
Log-rank p-value		0.002

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (93.4, 98.7)	99.5 (98.8, 100.0)
6 months	96.1 (93.4, 98.7)	98.8 (97.2, 100.0)
9 months	96.1 (93.4, 98.7)	98.8 (97.2, 100.0)
12 months	96.1 (93.4, 98.7)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	98.8 (97.2, 100.0)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	0	12 (2.8)
Number of Subjects Censored, n (%)	219 (100.0)	423 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.018

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
6 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
9 months	100.0 (100.0, 100.0)	95.9 (92.8, 99.0)
12 months	100.0 (100.0, 100.0)	95.9 (92.8, 99.0)
18 months	NE (NE, NE)	95.9 (92.8, 99.0)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	59 (26.9)	187 (43.0)
Number of Subjects Censored, n (%)	160 (73.1)	248 (57.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.95, NE)	1.38 (0.95, 1.64)
Median (95% CI)	10.18 (NE, NE)	6.44 (5.16, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.414 (0.151)
95% CI		(1.052, 1.900)
Log-rank p-value		0.021

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.2 (67.1, 79.3)	60.3 (55.5, 65.0)
6 months	68.0 (58.8, 77.2)	53.3 (47.8, 58.7)
9 months	68.0 (58.8, 77.2)	48.4 (42.2, 54.7)
12 months	0.0 (NE, NE)	46.0 (38.5, 53.5)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	37 (16.9)	117 (26.9)
Number of Subjects Censored, n (%)	182 (83.1)	318 (73.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.99 (1.94, 6.24)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.403 (0.191)
95% CI		(0.966, 2.039)
Log-rank p-value		0.079

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (77.4, 87.8)	74.4 (70.1, 78.7)
6 months	79.4 (71.6, 87.3)	71.0 (66.3, 75.7)
9 months	79.4 (71.6, 87.3)	68.5 (63.2, 73.9)
12 months	79.4 (71.6, 87.3)	66.4 (59.8, 73.0)
18 months	NE (NE, NE)	66.4 (59.8, 73.0)
Median Follow-up Time (months)	2.76	2.89

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	26 (6.0)
Number of Subjects Censored, n (%)	215 (98.2)	409 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.778 (0.540)
95% CI		(0.964, 8.003)
Log-rank p-value		0.048

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.4, 99.9)	93.9 (91.5, 96.3)
6 months	98.2 (96.4, 99.9)	93.5 (90.9, 96.0)
9 months	98.2 (96.4, 99.9)	92.2 (88.7, 95.7)
12 months	98.2 (96.4, 99.9)	92.2 (88.7, 95.7)
18 months	NE (NE, NE)	92.2 (88.7, 95.7)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	18 (4.1)
Number of Subjects Censored, n (%)	214 (97.7)	417 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.317 (0.517)
95% CI		(0.479, 3.625)
Log-rank p-value		0.579

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	96.6 (94.9, 98.4)
6 months	96.3 (92.4, 100.0)	94.9 (92.4, 97.5)
9 months	96.3 (92.4, 100.0)	93.8 (90.4, 97.2)
12 months	96.3 (92.4, 100.0)	93.8 (90.4, 97.2)
18 months	NE (NE, NE)	93.8 (90.4, 97.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	14 (3.2)
Number of Subjects Censored, n (%)	215 (98.2)	421 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.481 (0.574)
95% CI		(0.481, 4.559)
Log-rank p-value		0.476

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.0, 100.0)	97.1 (95.4, 98.7)
6 months	98.0 (96.0, 100.0)	96.6 (94.8, 98.5)
9 months	98.0 (96.0, 100.0)	94.8 (90.9, 98.8)
12 months	98.0 (96.0, 100.0)	94.8 (90.9, 98.8)
18 months	NE (NE, NE)	94.8 (90.9, 98.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	15 (3.4)
Number of Subjects Censored, n (%)	216 (98.6)	420 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.186 (0.638)
95% CI		(0.626, 7.633)
Log-rank p-value		0.205

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.0, 100.0)	96.8 (95.1, 98.5)
6 months	98.6 (97.0, 100.0)	96.1 (94.0, 98.3)
9 months	98.6 (97.0, 100.0)	94.9 (91.8, 98.1)
12 months	98.6 (97.0, 100.0)	94.9 (91.8, 98.1)
18 months	NE (NE, NE)	94.9 (91.8, 98.1)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	0	17 (3.9)
Number of Subjects Censored, n (%)	219 (100.0)	418 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.011

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (95.2, 98.5)
6 months	100.0 (100.0, 100.0)	95.2 (92.7, 97.7)
9 months	100.0 (100.0, 100.0)	94.1 (90.7, 97.4)
12 months	100.0 (100.0, 100.0)	94.1 (90.7, 97.4)
18 months	NE (NE, NE)	94.1 (90.7, 97.4)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	217 (99.1)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.240 (0.775)
95% CI		(0.491, 10.233)
Log-rank p-value		0.281

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.7, 100.0)	97.6 (96.1, 99.1)
6 months	98.7 (96.7, 100.0)	97.6 (96.1, 99.1)
9 months	98.7 (96.7, 100.0)	96.8 (94.6, 98.9)
12 months	98.7 (96.7, 100.0)	96.8 (94.6, 98.9)
18 months	NE (NE, NE)	96.8 (94.6, 98.9)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	13 (3.0)
Number of Subjects Censored, n (%)	217 (99.1)	422 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.368 (0.772)
95% CI		(0.521, 10.759)
Log-rank p-value		0.224

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.8 (96.4, 99.2)
6 months	99.1 (97.8, 100.0)	96.7 (94.7, 98.8)
9 months	99.1 (97.8, 100.0)	94.2 (90.0, 98.4)
12 months	99.1 (97.8, 100.0)	94.2 (90.0, 98.4)
18 months	NE (NE, NE)	94.2 (90.0, 98.4)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	11 (2.5)
Number of Subjects Censored, n (%)	216 (98.6)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.597 (0.661)
95% CI		(0.437, 5.838)
Log-rank p-value		0.497

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.3 (95.8, 98.9)
6 months	99.1 (97.8, 100.0)	97.3 (95.8, 98.9)
9 months	99.1 (97.8, 100.0)	97.3 (95.8, 98.9)
12 months	0.0 (NE, NE)	97.3 (95.8, 98.9)
18 months	0.0 (NE, NE)	97.3 (95.8, 98.9)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	9 (2.1)
Number of Subjects Censored, n (%)	218 (99.5)	426 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.390 (1.071)
95% CI		(0.293, 19.508)
Log-rank p-value		0.417

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	98.9 (97.8, 100.0)
6 months	99.5 (98.5, 100.0)	96.1 (93.4, 98.8)
9 months	99.5 (98.5, 100.0)	96.1 (93.4, 98.8)
12 months	99.5 (98.5, 100.0)	96.1 (93.4, 98.8)
18 months	NE (NE, NE)	96.1 (93.4, 98.8)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	60 (27.4)	176 (40.5)
Number of Subjects Censored, n (%)	159 (72.6)	259 (59.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (1.05, 5.59)	1.61 (0.99, 1.84)
Median (95% CI)	NE (5.59, NE)	7.85 (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.294 (0.152)
95% CI		(0.961, 1.741)
Log-rank p-value		0.088

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.8 (66.6, 79.0)	63.4 (58.8, 68.1)
6 months	52.3 (30.6, 73.9)	56.3 (50.7, 61.8)
9 months	NE (NE, NE)	48.9 (42.2, 55.6)
12 months	NE (NE, NE)	48.9 (42.2, 55.6)
18 months	NE (NE, NE)	36.7 (15.3, 58.0)
Median Follow-up Time (months)	2.69	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	20 (9.1)	52 (12.0)
Number of Subjects Censored, n (%)	199 (90.9)	383 (88.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.034 (0.269)
95% CI		(0.610, 1.751)
Log-rank p-value		0.935

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (85.4, 94.4)	89.5 (86.4, 92.5)
6 months	71.9 (47.8, 96.0)	86.1 (82.1, 90.0)
9 months	NE (NE, NE)	83.1 (78.1, 88.2)
12 months	NE (NE, NE)	83.1 (78.1, 88.2)
18 months	NE (NE, NE)	83.1 (78.1, 88.2)
Median Follow-up Time (months)	2.83	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	11 (5.0)	47 (10.8)
Number of Subjects Censored, n (%)	208 (95.0)	388 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.674 (0.340)
95% CI		(0.860, 3.262)
Log-rank p-value		0.132

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (92.4, 98.1)	90.6 (87.7, 93.5)
6 months	88.9 (76.6, 100.0)	87.5 (83.8, 91.3)
9 months	NE (NE, NE)	84.8 (80.0, 89.5)
12 months	NE (NE, NE)	84.8 (80.0, 89.5)
18 months	NE (NE, NE)	84.8 (80.0, 89.5)
Median Follow-up Time (months)	2.83	3.71

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	9 (4.1)	46 (10.6)
Number of Subjects Censored, n (%)	210 (95.9)	389 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.000 (0.370)
95% CI		(0.969, 4.130)
Log-rank p-value		0.058

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.7, 98.8)	91.2 (88.4, 94.0)
6 months	89.8 (77.5, 100.0)	88.3 (84.8, 91.9)
9 months	NE (NE, NE)	84.7 (79.8, 89.6)
12 months	NE (NE, NE)	84.7 (79.8, 89.6)
18 months	NE (NE, NE)	84.7 (79.8, 89.6)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	11 (5.0)	32 (7.4)
Number of Subjects Censored, n (%)	208 (95.0)	403 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.121 (0.356)
95% CI		(0.558, 2.254)
Log-rank p-value		0.845

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.9, 97.8)	94.1 (91.9, 96.4)
6 months	94.9 (91.9, 97.8)	91.4 (88.3, 94.5)
9 months	94.9 (91.9, 97.8)	89.4 (85.3, 93.5)
12 months	94.9 (91.9, 97.8)	89.4 (85.3, 93.5)
18 months	NE (NE, NE)	89.4 (85.3, 93.5)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	31 (7.1)
Number of Subjects Censored, n (%)	216 (98.6)	404 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.130 (0.609)
95% CI		(1.252, 13.624)
Log-rank p-value		0.013

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.3, 100.0)	93.6 (91.2, 96.0)
6 months	96.5 (91.7, 100.0)	92.3 (89.3, 95.3)
9 months	96.5 (91.7, 100.0)	89.0 (84.1, 93.9)
12 months	96.5 (91.7, 100.0)	89.0 (84.1, 93.9)
18 months	NE (NE, NE)	89.0 (84.1, 93.9)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	10 (4.6)	23 (5.3)
Number of Subjects Censored, n (%)	209 (95.4)	412 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.933 (0.385)
95% CI		(0.438, 1.985)
Log-rank p-value		0.808

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (91.7, 98.0)	95.1 (93.0, 97.2)
6 months	94.8 (91.7, 98.0)	94.0 (91.3, 96.6)
9 months	94.8 (91.7, 98.0)	93.2 (90.2, 96.2)
12 months	94.8 (91.7, 98.0)	93.2 (90.2, 96.2)
18 months	NE (NE, NE)	93.2 (90.2, 96.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	25 (5.7)
Number of Subjects Censored, n (%)	217 (99.1)	410 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.328 (0.738)
95% CI		(1.255, 22.626)
Log-rank p-value		0.012

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.7, 100.0)	94.3 (92.1, 96.6)
6 months	99.5 (98.7, 100.0)	93.3 (90.6, 96.0)
9 months	NE (NE, NE)	93.3 (90.6, 96.0)
12 months	NE (NE, NE)	93.3 (90.6, 96.0)
18 months	NE (NE, NE)	93.3 (90.6, 96.0)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	19 (4.4)
Number of Subjects Censored, n (%)	214 (97.7)	416 (95.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.453 (0.511)
95% CI		(0.534, 3.951)
Log-rank p-value		0.477

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 100.0)	96.2 (94.3, 98.1)
6 months	95.5 (90.7, 100.0)	94.6 (92.0, 97.2)
9 months	95.5 (90.7, 100.0)	93.9 (90.9, 96.8)
12 months	95.5 (90.7, 100.0)	93.9 (90.9, 96.8)
18 months	NE (NE, NE)	93.9 (90.9, 96.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.5)
Number of Subjects Censored, n (%)	218 (99.5)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.360 (1.050)
95% CI		(0.557, 34.145)
Log-rank p-value		0.128

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.4 (95.8, 99.0)
6 months	99.5 (98.6, 100.0)	97.4 (95.8, 99.0)
9 months	99.5 (98.6, 100.0)	96.4 (93.8, 98.9)
12 months	99.5 (98.6, 100.0)	96.4 (93.8, 98.9)
18 months	NE (NE, NE)	96.4 (93.8, 98.9)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.3)
Number of Subjects Censored, n (%)	217 (99.1)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.026 (0.782)
95% CI		(0.438, 9.375)
Log-rank p-value		0.349

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.7, 100.0)	97.7 (96.3, 99.2)
6 months	99.1 (97.7, 100.0)	97.7 (96.3, 99.2)
9 months	99.1 (97.7, 100.0)	96.7 (94.2, 99.2)
12 months	99.1 (97.7, 100.0)	96.7 (94.2, 99.2)
18 months	NE (NE, NE)	96.7 (94.2, 99.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	53 (24.2)	167 (38.4)
Number of Subjects Censored, n (%)	166 (75.8)	268 (61.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (1.48, NE)	0.85 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.535 (0.159)
95% CI		(1.123, 2.096)
Log-rank p-value		0.008

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.1 (67.9, 80.2)	64.9 (60.3, 69.4)
6 months	74.1 (67.9, 80.2)	59.9 (54.7, 65.1)
9 months	74.1 (67.9, 80.2)	56.4 (50.5, 62.4)
12 months	74.1 (67.9, 80.2)	48.2 (37.7, 58.7)
18 months	NE (NE, NE)	48.2 (37.7, 58.7)
Median Follow-up Time (months)	2.46	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	11 (5.0)	73 (16.8)
Number of Subjects Censored, n (%)	208 (95.0)	362 (83.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.431 (0.324)
95% CI		(1.818, 6.474)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (91.4, 97.7)	83.2 (79.7, 86.7)
6 months	94.5 (91.4, 97.7)	82.8 (79.2, 86.4)
9 months	94.5 (91.4, 97.7)	82.8 (79.2, 86.4)
12 months	94.5 (91.4, 97.7)	82.8 (79.2, 86.4)
18 months	NE (NE, NE)	82.8 (79.2, 86.4)
Median Follow-up Time (months)	2.83	3.22

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	20 (9.1)	40 (9.2)
Number of Subjects Censored, n (%)	199 (90.9)	395 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.280)
95% CI		(0.469, 1.406)
Log-rank p-value		0.438

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (86.5, 94.5)	92.3 (89.7, 94.9)
6 months	90.5 (86.5, 94.5)	90.2 (87.0, 93.5)
9 months	90.5 (86.5, 94.5)	88.7 (85.0, 92.5)
12 months	90.5 (86.5, 94.5)	85.6 (78.5, 92.7)
18 months	NE (NE, NE)	71.3 (45.1, 97.5)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	20 (9.1)	36 (8.3)
Number of Subjects Censored, n (%)	199 (90.9)	399 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.773 (0.283)
95% CI		(0.443, 1.346)
Log-rank p-value		0.354

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (86.1, 94.3)	92.3 (89.8, 94.9)
6 months	90.2 (86.1, 94.3)	91.4 (88.6, 94.3)
9 months	90.2 (86.1, 94.3)	90.6 (87.4, 93.9)
12 months	90.2 (86.1, 94.3)	85.9 (76.3, 95.5)
18 months	NE (NE, NE)	85.9 (76.3, 95.5)
Median Follow-up Time (months)	2.76	3.71

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	17 (3.9)
Number of Subjects Censored, n (%)	216 (98.6)	418 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.622 (0.627)
95% CI		(0.767, 8.964)
Log-rank p-value		0.120

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.1, 100.0)	95.9 (94.0, 97.8)
6 months	98.6 (97.1, 100.0)	95.9 (94.0, 97.8)
9 months	98.6 (97.1, 100.0)	95.9 (94.0, 97.8)
12 months	98.6 (97.1, 100.0)	95.9 (94.0, 97.8)
18 months	NE (NE, NE)	95.9 (94.0, 97.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	9 (2.1)
Number of Subjects Censored, n (%)	217 (99.1)	426 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.557 (0.804)
95% CI		(0.322, 7.529)
Log-rank p-value		0.606

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	98.6 (97.5, 99.7)
6 months	99.0 (97.6, 100.0)	98.0 (96.4, 99.6)
9 months	99.0 (97.6, 100.0)	96.2 (93.1, 99.2)
12 months	99.0 (97.6, 100.0)	96.2 (93.1, 99.2)
18 months	NE (NE, NE)	96.2 (93.1, 99.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	33 (15.1)	173 (39.8)
Number of Subjects Censored, n (%)	186 (84.9)	262 (60.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.846 (0.191)
95% CI		(1.958, 4.137)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.3 (79.3, 89.4)	61.3 (56.6, 66.0)
6 months	81.8 (75.0, 88.7)	57.5 (52.3, 62.8)
9 months	NE (NE, NE)	52.9 (46.4, 59.5)
12 months	NE (NE, NE)	52.9 (46.4, 59.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.69

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	20 (9.1)	164 (37.7)
Number of Subjects Censored, n (%)	199 (90.9)	271 (62.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.518 (0.238)
95% CI		(2.835, 7.197)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (85.8, 94.2)	63.2 (58.6, 67.9)
6 months	90.0 (85.8, 94.2)	60.7 (55.7, 65.7)
9 months	NE (NE, NE)	54.8 (48.1, 61.5)
12 months	NE (NE, NE)	54.8 (48.1, 61.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.76

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	43 (19.6)	145 (33.3)
Number of Subjects Censored, n (%)	176 (80.4)	290 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (2.83, NE)	1.77 (1.05, 2.50)
Median (95% CI)	NE (5.59, NE)	NE (9.76, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.575 (0.175)
95% CI		(1.117, 2.220)
Log-rank p-value		0.009

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.3 (74.7, 85.9)	68.6 (64.1, 73.1)
6 months	68.0 (52.1, 83.9)	63.4 (58.1, 68.7)
9 months	NE (NE, NE)	57.9 (50.6, 65.2)
12 months	NE (NE, NE)	55.1 (46.4, 63.9)
18 months	NE (NE, NE)	55.1 (46.4, 63.9)
Median Follow-up Time (months)	2.56	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	15 (6.8)	46 (10.6)
Number of Subjects Censored, n (%)	204 (93.2)	389 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.287 (0.301)
95% CI		(0.714, 2.319)
Log-rank p-value		0.380

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (89.3, 96.3)	90.3 (87.4, 93.2)
6 months	92.8 (89.3, 96.3)	87.5 (83.8, 91.1)
9 months	92.8 (89.3, 96.3)	86.7 (82.8, 90.6)
12 months	92.8 (89.3, 96.3)	86.7 (82.8, 90.6)
18 months	NE (NE, NE)	86.7 (82.8, 90.6)
Median Follow-up Time (months)	2.79	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	10 (4.6)	49 (11.3)
Number of Subjects Censored, n (%)	209 (95.4)	386 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.075 (0.351)
95% CI		(1.043, 4.128)
Log-rank p-value		0.038

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.9, 98.4)	90.1 (87.3, 93.0)
6 months	89.3 (77.0, 100.0)	87.4 (83.7, 91.1)
9 months	NE (NE, NE)	83.8 (78.3, 89.2)
12 months	NE (NE, NE)	83.8 (78.3, 89.2)
18 months	NE (NE, NE)	83.8 (78.3, 89.2)
Median Follow-up Time (months)	2.83	3.52

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	25 (5.7)
Number of Subjects Censored, n (%)	214 (97.7)	410 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.296 (0.493)
95% CI		(0.874, 6.035)
Log-rank p-value		0.083

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.8, 100.0)	94.5 (92.3, 96.7)
6 months	93.8 (87.3, 100.0)	93.2 (90.4, 96.0)
9 months	93.8 (87.3, 100.0)	93.2 (90.4, 96.0)
12 months	93.8 (87.3, 100.0)	93.2 (90.4, 96.0)
18 months	NE (NE, NE)	93.2 (90.4, 96.0)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	14 (3.2)
Number of Subjects Censored, n (%)	214 (97.7)	421 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.236 (0.526)
95% CI		(0.441, 3.464)
Log-rank p-value		0.716

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.6, 99.7)	96.9 (95.2, 98.5)
6 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
9 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
12 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
18 months	NE (NE, NE)	96.1 (93.9, 98.3)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.3)
Number of Subjects Censored, n (%)	217 (99.1)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.593 (0.800)
95% CI		(0.332, 7.646)
Log-rank p-value		0.548

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	98.6 (97.4, 99.7)
6 months	99.1 (97.8, 100.0)	97.9 (96.1, 99.6)
9 months	99.1 (97.8, 100.0)	93.8 (88.7, 98.8)
12 months	99.1 (97.8, 100.0)	93.8 (88.7, 98.8)
18 months	NE (NE, NE)	93.8 (88.7, 98.8)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	0	10 (2.3)
Number of Subjects Censored, n (%)	219 (100.0)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.043

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.0)
6 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.0)
9 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.0)
12 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.0)
18 months	NE (NE, NE)	97.5 (96.0, 99.0)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	25 (11.4)	151 (34.7)
Number of Subjects Censored, n (%)	194 (88.6)	284 (65.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.99, 1.84)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.103 (0.217)
95% CI		(2.029, 4.746)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (84.3, 92.9)	67.2 (62.7, 71.8)
6 months	86.1 (79.7, 92.5)	62.0 (56.7, 67.2)
9 months	86.1 (79.7, 92.5)	59.7 (53.7, 65.7)
12 months	86.1 (79.7, 92.5)	59.7 (53.7, 65.7)
18 months	NE (NE, NE)	44.8 (19.1, 70.5)
Median Follow-up Time (months)	2.79	2.83

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	85 (19.5)
Number of Subjects Censored, n (%)	214 (97.7)	350 (80.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.370 (0.461)
95% CI		(3.391, 20.658)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.6, 99.7)	82.3 (78.6, 85.9)
6 months	97.6 (95.6, 99.7)	77.4 (72.8, 82.1)
9 months	97.6 (95.6, 99.7)	76.1 (70.8, 81.4)
12 months	97.6 (95.6, 99.7)	76.1 (70.8, 81.4)
18 months	NE (NE, NE)	76.1 (70.8, 81.4)
Median Follow-up Time (months)	2.83	2.99

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	8 (3.7)	17 (3.9)
Number of Subjects Censored, n (%)	211 (96.3)	418 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.974 (0.431)
95% CI		(0.419, 2.267)
Log-rank p-value		0.935

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.7, 98.8)	95.9 (94.0, 97.8)
6 months	96.3 (93.7, 98.8)	95.9 (94.0, 97.8)
9 months	96.3 (93.7, 98.8)	95.9 (94.0, 97.8)
12 months	96.3 (93.7, 98.8)	95.9 (94.0, 97.8)
18 months	NE (NE, NE)	95.9 (94.0, 97.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	12 (2.8)
Number of Subjects Censored, n (%)	216 (98.6)	423 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.767 (0.650)
95% CI		(0.494, 6.315)
Log-rank p-value		0.404

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	97.3 (95.8, 98.9)
6 months	96.6 (91.9, 100.0)	96.9 (95.2, 98.7)
9 months	96.6 (91.9, 100.0)	96.9 (95.2, 98.7)
12 months	96.6 (91.9, 100.0)	96.9 (95.2, 98.7)
18 months	NE (NE, NE)	96.9 (95.2, 98.7)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	36 (16.4)	111 (25.5)
Number of Subjects Censored, n (%)	183 (83.6)	324 (74.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.01 (2.27, 6.21)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.404 (0.194)
95% CI		(0.960, 2.053)
Log-rank p-value		0.098

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (76.9, 87.6)	77.1 (73.1, 81.2)
6 months	82.2 (76.9, 87.6)	70.8 (65.7, 75.9)
9 months	82.2 (76.9, 87.6)	70.0 (64.7, 75.3)
12 months	82.2 (76.9, 87.6)	66.7 (58.6, 74.8)
18 months	NE (NE, NE)	66.7 (58.6, 74.8)
Median Follow-up Time (months)	2.69	2.86

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	10 (4.6)	39 (9.0)
Number of Subjects Censored, n (%)	209 (95.4)	396 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.835 (0.357)
95% CI		(0.911, 3.696)
Log-rank p-value		0.090

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.8, 98.0)	91.8 (89.2, 94.4)
6 months	94.9 (91.8, 98.0)	90.8 (87.8, 93.7)
9 months	94.9 (91.8, 98.0)	90.0 (86.7, 93.3)
12 months	94.9 (91.8, 98.0)	90.0 (86.7, 93.3)
18 months	NE (NE, NE)	90.0 (86.7, 93.3)
Median Follow-up Time (months)	2.83	3.65

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	7 (3.2)	10 (2.3)
Number of Subjects Censored, n (%)	212 (96.8)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.652 (0.495)
95% CI		(0.247, 1.720)
Log-rank p-value		0.366

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.4, 99.1)	97.6 (96.1, 99.1)
6 months	96.7 (94.4, 99.1)	97.6 (96.1, 99.1)
9 months	96.7 (94.4, 99.1)	97.6 (96.1, 99.1)
12 months	96.7 (94.4, 99.1)	97.6 (96.1, 99.1)
18 months	NE (NE, NE)	97.6 (96.1, 99.1)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	4 (1.8)	12 (2.8)
Number of Subjects Censored, n (%)	215 (98.2)	423 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.517 (0.578)
95% CI		(0.489, 4.706)
Log-rank p-value		0.469

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.7)
6 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.7)
9 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.7)
12 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.7)
18 months	NE (NE, NE)	97.2 (95.6, 98.7)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	29 (13.2)	110 (25.3)
Number of Subjects Censored, n (%)	190 (86.8)	325 (74.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.91 (2.79, 6.47)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.602 (0.212)
95% CI		(1.058, 2.425)
Log-rank p-value		0.030

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (81.0, 90.8)	78.2 (74.1, 82.2)
6 months	83.4 (76.7, 90.2)	70.6 (65.4, 75.9)
9 months	83.4 (76.7, 90.2)	67.8 (61.8, 73.7)
12 months	83.4 (76.7, 90.2)	61.0 (47.3, 74.7)
18 months	NE (NE, NE)	45.8 (17.9, 73.6)
Median Follow-up Time (months)	2.76	3.02

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	11 (5.0)	77 (17.7)
Number of Subjects Censored, n (%)	208 (95.0)	358 (82.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.022 (0.325)
95% CI		(1.600, 5.710)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (91.5, 97.7)	84.3 (80.7, 87.8)
6 months	94.6 (91.5, 97.7)	79.5 (75.0, 84.0)
9 months	94.6 (91.5, 97.7)	76.7 (70.9, 82.5)
12 months	94.6 (91.5, 97.7)	76.7 (70.9, 82.5)
18 months	NE (NE, NE)	57.5 (24.7, 90.4)
Median Follow-up Time (months)	2.83	3.32

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	5 (2.3)	10 (2.3)
Number of Subjects Censored, n (%)	214 (97.7)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.808 (0.559)
95% CI		(0.270, 2.415)
Log-rank p-value		0.698

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.5, 99.7)	97.9 (96.5, 99.2)
6 months	97.6 (95.5, 99.7)	97.4 (95.8, 99.1)
9 months	97.6 (95.5, 99.7)	97.4 (95.8, 99.1)
12 months	97.6 (95.5, 99.7)	97.4 (95.8, 99.1)
18 months	NE (NE, NE)	97.4 (95.8, 99.1)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	27 (12.3)	93 (21.4)
Number of Subjects Censored, n (%)	192 (87.7)	342 (78.6)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.91 (4.63, 6.93)
Median (95% CI)	NE (5.78, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.185 (0.226)
95% CI		(0.761, 1.844)
Log-rank p-value		0.392

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.7 (84.3, 93.1)	84.5 (80.9, 88.0)
6 months	68.9 (46.3, 91.6)	74.3 (68.8, 79.8)
9 months	68.9 (46.3, 91.6)	64.6 (56.9, 72.3)
12 months	68.9 (46.3, 91.6)	60.3 (49.4, 71.2)
18 months	NE (NE, NE)	45.2 (18.4, 72.1)
Median Follow-up Time (months)	2.79	3.29

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	8 (3.7)	19 (4.4)
Number of Subjects Censored, n (%)	211 (96.3)	416 (95.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.766 (0.441)
95% CI		(0.323, 1.820)
Log-rank p-value		0.641

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.4, 99.9)	96.9 (95.2, 98.6)
6 months	87.2 (76.4, 97.9)	95.0 (92.3, 97.7)
9 months	87.2 (76.4, 97.9)	92.3 (88.3, 96.3)
12 months	87.2 (76.4, 97.9)	92.3 (88.3, 96.3)
18 months	NE (NE, NE)	92.3 (88.3, 96.3)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	6 (2.7)	11 (2.5)
Number of Subjects Censored, n (%)	213 (97.3)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.462 (0.539)
95% CI		(0.161, 1.330)
Log-rank p-value		0.131

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (95.2, 99.7)	99.0 (98.0, 100.0)
6 months	93.8 (86.5, 100.0)	96.5 (94.1, 98.9)
9 months	93.8 (86.5, 100.0)	95.6 (92.6, 98.5)
12 months	93.8 (86.5, 100.0)	90.8 (81.3, 100.0)
18 months	NE (NE, NE)	90.8 (81.3, 100.0)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.3)
Number of Subjects Censored, n (%)	218 (99.5)	425 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.901 (1.054)
95% CI		(0.494, 30.781)
Log-rank p-value		0.170

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.6 (96.0, 99.2)
6 months	99.5 (98.6, 100.0)	96.9 (94.9, 99.0)
9 months	99.5 (98.6, 100.0)	96.9 (94.9, 99.0)
12 months	99.5 (98.6, 100.0)	96.9 (94.9, 99.0)
18 months	NE (NE, NE)	96.9 (94.9, 99.0)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	35 (16.0)	67 (15.4)
Number of Subjects Censored, n (%)	184 (84.0)	368 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.795 (0.213)
95% CI		(0.524, 1.205)
Log-rank p-value		0.304

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.3 (76.9, 87.7)	86.4 (83.0, 89.7)
6 months	82.3 (76.9, 87.7)	82.1 (77.7, 86.5)
9 months	82.3 (76.9, 87.7)	79.5 (74.3, 84.6)
12 months	82.3 (76.9, 87.7)	79.5 (74.3, 84.6)
18 months	NE (NE, NE)	79.5 (74.3, 84.6)
Median Follow-up Time (months)	2.76	3.48

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	26 (11.9)	36 (8.3)
Number of Subjects Censored, n (%)	193 (88.1)	399 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.496 (0.267)
95% CI		(0.294, 0.838)
Log-rank p-value		0.009

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (81.6, 91.4)	93.8 (91.4, 96.2)
6 months	86.5 (81.6, 91.4)	89.5 (85.7, 93.3)
9 months	86.5 (81.6, 91.4)	87.9 (83.7, 92.2)
12 months	86.5 (81.6, 91.4)	87.9 (83.7, 92.2)
18 months	NE (NE, NE)	58.6 (11.6, 100.0)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	30 (6.9)
Number of Subjects Censored, n (%)	217 (99.1)	405 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.521 (0.731)
95% CI		(1.796, 31.500)
Log-rank p-value		0.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	92.8 (90.3, 95.3)
6 months	99.1 (97.8, 100.0)	92.8 (90.3, 95.3)
9 months	99.1 (97.8, 100.0)	92.8 (90.3, 95.3)
12 months	99.1 (97.8, 100.0)	92.8 (90.3, 95.3)
18 months	NE (NE, NE)	92.8 (90.3, 95.3)
Median Follow-up Time (months)	2.83	3.71

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	95 (21.8)
Number of Subjects Censored, n (%)	218 (99.5)	340 (78.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.84, 6.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		39.560 (1.006)
95% CI		(5.507, 284.163)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	82.2 (78.4, 85.9)
6 months	99.5 (98.6, 100.0)	71.3 (65.6, 77.1)
9 months	99.5 (98.6, 100.0)	68.5 (62.1, 74.9)
12 months	99.5 (98.6, 100.0)	66.0 (58.1, 73.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	90 (20.7)
Number of Subjects Censored, n (%)	218 (99.5)	345 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (4.07, 9.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		36.735 (1.006)
95% CI		(5.110, 264.090)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	83.4 (79.7, 87.0)
6 months	99.5 (98.6, 100.0)	73.2 (67.6, 78.8)
9 months	99.5 (98.6, 100.0)	69.1 (62.5, 75.7)
12 months	99.5 (98.6, 100.0)	66.6 (58.7, 74.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.15

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	15 (6.8)	55 (12.6)
Number of Subjects Censored, n (%)	204 (93.2)	380 (87.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.448 (0.294)
95% CI		(0.813, 2.578)
Log-rank p-value		0.196

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (89.4, 96.6)	88.8 (85.7, 92.0)
6 months	91.4 (86.6, 96.1)	84.0 (79.7, 88.2)
9 months	91.4 (86.6, 96.1)	83.1 (78.5, 87.6)
12 months	91.4 (86.6, 96.1)	83.1 (78.5, 87.6)
18 months	NE (NE, NE)	83.1 (78.5, 87.6)
Median Follow-up Time (months)	2.83	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	12 (5.5)	24 (5.5)
Number of Subjects Censored, n (%)	207 (94.5)	411 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.739 (0.358)
95% CI		(0.366, 1.492)
Log-rank p-value		0.438

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.8, 97.4)	94.9 (92.7, 97.2)
6 months	94.1 (90.8, 97.4)	93.2 (90.4, 96.0)
9 months	94.1 (90.8, 97.4)	92.3 (88.9, 95.6)
12 months	94.1 (90.8, 97.4)	92.3 (88.9, 95.6)
18 months	NE (NE, NE)	92.3 (88.9, 95.6)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	217 (99.1)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.244 (0.774)
95% CI		(0.492, 10.238)
Log-rank p-value		0.312

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	97.4 (95.7, 99.0)
6 months	97.8 (94.4, 100.0)	96.8 (94.7, 98.8)
9 months	97.8 (94.4, 100.0)	96.8 (94.7, 98.8)
12 months	97.8 (94.4, 100.0)	96.8 (94.7, 98.8)
18 months	NE (NE, NE)	96.8 (94.7, 98.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.5)
Number of Subjects Censored, n (%)	218 (99.5)	424 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.773 (1.049)
95% CI		(0.611, 37.309)
Log-rank p-value		0.101

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	97.8 (96.4, 99.2)
6 months	99.4 (98.2, 100.0)	96.7 (94.7, 98.8)
9 months	99.4 (98.2, 100.0)	96.7 (94.7, 98.8)
12 months	99.4 (98.2, 100.0)	96.7 (94.7, 98.8)
18 months	NE (NE, NE)	96.7 (94.7, 98.8)
Median Follow-up Time (months)	2.83	3.78

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	23 (10.5)	48 (11.0)
Number of Subjects Censored, n (%)	196 (89.5)	387 (89.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.800 (0.259)
95% CI		(0.482, 1.328)
Log-rank p-value		0.423

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.6 (85.4, 93.7)	90.2 (87.2, 93.1)
6 months	88.0 (82.9, 93.1)	86.5 (82.6, 90.5)
9 months	88.0 (82.9, 93.1)	85.4 (80.9, 89.9)
12 months	88.0 (82.9, 93.1)	83.1 (76.8, 89.3)
18 months	NE (NE, NE)	83.1 (76.8, 89.3)
Median Follow-up Time (months)	2.83	3.68

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	3 (1.4)	18 (4.1)
Number of Subjects Censored, n (%)	216 (98.6)	417 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.220 (0.630)
95% CI		(0.646, 7.632)
Log-rank p-value		0.214

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.7, 100.0)	96.0 (94.1, 98.0)
6 months	98.5 (96.7, 100.0)	94.9 (92.4, 97.4)
9 months	98.5 (96.7, 100.0)	94.9 (92.4, 97.4)
12 months	98.5 (96.7, 100.0)	92.4 (86.8, 97.9)
18 months	NE (NE, NE)	92.4 (86.8, 97.9)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	2 (0.9)	14 (3.2)
Number of Subjects Censored, n (%)	217 (99.1)	421 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.525 (0.765)
95% CI		(0.564, 11.304)
Log-rank p-value		0.198

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.3 (95.8, 98.9)
6 months	99.1 (97.8, 100.0)	96.2 (94.0, 98.4)
9 months	99.1 (97.8, 100.0)	95.0 (91.8, 98.2)
12 months	99.1 (97.8, 100.0)	95.0 (91.8, 98.2)
18 months	NE (NE, NE)	95.0 (91.8, 98.2)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	23 (51.1)	39 (65.0)
Number of Subjects Censored, n (%)	22 (48.9)	21 (35.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.53 (0.07, 0.72)	0.69 (0.30, 0.69)
Median (95% CI)	2.76 (0.72, NE)	1.23 (0.69, 3.55)
75% percentile (95% CI)	NE (NE, NE)	NE (3.55, NE)

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Min, Max	0.0, 13.0*	0.1, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.221 (0.292)
95% CI		(0.689, 2.163)
Log-rank p-value		0.600

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	48.5 (33.8, 63.2)	38.0 (25.6, 50.4)
6 months	48.5 (33.8, 63.2)	33.7 (21.4, 46.1)
9 months	48.5 (33.8, 63.2)	33.7 (21.4, 46.1)
12 months	48.5 (33.8, 63.2)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	1.23

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (17.8)	22 (36.7)
Number of Subjects Censored, n (%)	37 (82.2)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	0.84 (0.69, 3.12)
Median (95% CI)	NE (NE, NE)	NE (3.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 10.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.191 (0.431)
95% CI		(0.941, 5.101)
Log-rank p-value		0.088

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (70.8, 93.3)	64.7 (52.6, 76.9)
6 months	82.1 (70.8, 93.3)	62.7 (50.2, 75.1)
9 months	82.1 (70.8, 93.3)	62.7 (50.2, 75.1)
12 months	82.1 (70.8, 93.3)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.20

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	9 (20.0)	10 (16.7)
Number of Subjects Censored, n (%)	36 (80.0)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (1.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.846 (0.550)
95% CI		(0.288, 2.486)
Log-rank p-value		0.753

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.6 (67.7, 91.5)	83.2 (73.7, 92.7)
6 months	79.6 (67.7, 91.5)	83.2 (73.7, 92.7)
9 months	79.6 (67.7, 91.5)	83.2 (73.7, 92.7)
12 months	79.6 (67.7, 91.5)	83.2 (73.7, 92.7)
18 months	NE (NE, NE)	83.2 (73.7, 92.7)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	7 (11.7)
Number of Subjects Censored, n (%)	39 (86.7)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.694 (0.668)
95% CI		(0.187, 2.571)
Log-rank p-value		0.592

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (76.4, 96.6)	91.3 (83.9, 98.6)
6 months	86.5 (76.4, 96.6)	89.0 (80.7, 97.4)
9 months	86.5 (76.4, 96.6)	84.6 (73.0, 96.2)
12 months	86.5 (76.4, 96.6)	84.6 (73.0, 96.2)
18 months	NE (NE, NE)	84.6 (73.0, 96.2)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	7 (11.7)
Number of Subjects Censored, n (%)	44 (97.8)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.056 (1.074)
95% CI		(0.616, 41.460)
Log-rank p-value		0.099

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	88.3 (80.2, 96.4)
6 months	97.8 (93.5, 100.0)	88.3 (80.2, 96.4)
9 months	97.8 (93.5, 100.0)	88.3 (80.2, 96.4)
12 months	97.8 (93.5, 100.0)	88.3 (80.2, 96.4)
18 months	NE (NE, NE)	88.3 (80.2, 96.4)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	1 (1.7)
Number of Subjects Censored, n (%)	41 (91.1)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.214 (1.139)
95% CI		(0.023, 1.991)
Log-rank p-value		0.154

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
6 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
9 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
12 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
18 months	NE (NE, NE)	98.1 (94.6, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	2 (3.3)
Number of Subjects Censored, n (%)	41 (91.1)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.294 (0.888)
95% CI		(0.052, 1.676)
Log-rank p-value		0.161

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (82.8, 99.4)	96.7 (92.1, 100.0)
6 months	91.1 (82.8, 99.4)	96.7 (92.1, 100.0)
9 months	91.1 (82.8, 99.4)	96.7 (92.1, 100.0)
12 months	91.1 (82.8, 99.4)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
9 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
12 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
18 months	NE (NE, NE)	97.7 (93.3, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	45 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.232

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.330

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	21 (46.7)	42 (70.0)
Number of Subjects Censored, n (%)	24 (53.3)	18 (30.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.07, 1.38)	0.46 (0.26, 0.69)
Median (95% CI)	5.59 (1.31, NE)	0.99 (0.69, 3.58)
75% percentile (95% CI)	NE (5.59, NE)	NE (3.58, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.652 (0.294)
95% CI		(0.928, 2.939)
Log-rank p-value		0.059

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.6 (39.7, 69.4)	39.9 (27.4, 52.3)
6 months	NE (NE, NE)	28.7 (16.4, 41.0)
9 months	NE (NE, NE)	25.1 (12.5, 37.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	0.99

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	16 (26.7)
Number of Subjects Censored, n (%)	41 (91.1)	44 (73.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.183 (0.646)
95% CI		(1.179, 14.838)
Log-rank p-value		0.025

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (82.4, 99.4)	78.3 (67.9, 88.8)
6 months	90.9 (82.4, 99.4)	73.0 (60.8, 85.1)
9 months	90.9 (82.4, 99.4)	68.4 (54.1, 82.7)
12 months	90.9 (82.4, 99.4)	68.4 (54.1, 82.7)
18 months	NE (NE, NE)	68.4 (54.1, 82.7)
Median Follow-up Time (months)	2.83	3.76

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	7 (11.7)
Number of Subjects Censored, n (%)	40 (88.9)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.782 (0.661)
95% CI		(0.214, 2.857)
Log-rank p-value		0.641

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (79.6, 98.1)	89.5 (81.6, 97.5)
6 months	88.8 (79.6, 98.1)	87.3 (78.4, 96.2)
9 months	88.8 (79.6, 98.1)	87.3 (78.4, 96.2)
12 months	88.8 (79.6, 98.1)	87.3 (78.4, 96.2)
18 months	NE (NE, NE)	87.3 (78.4, 96.2)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	7 (15.6)	12 (20.0)
Number of Subjects Censored, n (%)	38 (84.4)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.38, NE)	6.41 (2.92, NE)
Median (95% CI)	NE (NE, NE)	12.25 (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.376 (0.566)
95% CI		(0.454, 4.175)
Log-rank p-value		0.624

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.9 (73.0, 94.9)	86.2 (77.2, 95.1)
6 months	83.9 (73.0, 94.9)	84.0 (74.3, 93.7)
9 months	83.9 (73.0, 94.9)	74.6 (59.7, 89.6)
12 months	83.9 (73.0, 94.9)	74.6 (59.7, 89.6)
18 months	NE (NE, NE)	37.3 (0.0, 89.6)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	9 (15.0)
Number of Subjects Censored, n (%)	40 (88.9)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.92, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.181 (0.645)
95% CI		(0.333, 4.182)
Log-rank p-value		0.727

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (79.7, 98.1)	85.5 (76.2, 94.9)
6 months	88.9 (79.7, 98.1)	82.0 (70.7, 93.2)
9 months	88.9 (79.7, 98.1)	82.0 (70.7, 93.2)
12 months	88.9 (79.7, 98.1)	82.0 (70.7, 93.2)
18 months	NE (NE, NE)	82.0 (70.7, 93.2)
Median Follow-up Time (months)	2.83	3.99

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	9 (15.0)
Number of Subjects Censored, n (%)	44 (97.8)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.33, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.226 (1.062)
95% CI		(0.901, 57.923)
Log-rank p-value		0.031

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (93.3, 100.0)	84.9 (75.8, 94.0)
6 months	97.7 (93.3, 100.0)	84.9 (75.8, 94.0)
9 months	97.7 (93.3, 100.0)	84.9 (75.8, 94.0)
12 months	97.7 (93.3, 100.0)	84.9 (75.8, 94.0)
18 months	NE (NE, NE)	84.9 (75.8, 94.0)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	8 (13.3)
Number of Subjects Censored, n (%)	43 (95.6)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.210 (0.842)
95% CI		(0.617, 16.702)
Log-rank p-value		0.160

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.3, 100.0)	88.3 (80.2, 96.5)
6 months	95.4 (89.3, 100.0)	86.2 (77.3, 95.1)
9 months	95.4 (89.3, 100.0)	86.2 (77.3, 95.1)
12 months	95.4 (89.3, 100.0)	86.2 (77.3, 95.1)
18 months	NE (NE, NE)	86.2 (77.3, 95.1)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	4 (6.7)
Number of Subjects Censored, n (%)	42 (93.3)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	1.5*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.356 (0.900)
95% CI		(0.061, 2.075)
Log-rank p-value		0.206

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	94.7 (88.9, 100.0)
6 months	NE (NE, NE)	92.3 (85.0, 99.7)
9 months	NE (NE, NE)	92.3 (85.0, 99.7)
12 months	NE (NE, NE)	92.3 (85.0, 99.7)
18 months	NE (NE, NE)	92.3 (85.0, 99.7)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	45 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.426

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	5 (8.3)
Number of Subjects Censored, n (%)	45 (100.0)	55 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.160

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
6 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
9 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
12 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
18 months	NE (NE, NE)	91.6 (84.5, 98.6)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	0
Number of Subjects Censored, n (%)	43 (95.6)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
6 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
9 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
12 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.584

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	14 (31.1)	22 (36.7)
Number of Subjects Censored, n (%)	31 (68.9)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.69, NE)	1.87 (0.72, 3.58)
Median (95% CI)	10.18 (NE, NE)	NE (3.58, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.3, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.981 (0.380)
95% CI		(0.466, 2.065)
Log-rank p-value		0.777

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (57.9, 84.4)	65.4 (53.1, 77.8)
6 months	71.1 (57.9, 84.4)	61.3 (48.4, 74.1)
9 months	71.1 (57.9, 84.4)	61.3 (48.4, 74.1)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (17.8)	10 (16.7)
Number of Subjects Censored, n (%)	37 (82.2)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.616 (0.507)
95% CI		(0.228, 1.663)
Log-rank p-value		0.318

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (70.5, 93.3)	84.1 (74.6, 93.7)
6 months	81.9 (70.5, 93.3)	82.0 (71.8, 92.2)
9 months	81.9 (70.5, 93.3)	82.0 (71.8, 92.2)
12 months	81.9 (70.5, 93.3)	82.0 (71.8, 92.2)
18 months	NE (NE, NE)	82.0 (71.8, 92.2)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.195

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
18 months	NE (NE, NE)	94.8 (89.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	45 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.408

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
9 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
12 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
18 months	NE (NE, NE)	96.6 (92.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.162

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	85.9 (65.6, 100.0)
12 months	100.0 (100.0, 100.0)	85.9 (65.6, 100.0)
18 months	NE (NE, NE)	85.9 (65.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.519

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
9 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
12 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
18 months	NE (NE, NE)	98.2 (94.7, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.192

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
9 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
12 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
18 months	NE (NE, NE)	95.0 (89.4, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	2 (3.3)
Number of Subjects Censored, n (%)	44 (97.8)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.408

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	96.6 (92.0, 100.0)
6 months	97.8 (93.5, 100.0)	96.6 (92.0, 100.0)
9 months	97.8 (93.5, 100.0)	96.6 (92.0, 100.0)
12 months	97.8 (93.5, 100.0)	96.6 (92.0, 100.0)
18 months	NE (NE, NE)	96.6 (92.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	2 (3.3)
Number of Subjects Censored, n (%)	44 (97.8)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.101 (1.294)
95% CI		(0.087, 13.899)
Log-rank p-value		0.850

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	98.3 (95.1, 100.0)
6 months	97.8 (93.5, 100.0)	98.3 (95.1, 100.0)
9 months	97.8 (93.5, 100.0)	87.4 (67.0, 100.0)
12 months	97.8 (93.5, 100.0)	87.4 (67.0, 100.0)
18 months	NE (NE, NE)	87.4 (67.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	2 (3.3)
Number of Subjects Censored, n (%)	42 (93.3)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.7, 10.2	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.701 (1.075)
95% CI		(0.085, 5.770)
Log-rank p-value		0.868

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	96.5 (91.8, 100.0)
6 months	95.6 (89.5, 100.0)	96.5 (91.8, 100.0)
9 months	95.6 (89.5, 100.0)	96.5 (91.8, 100.0)
12 months	0.0 (NE, NE)	96.5 (91.8, 100.0)
18 months	0.0 (NE, NE)	96.5 (91.8, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.342

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	14 (31.1)	22 (36.7)
Number of Subjects Censored, n (%)	31 (68.9)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, NE)	1.46 (0.69, 6.44)
Median (95% CI)	5.59 (5.59, NE)	16.79 (5.78, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (16.79, NE)
Min, Max	0.0, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.083 (0.403)
95% CI		(0.492, 2.386)
Log-rank p-value		0.775

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (57.9, 84.4)	67.3 (55.1, 79.5)
6 months	NE (NE, NE)	63.1 (49.1, 77.0)
9 months	NE (NE, NE)	58.6 (43.1, 74.0)
12 months	NE (NE, NE)	58.6 (43.1, 74.0)
18 months	NE (NE, NE)	29.3 (0.0, 70.6)
Median Follow-up Time (months)	2.79	3.47

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	7 (11.7)
Number of Subjects Censored, n (%)	40 (88.9)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (6.87, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.637 (0.696)
95% CI		(0.163, 2.492)
Log-rank p-value		0.626

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (81.0, 99.5)	88.8 (80.3, 97.4)
6 months	NE (NE, NE)	88.8 (80.3, 97.4)
9 months	NE (NE, NE)	82.9 (69.2, 96.7)
12 months	NE (NE, NE)	82.9 (69.2, 96.7)
18 months	NE (NE, NE)	82.9 (69.2, 96.7)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	9 (15.0)
Number of Subjects Censored, n (%)	42 (93.3)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (2.89, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.658 (0.856)
95% CI		(0.310, 8.878)
Log-rank p-value		0.496

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	86.0 (76.9, 95.1)
6 months	NE (NE, NE)	81.7 (69.7, 93.6)
9 months	NE (NE, NE)	81.7 (69.7, 93.6)
12 months	NE (NE, NE)	81.7 (69.7, 93.6)
18 months	NE (NE, NE)	81.7 (69.7, 93.6)
Median Follow-up Time (months)	2.83	4.63

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	6 (10.0)
Number of Subjects Censored, n (%)	42 (93.3)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.654 (0.872)
95% CI		(0.300, 9.138)
Log-rank p-value		0.581

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	89.5 (81.4, 97.5)
6 months	NE (NE, NE)	89.5 (81.4, 97.5)
9 months	NE (NE, NE)	89.5 (81.4, 97.5)
12 months	NE (NE, NE)	89.5 (81.4, 97.5)
18 months	NE (NE, NE)	89.5 (81.4, 97.5)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	4 (6.7)
Number of Subjects Censored, n (%)	42 (93.3)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.738 (0.848)
95% CI		(0.140, 3.890)
Log-rank p-value		0.763

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	93.1 (86.6, 99.6)
6 months	93.3 (86.0, 100.0)	93.1 (86.6, 99.6)
9 months	93.3 (86.0, 100.0)	93.1 (86.6, 99.6)
12 months	93.3 (86.0, 100.0)	93.1 (86.6, 99.6)
18 months	NE (NE, NE)	93.1 (86.6, 99.6)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	6 (10.0)
Number of Subjects Censored, n (%)	45 (100.0)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.065

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.4 (84.2, 98.6)
6 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
9 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
12 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
18 months	NE (NE, NE)	87.9 (78.2, 97.6)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	6 (10.0)
Number of Subjects Censored, n (%)	42 (93.3)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.568 (1.177)
95% CI		(0.256, 25.794)
Log-rank p-value		0.341

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (85.8, 100.0)	93.2 (86.7, 99.6)
6 months	93.2 (85.8, 100.0)	86.1 (74.6, 97.6)
9 months	93.2 (85.8, 100.0)	86.1 (74.6, 97.6)
12 months	93.2 (85.8, 100.0)	86.1 (74.6, 97.6)
18 months	NE (NE, NE)	86.1 (74.6, 97.6)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	2 (3.3)
Number of Subjects Censored, n (%)	43 (95.6)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 7.4	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.270 (1.346)
95% CI		(0.019, 3.778)
Log-rank p-value		0.377

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	96.7 (92.1, 100.0)
6 months	97.8 (93.5, 100.0)	96.7 (92.1, 100.0)
9 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
12 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
18 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.037

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
6 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
9 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
12 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
18 months	NE (NE, NE)	94.5 (88.4, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.342

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	13 (28.9)	23 (38.3)
Number of Subjects Censored, n (%)	32 (71.1)	37 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.36, NE)	1.38 (0.72, 3.25)
Median (95% CI)	NE (NE, NE)	NE (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.190 (0.372)
95% CI		(0.574, 2.469)
Log-rank p-value		0.677

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.8 (57.5, 84.2)	66.2 (54.2, 78.3)
6 months	70.8 (57.5, 84.2)	64.1 (51.7, 76.5)
9 months	70.8 (57.5, 84.2)	56.1 (41.1, 71.1)
12 months	70.8 (57.5, 84.2)	56.1 (41.1, 71.1)
18 months	NE (NE, NE)	56.1 (41.1, 71.1)
Median Follow-up Time (months)	2.79	3.27

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	7 (11.7)
Number of Subjects Censored, n (%)	41 (91.1)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.334 (0.648)
95% CI		(0.375, 4.749)
Log-rank p-value		0.647

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (82.5, 99.4)	88.2 (79.9, 96.4)
6 months	90.9 (82.5, 99.4)	88.2 (79.9, 96.4)
9 months	90.9 (82.5, 99.4)	88.2 (79.9, 96.4)
12 months	90.9 (82.5, 99.4)	88.2 (79.9, 96.4)
18 months	NE (NE, NE)	88.2 (79.9, 96.4)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	6 (10.0)
Number of Subjects Censored, n (%)	39 (86.7)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.599 (0.649)
95% CI		(0.168, 2.137)
Log-rank p-value		0.478

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (76.5, 96.6)	93.3 (87.0, 99.6)
6 months	86.5 (76.5, 96.6)	91.1 (83.6, 98.6)
9 months	86.5 (76.5, 96.6)	86.3 (74.8, 97.9)
12 months	86.5 (76.5, 96.6)	86.3 (74.8, 97.9)
18 months	NE (NE, NE)	86.3 (74.8, 97.9)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	7 (11.7)
Number of Subjects Censored, n (%)	39 (86.7)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.25, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.731 (0.590)
95% CI		(0.230, 2.323)
Log-rank p-value		0.607

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.7 (76.7, 96.6)	90.0 (82.4, 97.6)
6 months	86.7 (76.7, 96.6)	90.0 (82.4, 97.6)
9 months	86.7 (76.7, 96.6)	85.2 (73.7, 96.8)
12 months	86.7 (76.7, 96.6)	85.2 (73.7, 96.8)
18 months	NE (NE, NE)	85.2 (73.7, 96.8)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.280

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
18 months	NE (NE, NE)	94.8 (89.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	45 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.342

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (17.8)	24 (40.0)
Number of Subjects Censored, n (%)	37 (82.2)	36 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.41, NE)	0.94 (0.53, 2.07)
Median (95% CI)	NE (NE, NE)	NE (2.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.737 (0.440)
95% CI		(1.156, 6.478)
Log-rank p-value		0.023

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (71.0, 93.4)	59.2 (46.6, 71.8)
6 months	NE (NE, NE)	59.2 (46.6, 71.8)
9 months	NE (NE, NE)	59.2 (46.6, 71.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.81

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	23 (38.3)
Number of Subjects Censored, n (%)	39 (86.7)	37 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	1.30 (0.62, 2.50)
Median (95% CI)	NE (NE, NE)	NE (2.50, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.705 (0.503)
95% CI		(1.383, 9.927)
Log-rank p-value		0.007

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (76.3, 96.5)	60.6 (47.9, 73.2)
6 months	NE (NE, NE)	60.6 (47.9, 73.2)
9 months	NE (NE, NE)	60.6 (47.9, 73.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.81

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	10 (22.2)	28 (46.7)
Number of Subjects Censored, n (%)	35 (77.8)	32 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (1.61, NE)	0.99 (0.33, 1.77)
Median (95% CI)	5.59 (5.59, NE)	6.74 (1.77, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (9.76, NE)
Min, Max	0.0, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.181 (0.406)
95% CI		(0.984, 4.836)
Log-rank p-value		0.052

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.9 (66.5, 91.3)	57.7 (45.0, 70.3)
6 months	NE (NE, NE)	54.3 (40.7, 67.8)
9 months	NE (NE, NE)	49.3 (33.9, 64.7)
12 months	NE (NE, NE)	32.9 (4.6, 61.1)
18 months	NE (NE, NE)	32.9 (4.6, 61.1)
Median Follow-up Time (months)	2.83	2.58

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	8 (13.3)
Number of Subjects Censored, n (%)	43 (95.6)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.724 (1.096)
95% CI		(0.551, 40.482)
Log-rank p-value		0.119

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.3, 100.0)	89.9 (82.3, 97.6)
6 months	95.4 (89.3, 100.0)	86.7 (77.1, 96.3)
9 months	95.4 (89.3, 100.0)	81.9 (69.0, 94.8)
12 months	95.4 (89.3, 100.0)	81.9 (69.0, 94.8)
18 months	NE (NE, NE)	81.9 (69.0, 94.8)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	10 (16.7)
Number of Subjects Censored, n (%)	42 (93.3)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (2.79, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.040 (0.691)
95% CI		(0.527, 7.903)
Log-rank p-value		0.355

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.2, 100.0)	84.7 (75.4, 93.9)
6 months	NE (NE, NE)	84.7 (75.4, 93.9)
9 months	NE (NE, NE)	79.0 (65.3, 92.8)
12 months	NE (NE, NE)	79.0 (65.3, 92.8)
18 months	NE (NE, NE)	79.0 (65.3, 92.8)
Median Follow-up Time (months)	2.83	4.14

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.098

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.2, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (89.2, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (89.2, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (89.2, 100.0)
18 months	NE (NE, NE)	94.8 (89.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	4 (6.7)
Number of Subjects Censored, n (%)	44 (97.8)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.948 (1.134)
95% CI		(0.211, 17.969)
Log-rank p-value		0.542

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (93.3, 100.0)	93.1 (86.6, 99.6)
6 months	97.7 (93.3, 100.0)	93.1 (86.6, 99.6)
9 months	97.7 (93.3, 100.0)	93.1 (86.6, 99.6)
12 months	97.7 (93.3, 100.0)	93.1 (86.6, 99.6)
18 months	NE (NE, NE)	93.1 (86.6, 99.6)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	3 (5.0)
Number of Subjects Censored, n (%)	44 (97.8)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.656 (1.351)
95% CI		(0.047, 9.267)
Log-rank p-value		0.942

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	98.3 (94.9, 100.0)
6 months	97.8 (93.5, 100.0)	98.3 (94.9, 100.0)
9 months	97.8 (93.5, 100.0)	85.1 (67.5, 100.0)
12 months	97.8 (93.5, 100.0)	85.1 (67.5, 100.0)
18 months	NE (NE, NE)	85.1 (67.5, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	45 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.330

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
18 months	NE (NE, NE)	96.6 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	7 (15.6)	27 (45.0)
Number of Subjects Censored, n (%)	38 (84.4)	33 (55.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.61, NE)	1.05 (0.53, 1.61)
Median (95% CI)	NE (3.71, NE)	7.39 (1.61, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.39, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.669 (0.433)
95% CI		(1.142, 6.235)
Log-rank p-value		0.022

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.3 (76.1, 96.5)	59.5 (47.0, 72.1)
6 months	74.0 (50.0, 98.0)	54.0 (40.5, 67.5)
9 months	74.0 (50.0, 98.0)	43.2 (21.4, 65.0)
12 months	74.0 (50.0, 98.0)	43.2 (21.4, 65.0)
18 months	NE (NE, NE)	43.2 (21.4, 65.0)
Median Follow-up Time (months)	2.83	2.58

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	20 (33.3)
Number of Subjects Censored, n (%)	43 (95.6)	40 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.66, 7.39)
Median (95% CI)	NE (NE, NE)	NE (5.19, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.097 (0.750)
95% CI		(1.401, 26.529)
Log-rank p-value		0.005

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.2, 100.0)	73.2 (62.0, 84.5)
6 months	95.4 (89.2, 100.0)	62.1 (46.4, 77.9)
9 months	95.4 (89.2, 100.0)	51.8 (29.1, 74.5)
12 months	95.4 (89.2, 100.0)	51.8 (29.1, 74.5)
18 months	NE (NE, NE)	51.8 (29.1, 74.5)
Median Follow-up Time (months)	2.83	3.27

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	0
Number of Subjects Censored, n (%)	44 (97.8)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.293

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
6 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
9 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
12 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	0
Number of Subjects Censored, n (%)	42 (93.3)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.023

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.2, 100.0)	100.0 (100.0, 100.0)
6 months	84.8 (64.4, 100.0)	100.0 (100.0, 100.0)
9 months	84.8 (64.4, 100.0)	100.0 (100.0, 100.0)
12 months	84.8 (64.4, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	10 (22.2)	14 (23.3)
Number of Subjects Censored, n (%)	35 (77.8)	46 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.979 (0.441)
95% CI		(0.412, 2.326)
Log-rank p-value		0.877

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (65.6, 89.9)	78.2 (67.7, 88.7)
6 months	77.8 (65.6, 89.9)	75.2 (63.5, 86.8)
9 months	77.8 (65.6, 89.9)	75.2 (63.5, 86.8)
12 months	77.8 (65.6, 89.9)	75.2 (63.5, 86.8)
18 months	NE (NE, NE)	75.2 (63.5, 86.8)
Median Follow-up Time (months)	2.79	3.76

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	11 (18.3)
Number of Subjects Censored, n (%)	42 (93.3)	49 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.147 (0.786)
95% CI		(0.888, 19.364)
Log-rank p-value		0.068

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	83.3 (73.9, 92.8)
6 months	93.3 (86.0, 100.0)	80.4 (69.6, 91.1)
9 months	93.3 (86.0, 100.0)	80.4 (69.6, 91.1)
12 months	93.3 (86.0, 100.0)	80.4 (69.6, 91.1)
18 months	NE (NE, NE)	80.4 (69.6, 91.1)
Median Follow-up Time (months)	2.83	3.99

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	0
Number of Subjects Censored, n (%)	43 (95.6)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.089

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
6 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
9 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
12 months	95.6 (89.5, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	4 (6.7)
Number of Subjects Censored, n (%)	45 (100.0)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.179

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
6 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
9 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
12 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
18 months	NE (NE, NE)	93.2 (86.7, 99.6)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	14 (23.3)
Number of Subjects Censored, n (%)	40 (88.9)	46 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.315 (0.582)
95% CI		(0.739, 7.245)
Log-rank p-value		0.155

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (79.7, 98.1)	79.9 (69.7, 90.1)
6 months	88.9 (79.7, 98.1)	74.9 (63.3, 86.6)
9 months	88.9 (79.7, 98.1)	74.9 (63.3, 86.6)
12 months	88.9 (79.7, 98.1)	74.9 (63.3, 86.6)
18 months	NE (NE, NE)	74.9 (63.3, 86.6)
Median Follow-up Time (months)	2.83	3.70

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	11 (18.3)
Number of Subjects Censored, n (%)	42 (93.3)	49 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.883 (0.786)
95% CI		(0.832, 18.126)
Log-rank p-value		0.072

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	84.8 (75.6, 94.0)
6 months	93.3 (86.0, 100.0)	79.9 (69.0, 90.8)
9 months	93.3 (86.0, 100.0)	79.9 (69.0, 90.8)
12 months	93.3 (86.0, 100.0)	79.9 (69.0, 90.8)
18 months	NE (NE, NE)	79.9 (69.0, 90.8)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (17.8)	15 (25.0)
Number of Subjects Censored, n (%)	37 (82.2)	45 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (2.27, NE)	5.68 (1.87, 17.48)
Median (95% CI)	NE (3.71, NE)	17.48 (6.54, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.022 (0.507)
95% CI		(0.378, 2.764)
Log-rank p-value		0.717

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (76.3, 96.5)	84.9 (75.8, 94.0)
6 months	64.0 (35.7, 92.3)	71.2 (56.2, 86.3)
9 months	64.0 (35.7, 92.3)	65.7 (48.4, 83.0)
12 months	64.0 (35.7, 92.3)	65.7 (48.4, 83.0)
18 months	NE (NE, NE)	32.9 (0.0, 79.2)
Median Follow-up Time (months)	2.83	3.76

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.4)	2 (3.3)
Number of Subjects Censored, n (%)	43 (95.6)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.113 (1.488)
95% CI		(0.006, 2.089)
Log-rank p-value		0.233

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	98.3 (95.0, 100.0)
6 months	88.0 (69.4, 100.0)	93.8 (84.7, 100.0)
9 months	88.0 (69.4, 100.0)	93.8 (84.7, 100.0)
12 months	88.0 (69.4, 100.0)	93.8 (84.7, 100.0)
18 months	NE (NE, NE)	93.8 (84.7, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (6.7)	3 (5.0)
Number of Subjects Censored, n (%)	42 (93.3)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (6.54, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.631 (0.909)
95% CI		(0.106, 3.751)
Log-rank p-value		0.981

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	98.3 (95.1, 100.0)
6 months	81.5 (56.2, 100.0)	96.0 (90.6, 100.0)
9 months	81.5 (56.2, 100.0)	90.4 (78.5, 100.0)
12 months	81.5 (56.2, 100.0)	90.4 (78.5, 100.0)
18 months	NE (NE, NE)	90.4 (78.5, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	0
Number of Subjects Censored, n (%)	44 (97.8)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.173

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
6 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
9 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
12 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	6 (10.0)
Number of Subjects Censored, n (%)	39 (86.7)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.843 (0.594)
95% CI		(0.263, 2.700)
Log-rank p-value		0.747

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (75.5, 96.5)	89.9 (82.3, 97.6)
6 months	86.0 (75.5, 96.5)	89.9 (82.3, 97.6)
9 months	86.0 (75.5, 96.5)	89.9 (82.3, 97.6)
12 months	86.0 (75.5, 96.5)	89.9 (82.3, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.44

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (13.3)	4 (6.7)
Number of Subjects Censored, n (%)	39 (86.7)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	1.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.393 (0.723)
95% CI		(0.095, 1.619)
Log-rank p-value		0.174

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (75.5, 96.5)	94.9 (89.4, 100.0)
6 months	86.0 (75.5, 96.5)	94.9 (89.4, 100.0)
9 months	86.0 (75.5, 96.5)	94.9 (89.4, 100.0)
12 months	86.0 (75.5, 96.5)	94.9 (89.4, 100.0)
18 months	NE (NE, NE)	47.5 (0.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.107

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
9 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
12 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	12 (20.0)
Number of Subjects Censored, n (%)	45 (100.0)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.019

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.1 (74.5, 93.7)
6 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
9 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
12 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.89

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	12 (20.0)
Number of Subjects Censored, n (%)	45 (100.0)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.019

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.1 (74.5, 93.7)
6 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
9 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
12 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.89

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	10 (16.7)
Number of Subjects Censored, n (%)	40 (88.9)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.995 (0.643)
95% CI		(0.282, 3.507)
Log-rank p-value		0.976

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.3 (78.6, 98.0)	84.4 (75.0, 93.8)
6 months	88.3 (78.6, 98.0)	81.8 (71.3, 92.2)
9 months	88.3 (78.6, 98.0)	81.8 (71.3, 92.2)
12 months	88.3 (78.6, 98.0)	81.8 (71.3, 92.2)
18 months	NE (NE, NE)	81.8 (71.3, 92.2)
Median Follow-up Time (months)	2.83	3.99

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	4 (6.7)
Number of Subjects Censored, n (%)	40 (88.9)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.224 (0.920)
95% CI		(0.037, 1.357)
Log-rank p-value		0.097

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.3 (78.6, 98.0)	92.7 (85.7, 99.6)
6 months	88.3 (78.6, 98.0)	92.7 (85.7, 99.6)
9 months	88.3 (78.6, 98.0)	92.7 (85.7, 99.6)
12 months	88.3 (78.6, 98.0)	92.7 (85.7, 99.6)
18 months	NE (NE, NE)	92.7 (85.7, 99.6)
Median Follow-up Time (months)	2.83	4.65

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	1 (1.7)
Number of Subjects Censored, n (%)	44 (97.8)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.110 (1.419)
95% CI		(0.069, 17.912)
Log-rank p-value		0.920

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	98.3 (95.0, 100.0)
6 months	97.6 (93.0, 100.0)	98.3 (95.0, 100.0)
9 months	97.6 (93.0, 100.0)	98.3 (95.0, 100.0)
12 months	97.6 (93.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	8 (13.3)
Number of Subjects Censored, n (%)	41 (91.1)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.683)
95% CI		(0.236, 3.424)
Log-rank p-value		0.960

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (82.6, 99.4)	91.0 (83.4, 98.6)
6 months	91.0 (82.6, 99.4)	84.0 (72.1, 96.0)
9 months	91.0 (82.6, 99.4)	77.0 (59.9, 94.1)
12 months	91.0 (82.6, 99.4)	77.0 (59.9, 94.1)
18 months	NE (NE, NE)	77.0 (59.9, 94.1)
Median Follow-up Time (months)	2.83	4.14

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	2 (3.3)
Number of Subjects Censored, n (%)	44 (97.8)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.407 (1.405)
95% CI		(0.026, 6.384)
Log-rank p-value		0.567

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	97.8 (93.6, 100.0)
6 months	97.6 (93.0, 100.0)	93.4 (84.0, 100.0)
9 months	97.6 (93.0, 100.0)	93.4 (84.0, 100.0)
12 months	97.6 (93.0, 100.0)	93.4 (84.0, 100.0)
18 months	NE (NE, NE)	93.4 (84.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.189

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	89.2 (74.6, 100.0)
12 months	100.0 (100.0, 100.0)	89.2 (74.6, 100.0)
18 months	NE (NE, NE)	89.2 (74.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	105 (57.1)	276 (69.7)
Number of Subjects Censored, n (%)	79 (42.9)	120 (30.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.72)	0.36 (0.26, 0.49)
Median (95% CI)	1.64 (1.28, 3.19)	1.25 (0.92, 1.61)
75% percentile (95% CI)	NE (4.70, NE)	5.65 (4.47, 7.39)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.215 (0.116)
95% CI		(0.968, 1.526)
Log-rank p-value		0.123

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	42.8 (35.3, 50.3)	37.7 (32.9, 42.6)
6 months	31.2 (18.9, 43.5)	24.3 (19.0, 29.5)
9 months	NE (NE, NE)	17.5 (11.1, 23.9)
12 months	NE (NE, NE)	17.5 (11.1, 23.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.53	1.15

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	44 (23.9)	133 (33.6)
Number of Subjects Censored, n (%)	140 (76.1)	263 (66.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.95, NE)	1.41 (0.92, 2.53)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.294 (0.175)
95% CI		(0.918, 1.825)
Log-rank p-value		0.152

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.4 (68.8, 82.0)	68.2 (63.4, 72.9)
6 months	67.3 (54.4, 80.2)	63.9 (58.7, 69.1)
9 months	NE (NE, NE)	60.9 (54.4, 67.5)
12 months	NE (NE, NE)	60.9 (54.4, 67.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.35	2.83

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	27 (14.7)	81 (20.5)
Number of Subjects Censored, n (%)	157 (85.3)	315 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.251 (0.225)
95% CI		(0.806, 1.943)
Log-rank p-value		0.351

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (78.9, 89.8)	81.2 (77.3, 85.1)
6 months	84.4 (78.9, 89.8)	77.5 (72.9, 82.2)
9 months	NE (NE, NE)	75.1 (69.5, 80.7)
12 months	NE (NE, NE)	75.1 (69.5, 80.7)
18 months	NE (NE, NE)	75.1 (69.5, 80.7)
Median Follow-up Time (months)	2.46	3.02

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	17 (9.2)	39 (9.8)
Number of Subjects Censored, n (%)	167 (90.8)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.297)
95% CI		(0.502, 1.610)
Log-rank p-value		0.674

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (85.2, 94.8)	91.7 (88.9, 94.5)
6 months	84.0 (71.8, 96.2)	89.0 (85.4, 92.6)
9 months	NE (NE, NE)	88.1 (84.2, 92.1)
12 months	NE (NE, NE)	82.6 (71.5, 93.7)
18 months	NE (NE, NE)	82.6 (71.5, 93.7)
Median Follow-up Time (months)	2.78	3.55

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	55 (13.9)
Number of Subjects Censored, n (%)	179 (97.3)	341 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.549 (0.469)
95% CI		(1.814, 11.408)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.4, 99.6)	87.6 (84.3, 90.9)
6 months	97.0 (94.4, 99.6)	85.6 (81.8, 89.3)
9 months	NE (NE, NE)	82.9 (77.7, 88.1)
12 months	NE (NE, NE)	82.9 (77.7, 88.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.32

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	24 (13.0)	26 (6.6)
Number of Subjects Censored, n (%)	160 (87.0)	370 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.346 (0.294)
95% CI		(0.194, 0.616)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (81.0, 91.8)	95.7 (93.7, 97.8)
6 months	81.8 (73.7, 89.9)	91.0 (87.4, 94.7)
9 months	NE (NE, NE)	91.0 (87.4, 94.7)
12 months	NE (NE, NE)	91.0 (87.4, 94.7)
18 months	NE (NE, NE)	83.4 (68.8, 98.0)
Median Follow-up Time (months)	2.81	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	13 (7.1)	20 (5.1)
Number of Subjects Censored, n (%)	171 (92.9)	376 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.576 (0.365)
95% CI		(0.282, 1.180)
Log-rank p-value		0.135

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (88.1, 96.4)	95.2 (93.0, 97.4)
6 months	92.3 (88.1, 96.4)	95.2 (93.0, 97.4)
9 months	NE (NE, NE)	92.9 (87.9, 97.9)
12 months	NE (NE, NE)	89.4 (81.3, 97.6)
18 months	NE (NE, NE)	89.4 (81.3, 97.6)
Median Follow-up Time (months)	2.79	3.71

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	15 (3.8)
Number of Subjects Censored, n (%)	179 (97.3)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.849 (0.548)
95% CI		(0.290, 2.484)
Log-rank p-value		0.704

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.4, 99.6)	97.9 (96.4, 99.3)
6 months	97.0 (94.4, 99.6)	96.3 (94.0, 98.6)
9 months	NE (NE, NE)	94.8 (91.1, 98.5)
12 months	NE (NE, NE)	86.2 (76.2, 96.2)
18 months	NE (NE, NE)	86.2 (76.2, 96.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	9 (2.3)
Number of Subjects Censored, n (%)	180 (97.8)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.634 (0.622)
95% CI		(0.187, 2.144)
Log-rank p-value		0.411

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.2, 100.0)	98.3 (96.9, 99.6)
6 months	97.1 (94.2, 100.0)	97.1 (95.1, 99.2)
9 months	NE (NE, NE)	95.6 (92.0, 99.2)
12 months	NE (NE, NE)	95.6 (92.0, 99.2)
18 months	NE (NE, NE)	95.6 (92.0, 99.2)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	10 (2.5)
Number of Subjects Censored, n (%)	182 (98.9)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.820 (0.795)
95% CI		(0.383, 8.639)
Log-rank p-value		0.412

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	98.2 (96.9, 99.5)
6 months	98.9 (97.4, 100.0)	96.9 (94.6, 99.2)
9 months	NE (NE, NE)	94.7 (90.0, 99.5)
12 months	NE (NE, NE)	94.7 (90.0, 99.5)
18 months	NE (NE, NE)	94.7 (90.0, 99.5)
Median Follow-up Time (months)	2.83	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	109 (59.2)	267 (67.4)
Number of Subjects Censored, n (%)	75 (40.8)	129 (32.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.30, 0.69)	0.53 (0.46, 0.69)
Median (95% CI)	1.58 (1.02, 2.00)	1.58 (1.05, 1.91)
75% percentile (95% CI)	5.36 (3.75, NE)	5.95 (4.90, 7.79)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.978 (0.116)
95% CI		(0.779, 1.227)
Log-rank p-value		0.932

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	36.8 (28.5, 45.0)	38.4 (33.4, 43.3)
6 months	14.3 (0.0, 35.1)	24.4 (18.6, 30.2)
9 months	NE (NE, NE)	17.0 (10.1, 23.8)
12 months	NE (NE, NE)	13.6 (5.5, 21.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.22	1.38

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	20 (10.9)	94 (23.7)
Number of Subjects Censored, n (%)	164 (89.1)	302 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.89, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.896 (0.249)
95% CI		(1.164, 3.089)
Log-rank p-value		0.011

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (84.2, 93.4)	79.2 (75.1, 83.3)
6 months	88.8 (84.2, 93.4)	72.1 (66.4, 77.7)
9 months	NE (NE, NE)	68.5 (61.9, 75.2)
12 months	NE (NE, NE)	62.3 (49.2, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	2.84

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	37 (20.1)	72 (18.2)
Number of Subjects Censored, n (%)	147 (79.9)	324 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.87, NE)	9.00 (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.637 (0.208)
95% CI		(0.423, 0.957)
Log-rank p-value		0.023

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.3 (73.1, 85.4)	84.5 (80.7, 88.2)
6 months	74.6 (64.0, 85.2)	78.4 (73.3, 83.5)
9 months	NE (NE, NE)	75.0 (68.8, 81.3)
12 months	NE (NE, NE)	70.6 (62.3, 79.0)
18 months	NE (NE, NE)	70.6 (62.3, 79.0)
Median Follow-up Time (months)	2.46	3.22

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	30 (16.3)	71 (17.9)
Number of Subjects Censored, n (%)	154 (83.7)	325 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	9.23 (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.223)
95% CI		(0.547, 1.313)
Log-rank p-value		0.552

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (74.8, 88.2)	84.7 (80.9, 88.4)
6 months	76.9 (66.2, 87.6)	79.2 (74.4, 84.1)
9 months	NE (NE, NE)	75.3 (68.9, 81.7)
12 months	NE (NE, NE)	69.5 (59.6, 79.4)
18 months	NE (NE, NE)	69.5 (59.6, 79.4)
Median Follow-up Time (months)	2.60	3.22

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	17 (9.2)	69 (17.4)
Number of Subjects Censored, n (%)	167 (90.8)	327 (82.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.472 (0.276)
95% CI		(0.857, 2.528)
Log-rank p-value		0.162

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (83.2, 94.9)	85.3 (81.7, 89.0)
6 months	86.9 (79.8, 93.9)	79.4 (74.5, 84.3)
9 months	NE (NE, NE)	75.8 (69.6, 81.9)
12 months	NE (NE, NE)	73.3 (65.6, 80.9)
18 months	NE (NE, NE)	73.3 (65.6, 80.9)
Median Follow-up Time (months)	2.71	3.22

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	27 (14.7)	57 (14.4)
Number of Subjects Censored, n (%)	157 (85.3)	339 (85.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	10.18 (7.10, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.666 (0.243)
95% CI		(0.414, 1.072)
Log-rank p-value		0.083

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (79.7, 90.6)	89.5 (86.4, 92.7)
6 months	76.7 (63.6, 89.7)	83.3 (78.6, 88.0)
9 months	NE (NE, NE)	79.0 (73.0, 85.1)
12 months	NE (NE, NE)	73.5 (64.1, 82.9)
18 months	NE (NE, NE)	73.5 (64.1, 82.9)
Median Follow-up Time (months)	2.69	3.40

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.3)	59 (14.9)
Number of Subjects Censored, n (%)	178 (96.7)	337 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.502 (0.430)
95% CI		(1.937, 10.466)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.5, 99.2)	86.3 (82.8, 89.7)
6 months	96.3 (93.5, 99.2)	84.0 (80.0, 88.0)
9 months	NE (NE, NE)	81.4 (76.1, 86.7)
12 months	NE (NE, NE)	81.4 (76.1, 86.7)
18 months	NE (NE, NE)	81.4 (76.1, 86.7)
Median Follow-up Time (months)	2.79	3.24

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	30 (7.6)
Number of Subjects Censored, n (%)	179 (97.3)	366 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.286 (0.488)
95% CI		(0.878, 5.952)
Log-rank p-value		0.086

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.6, 99.6)	93.7 (91.2, 96.1)
6 months	97.1 (94.6, 99.6)	90.8 (87.4, 94.3)
9 months	NE (NE, NE)	89.3 (84.7, 93.8)
12 months	NE (NE, NE)	89.3 (84.7, 93.8)
18 months	NE (NE, NE)	89.3 (84.7, 93.8)
Median Follow-up Time (months)	2.79	3.55

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	14 (3.5)
Number of Subjects Censored, n (%)	180 (97.8)	382 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.224 (0.579)
95% CI		(0.393, 3.808)
Log-rank p-value		0.770

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.3, 99.9)	97.2 (95.5, 98.8)
6 months	97.6 (95.3, 99.9)	95.9 (93.4, 98.3)
9 months	NE (NE, NE)	94.4 (90.6, 98.1)
12 months	NE (NE, NE)	94.4 (90.6, 98.1)
18 months	NE (NE, NE)	94.4 (90.6, 98.1)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	6 (1.5)
Number of Subjects Censored, n (%)	180 (97.8)	390 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.603 (0.651)
95% CI		(0.168, 2.158)
Log-rank p-value		0.510

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.0, 100.0)	98.3 (97.0, 99.7)
6 months	97.5 (95.0, 100.0)	98.3 (97.0, 99.7)
9 months	NE (NE, NE)	98.3 (97.0, 99.7)
12 months	NE (NE, NE)	98.3 (97.0, 99.7)
18 months	NE (NE, NE)	98.3 (97.0, 99.7)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	9 (4.9)	3 (0.8)
Number of Subjects Censored, n (%)	175 (95.1)	393 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.107 (0.697)
95% CI		(0.027, 0.418)
Log-rank p-value		<.001

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (91.0, 98.0)	99.5 (98.7, 100.0)
6 months	94.5 (91.0, 98.0)	98.6 (96.8, 100.0)
9 months	NE (NE, NE)	98.6 (96.8, 100.0)
12 months	NE (NE, NE)	98.6 (96.8, 100.0)
18 months	NE (NE, NE)	98.6 (96.8, 100.0)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	12 (3.0)
Number of Subjects Censored, n (%)	184 (100.0)	384 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.032

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.3, 98.8)
6 months	100.0 (100.0, 100.0)	97.0 (95.3, 98.8)
9 months	NE (NE, NE)	95.4 (91.8, 99.0)
12 months	NE (NE, NE)	95.4 (91.8, 99.0)
18 months	NE (NE, NE)	95.4 (91.8, 99.0)
Median Follow-up Time (months)	2.83	3.71

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	49 (26.6)	174 (43.9)
Number of Subjects Censored, n (%)	135 (73.4)	222 (56.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.99, NE)	1.08 (0.92, 1.61)
Median (95% CI)	NE (NE, NE)	6.24 (4.63, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.488 (0.163)
95% CI		(1.080, 2.049)
Log-rank p-value		0.019

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.7 (65.9, 79.5)	59.5 (54.5, 64.5)
6 months	66.0 (54.9, 77.2)	51.9 (46.0, 57.7)
9 months	NE (NE, NE)	46.4 (39.6, 53.2)
12 months	NE (NE, NE)	43.6 (35.4, 51.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.78

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	32 (17.4)	114 (28.8)
Number of Subjects Censored, n (%)	152 (82.6)	282 (71.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.73 (1.68, 3.94)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.492 (0.202)
95% CI		(1.004, 2.217)
Log-rank p-value		0.054

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.2, 87.8)	72.7 (68.1, 77.3)
6 months	77.7 (67.8, 87.5)	68.5 (63.3, 73.7)
9 months	NE (NE, NE)	65.7 (59.7, 71.6)
12 months	NE (NE, NE)	63.0 (55.4, 70.6)
18 months	NE (NE, NE)	63.0 (55.4, 70.6)
Median Follow-up Time (months)	2.56	2.83

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	25 (6.3)
Number of Subjects Censored, n (%)	180 (97.8)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.358 (0.543)
95% CI		(0.813, 6.839)
Log-rank p-value		0.089

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	93.8 (91.3, 96.4)
6 months	97.8 (95.7, 99.9)	92.8 (90.0, 95.7)
9 months	NE (NE, NE)	91.4 (87.3, 95.4)
12 months	NE (NE, NE)	91.4 (87.3, 95.4)
18 months	NE (NE, NE)	91.4 (87.3, 95.4)
Median Follow-up Time (months)	2.81	3.71

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	18 (4.5)
Number of Subjects Censored, n (%)	179 (97.3)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.196 (0.519)
95% CI		(0.432, 3.310)
Log-rank p-value		0.721

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.6, 99.9)	96.5 (94.6, 98.4)
6 months	95.4 (90.3, 100.0)	94.0 (91.0, 97.1)
9 months	NE (NE, NE)	92.7 (88.7, 96.7)
12 months	NE (NE, NE)	92.7 (88.7, 96.7)
18 months	NE (NE, NE)	92.7 (88.7, 96.7)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	11 (2.8)
Number of Subjects Censored, n (%)	180 (97.8)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.173 (0.589)
95% CI		(0.370, 3.720)
Log-rank p-value		0.749

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.1, 100.0)	97.3 (95.6, 98.9)
6 months	97.5 (95.1, 100.0)	96.8 (94.9, 98.7)
9 months	NE (NE, NE)	96.8 (94.9, 98.7)
12 months	NE (NE, NE)	96.8 (94.9, 98.7)
18 months	NE (NE, NE)	96.8 (94.9, 98.7)
Median Follow-up Time (months)	2.79	3.75

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	14 (3.5)
Number of Subjects Censored, n (%)	181 (98.4)	382 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.786 (0.646)
95% CI		(0.504, 6.331)
Log-rank p-value		0.375

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

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.5, 100.0)	96.7 (94.9, 98.6)
6 months	98.3 (96.5, 100.0)	96.0 (93.7, 98.3)
9 months	NE (NE, NE)	94.6 (91.2, 98.1)
12 months	NE (NE, NE)	94.6 (91.2, 98.1)
18 months	NE (NE, NE)	94.6 (91.2, 98.1)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	15 (3.8)
Number of Subjects Censored, n (%)	184 (100.0)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.8)
6 months	100.0 (100.0, 100.0)	95.2 (92.4, 97.9)
9 months	NE (NE, NE)	93.9 (90.1, 97.6)
12 months	NE (NE, NE)	93.9 (90.1, 97.6)
18 months	NE (NE, NE)	93.9 (90.1, 97.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	182 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.023 (0.776)
95% CI		(0.442, 9.252)
Log-rank p-value		0.370

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	97.3 (95.6, 98.9)
6 months	98.3 (95.9, 100.0)	97.3 (95.6, 98.9)
9 months	NE (NE, NE)	96.4 (94.0, 98.8)
12 months	NE (NE, NE)	96.4 (94.0, 98.8)
18 months	NE (NE, NE)	96.4 (94.0, 98.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.8)
Number of Subjects Censored, n (%)	183 (99.5)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.761 (1.053)
95% CI		(0.477, 29.649)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.4, 100.0)	97.8 (96.3, 99.3)
6 months	99.4 (98.4, 100.0)	96.6 (94.4, 98.9)
9 months	NE (NE, NE)	95.8 (92.9, 98.6)
12 months	NE (NE, NE)	95.8 (92.9, 98.6)
18 months	NE (NE, NE)	95.8 (92.9, 98.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	9 (2.3)
Number of Subjects Censored, n (%)	184 (100.0)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (96.1, 99.2)
6 months	100.0 (100.0, 100.0)	97.6 (96.1, 99.2)
9 months	NE (NE, NE)	97.6 (96.1, 99.2)
12 months	NE (NE, NE)	97.6 (96.1, 99.2)
18 months	NE (NE, NE)	97.6 (96.1, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.5)
Number of Subjects Censored, n (%)	183 (99.5)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.348 (1.073)
95% CI		(0.287, 19.224)
Log-rank p-value		0.481

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	98.8 (97.6, 100.0)
6 months	99.4 (98.1, 100.0)	95.1 (91.9, 98.3)
9 months	NE (NE, NE)	95.1 (91.9, 98.3)
12 months	NE (NE, NE)	95.1 (91.9, 98.3)
18 months	NE (NE, NE)	95.1 (91.9, 98.3)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	49 (26.6)	164 (41.4)
Number of Subjects Censored, n (%)	135 (73.4)	232 (58.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.17 (1.35, 5.82)	1.58 (0.95, 1.68)
Median (95% CI)	NE (5.82, NE)	6.90 (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.385 (0.165)
95% CI		(1.002, 1.913)
Log-rank p-value		0.040

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.7 (65.9, 79.6)	62.5 (57.5, 67.4)
6 months	57.4 (38.1, 76.8)	54.6 (48.7, 60.4)
9 months	NE (NE, NE)	46.8 (39.6, 54.0)
12 months	NE (NE, NE)	46.8 (39.6, 54.0)
18 months	NE (NE, NE)	46.8 (39.6, 54.0)
Median Follow-up Time (months)	2.51	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	16 (8.7)	49 (12.4)
Number of Subjects Censored, n (%)	168 (91.3)	347 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.172 (0.294)
95% CI		(0.659, 2.084)
Log-rank p-value		0.614

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (84.4, 94.7)	89.4 (86.3, 92.5)
6 months	78.3 (57.3, 99.3)	85.1 (80.8, 89.5)
9 months	NE (NE, NE)	82.8 (77.5, 88.2)
12 months	NE (NE, NE)	82.8 (77.5, 88.2)
18 months	NE (NE, NE)	82.8 (77.5, 88.2)
Median Follow-up Time (months)	2.74	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	39 (9.8)
Number of Subjects Censored, n (%)	176 (95.7)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.801 (0.394)
95% CI		(0.832, 3.898)
Log-rank p-value		0.136

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.4, 98.5)	91.6 (88.7, 94.5)
6 months	95.5 (92.4, 98.5)	88.9 (85.3, 92.6)
9 months	NE (NE, NE)	85.7 (80.7, 90.8)
12 months	NE (NE, NE)	85.7 (80.7, 90.8)
18 months	NE (NE, NE)	85.7 (80.7, 90.8)
Median Follow-up Time (months)	2.81	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.3)	41 (10.4)
Number of Subjects Censored, n (%)	178 (96.7)	355 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.443 (0.443)
95% CI		(1.026, 5.818)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (94.0, 99.3)	91.7 (88.9, 94.5)
6 months	96.6 (94.0, 99.3)	88.4 (84.7, 92.2)
9 months	NE (NE, NE)	84.3 (78.8, 89.7)
12 months	NE (NE, NE)	84.3 (78.8, 89.7)
18 months	NE (NE, NE)	84.3 (78.8, 89.7)
Median Follow-up Time (months)	2.81	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	32 (8.1)
Number of Subjects Censored, n (%)	176 (95.7)	364 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.359 (0.402)
95% CI		(0.618, 2.987)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.5, 98.6)	93.8 (91.3, 96.3)
6 months	95.5 (92.5, 98.6)	90.1 (86.6, 93.7)
9 months	NE (NE, NE)	87.8 (83.1, 92.5)
12 months	NE (NE, NE)	87.8 (83.1, 92.5)
18 months	NE (NE, NE)	87.8 (83.1, 92.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	26 (6.6)
Number of Subjects Censored, n (%)	181 (98.4)	370 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.330 (0.616)
95% CI		(0.995, 11.148)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	94.0 (91.5, 96.4)
6 months	95.5 (89.3, 100.0)	93.2 (90.2, 96.1)
9 months	NE (NE, NE)	89.4 (84.1, 94.8)
12 months	NE (NE, NE)	89.4 (84.1, 94.8)
18 months	NE (NE, NE)	89.4 (84.1, 94.8)
Median Follow-up Time (months)	2.81	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.8)	18 (4.5)
Number of Subjects Censored, n (%)	177 (96.2)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.036 (0.453)
95% CI		(0.426, 2.518)
Log-rank p-value		0.956

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.2, 98.8)	95.7 (93.6, 97.8)
6 months	95.5 (92.2, 98.8)	95.0 (92.6, 97.5)
9 months	NE (NE, NE)	94.1 (91.2, 97.1)
12 months	NE (NE, NE)	94.1 (91.2, 97.1)
18 months	NE (NE, NE)	94.1 (91.2, 97.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	25 (6.3)
Number of Subjects Censored, n (%)	184 (100.0)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.0 (91.6, 96.5)
6 months	100.0 (100.0, 100.0)	92.4 (89.3, 95.4)
9 months	NE (NE, NE)	92.4 (89.3, 95.4)
12 months	NE (NE, NE)	92.4 (89.3, 95.4)
18 months	NE (NE, NE)	92.4 (89.3, 95.4)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	17 (4.3)
Number of Subjects Censored, n (%)	179 (97.3)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.087 (0.518)
95% CI		(0.394, 2.998)
Log-rank p-value		0.902

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.6, 100.0)	96.4 (94.5, 98.4)
6 months	94.3 (88.1, 100.0)	94.6 (91.9, 97.4)
9 months	NE (NE, NE)	93.8 (90.6, 97.0)
12 months	NE (NE, NE)	93.8 (90.6, 97.0)
18 months	NE (NE, NE)	93.8 (90.6, 97.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	12 (3.0)
Number of Subjects Censored, n (%)	183 (99.5)	384 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.267 (1.049)
95% CI		(0.547, 33.311)
Log-rank p-value		0.132

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	97.1 (95.3, 98.9)
6 months	99.4 (98.3, 100.0)	96.5 (94.4, 98.6)
9 months	NE (NE, NE)	95.3 (92.2, 98.4)
12 months	NE (NE, NE)	95.3 (92.2, 98.4)
18 months	NE (NE, NE)	95.3 (92.2, 98.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	182 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.189 (0.775)
95% CI		(0.479, 10.006)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.3, 100.0)	97.2 (95.5, 98.9)
6 months	98.9 (97.3, 100.0)	97.2 (95.5, 98.9)
9 months	NE (NE, NE)	96.0 (93.2, 98.9)
12 months	NE (NE, NE)	96.0 (93.2, 98.9)
18 months	NE (NE, NE)	96.0 (93.2, 98.9)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	44 (23.9)	152 (38.4)
Number of Subjects Censored, n (%)	140 (76.1)	244 (61.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (1.48, NE)	0.72 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.577 (0.173)
95% CI		(1.123, 2.216)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.7 (66.9, 80.6)	65.0 (60.3, 69.8)
6 months	73.7 (66.9, 80.6)	58.9 (53.3, 64.5)
9 months	NE (NE, NE)	56.6 (50.3, 62.8)
12 months	NE (NE, NE)	46.9 (35.1, 58.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.23	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	67 (16.9)
Number of Subjects Censored, n (%)	176 (95.7)	329 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.205 (0.376)
95% CI		(2.013, 8.785)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.8, 98.5)	83.1 (79.3, 86.8)
6 months	95.1 (91.8, 98.5)	82.6 (78.8, 86.4)
9 months	NE (NE, NE)	82.6 (78.8, 86.4)
12 months	NE (NE, NE)	82.6 (78.8, 86.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	16 (8.7)	37 (9.3)
Number of Subjects Censored, n (%)	168 (91.3)	359 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.815 (0.307)
95% CI		(0.447, 1.487)
Log-rank p-value		0.514

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (86.3, 95.1)	92.3 (89.5, 95.0)
6 months	90.7 (86.3, 95.1)	89.4 (85.8, 93.1)
9 months	NE (NE, NE)	88.6 (84.7, 92.6)
12 months	NE (NE, NE)	84.8 (76.5, 93.1)
18 months	NE (NE, NE)	63.6 (27.1, 100.0)
Median Follow-up Time (months)	2.78	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	15 (8.2)	31 (7.8)
Number of Subjects Censored, n (%)	169 (91.8)	365 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.841 (0.320)
95% CI		(0.449, 1.573)
Log-rank p-value		0.641

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (86.6, 95.4)	92.6 (90.0, 95.3)
6 months	91.0 (86.6, 95.4)	91.6 (88.6, 94.6)
9 months	NE (NE, NE)	91.6 (88.6, 94.6)
12 months	NE (NE, NE)	85.8 (74.6, 97.1)
18 months	NE (NE, NE)	85.8 (74.6, 97.1)
Median Follow-up Time (months)	2.60	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	15 (3.8)
Number of Subjects Censored, n (%)	181 (98.4)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.189 (0.634)
95% CI		(0.632, 7.581)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.5, 100.0)	96.0 (94.1, 98.0)
6 months	98.3 (96.5, 100.0)	96.0 (94.1, 98.0)
9 months	NE (NE, NE)	96.0 (94.1, 98.0)
12 months	NE (NE, NE)	96.0 (94.1, 98.0)
18 months	NE (NE, NE)	96.0 (94.1, 98.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	9 (2.3)
Number of Subjects Censored, n (%)	182 (98.9)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.518 (0.806)
95% CI		(0.313, 7.371)
Log-rank p-value		0.655

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.0, 100.0)	98.5 (97.3, 99.7)
6 months	98.8 (97.0, 100.0)	97.8 (96.0, 99.6)
9 months	NE (NE, NE)	95.7 (92.2, 99.1)
12 months	NE (NE, NE)	95.7 (92.2, 99.1)
18 months	NE (NE, NE)	95.7 (92.2, 99.1)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	26 (14.1)	155 (39.1)
Number of Subjects Censored, n (%)	158 (85.9)	241 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.803 (0.213)
95% CI		(1.846, 4.254)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (79.6, 90.6)	62.2 (57.3, 67.2)
6 months	81.7 (73.3, 90.1)	57.9 (52.3, 63.5)
9 months	NE (NE, NE)	52.5 (45.4, 59.7)
12 months	NE (NE, NE)	52.5 (45.4, 59.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.50	2.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	14 (7.6)	145 (36.6)
Number of Subjects Censored, n (%)	170 (92.4)	251 (63.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.72, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.989 (0.281)
95% CI		(2.878, 8.647)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.5 (87.1, 95.8)	64.7 (59.8, 69.5)
6 months	91.5 (87.1, 95.8)	61.8 (56.5, 67.0)
9 months	NE (NE, NE)	55.0 (47.7, 62.4)
12 months	NE (NE, NE)	55.0 (47.7, 62.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	37 (20.1)	125 (31.6)
Number of Subjects Censored, n (%)	147 (79.9)	271 (68.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	1.84 (1.22, 2.76)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.402 (0.189)
95% CI		(0.968, 2.031)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.9 (72.6, 85.2)	70.0 (65.3, 74.6)
6 months	75.8 (67.4, 84.3)	64.9 (59.3, 70.4)
9 months	NE (NE, NE)	59.6 (51.8, 67.5)
12 months	NE (NE, NE)	59.6 (51.8, 67.5)
18 months	NE (NE, NE)	59.6 (51.8, 67.5)
Median Follow-up Time (months)	2.38	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	15 (8.2)	39 (9.8)
Number of Subjects Censored, n (%)	169 (91.8)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.953 (0.308)
95% CI		(0.521, 1.741)
Log-rank p-value		0.971

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.5 (87.4, 95.6)	90.7 (87.7, 93.7)
6 months	91.5 (87.4, 95.6)	88.0 (84.3, 91.8)
9 months	NE (NE, NE)	88.0 (84.3, 91.8)
12 months	NE (NE, NE)	88.0 (84.3, 91.8)
18 months	NE (NE, NE)	88.0 (84.3, 91.8)
Median Follow-up Time (months)	2.74	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.8)	40 (10.1)
Number of Subjects Censored, n (%)	177 (96.2)	356 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.205 (0.414)
95% CI		(0.979, 4.964)
Log-rank p-value		0.052

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (93.1, 98.9)	91.3 (88.4, 94.1)
6 months	96.0 (93.1, 98.9)	88.2 (84.3, 92.1)
9 months	NE (NE, NE)	85.1 (79.5, 90.8)
12 months	NE (NE, NE)	85.1 (79.5, 90.8)
18 months	NE (NE, NE)	85.1 (79.5, 90.8)
Median Follow-up Time (months)	2.79	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	23 (5.8)
Number of Subjects Censored, n (%)	180 (97.8)	373 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.351 (0.545)
95% CI		(0.807, 6.845)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.1, 100.0)	94.5 (92.2, 96.8)
6 months	95.1 (88.9, 100.0)	93.0 (90.0, 96.1)
9 months	NE (NE, NE)	93.0 (90.0, 96.1)
12 months	NE (NE, NE)	93.0 (90.0, 96.1)
18 months	NE (NE, NE)	93.0 (90.0, 96.1)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	10 (2.5)
Number of Subjects Censored, n (%)	180 (97.8)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.026 (0.601)
95% CI		(0.316, 3.335)
Log-rank p-value		0.999

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.6, 99.9)	97.6 (96.1, 99.2)
6 months	97.8 (95.6, 99.9)	96.8 (94.5, 99.0)
9 months	NE (NE, NE)	96.8 (94.5, 99.0)
12 months	NE (NE, NE)	96.8 (94.5, 99.0)
18 months	NE (NE, NE)	96.8 (94.5, 99.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	9 (2.3)
Number of Subjects Censored, n (%)	183 (99.5)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.053 (1.066)
95% CI		(0.378, 24.689)
Log-rank p-value		0.279

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.4, 100.0)	98.2 (96.9, 99.5)
6 months	99.4 (98.4, 100.0)	97.4 (95.4, 99.4)
9 months	NE (NE, NE)	95.2 (90.5, 99.9)
12 months	NE (NE, NE)	95.2 (90.5, 99.9)
18 months	NE (NE, NE)	95.2 (90.5, 99.9)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	9 (2.3)
Number of Subjects Censored, n (%)	184 (100.0)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
6 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
9 months	NE (NE, NE)	97.5 (95.9, 99.1)
12 months	NE (NE, NE)	97.5 (95.9, 99.1)
18 months	NE (NE, NE)	97.5 (95.9, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	20 (10.9)	130 (32.8)
Number of Subjects Censored, n (%)	164 (89.1)	266 (67.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (1.02, 2.10)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.115 (0.241)
95% CI		(1.941, 4.999)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (84.1, 93.4)	68.6 (63.9, 73.3)
6 months	88.8 (84.1, 93.4)	63.7 (58.2, 69.2)
9 months	NE (NE, NE)	62.7 (56.9, 68.5)
12 months	NE (NE, NE)	62.7 (56.9, 68.5)
18 months	NE (NE, NE)	31.4 (0.0, 74.9)
Median Follow-up Time (months)	2.66	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	68 (17.2)
Number of Subjects Censored, n (%)	180 (97.8)	328 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.906 (0.515)
95% CI		(2.879, 21.711)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	83.8 (80.1, 87.5)
6 months	97.8 (95.7, 99.9)	80.3 (75.8, 84.8)
9 months	NE (NE, NE)	80.3 (75.8, 84.8)
12 months	NE (NE, NE)	80.3 (75.8, 84.8)
18 months	NE (NE, NE)	80.3 (75.8, 84.8)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.8)	18 (4.5)
Number of Subjects Censored, n (%)	177 (96.2)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.164 (0.447)
95% CI		(0.485, 2.797)
Log-rank p-value		0.752

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (93.3, 98.9)	95.2 (93.1, 97.4)
6 months	96.1 (93.3, 98.9)	95.2 (93.1, 97.4)
9 months	NE (NE, NE)	95.2 (93.1, 97.4)
12 months	NE (NE, NE)	95.2 (93.1, 97.4)
18 months	NE (NE, NE)	95.2 (93.1, 97.4)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	13 (3.3)
Number of Subjects Censored, n (%)	184 (100.0)	383 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (95.0, 98.6)
6 months	100.0 (100.0, 100.0)	96.3 (94.3, 98.3)
9 months	NE (NE, NE)	96.3 (94.3, 98.3)
12 months	NE (NE, NE)	96.3 (94.3, 98.3)
18 months	NE (NE, NE)	96.3 (94.3, 98.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	27 (14.7)	101 (25.5)
Number of Subjects Censored, n (%)	157 (85.3)	295 (74.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.01 (2.27, 6.21)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.529 (0.219)
95% CI		(0.995, 2.349)
Log-rank p-value		0.071

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (77.7, 89.3)	77.4 (73.1, 81.6)
6 months	83.5 (77.7, 89.3)	70.9 (65.5, 76.3)
9 months	NE (NE, NE)	69.1 (63.4, 74.9)
12 months	NE (NE, NE)	65.5 (56.7, 74.4)
18 months	NE (NE, NE)	65.5 (56.7, 74.4)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	30 (7.6)
Number of Subjects Censored, n (%)	176 (95.7)	366 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.493 (0.403)
95% CI		(0.678, 3.288)
Log-rank p-value		0.322

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.4, 98.4)	93.3 (90.8, 95.8)
6 months	94.9 (91.4, 98.4)	92.7 (90.0, 95.4)
9 months	NE (NE, NE)	91.0 (87.4, 94.6)
12 months	NE (NE, NE)	91.0 (87.4, 94.6)
18 months	NE (NE, NE)	91.0 (87.4, 94.6)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	10 (2.5)
Number of Subjects Censored, n (%)	179 (97.3)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.876 (0.550)
95% CI		(0.298, 2.572)
Log-rank p-value		0.762

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.8, 99.6)	97.3 (95.7, 99.0)
6 months	97.2 (94.8, 99.6)	97.3 (95.7, 99.0)
9 months	NE (NE, NE)	97.3 (95.7, 99.0)
12 months	NE (NE, NE)	97.3 (95.7, 99.0)
18 months	NE (NE, NE)	97.3 (95.7, 99.0)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.2)	8 (2.0)
Number of Subjects Censored, n (%)	180 (97.8)	388 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.819 (0.613)
95% CI		(0.246, 2.722)
Log-rank p-value		0.696

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.3, 99.9)	97.9 (96.5, 99.4)
6 months	97.6 (95.3, 99.9)	97.9 (96.5, 99.4)
9 months	NE (NE, NE)	97.9 (96.5, 99.4)
12 months	NE (NE, NE)	97.9 (96.5, 99.4)
18 months	NE (NE, NE)	97.9 (96.5, 99.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	24 (13.0)	98 (24.7)
Number of Subjects Censored, n (%)	160 (87.0)	298 (75.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (2.83, 6.54)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (0.231)
95% CI		(0.958, 2.370)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (80.3, 91.3)	78.5 (74.3, 82.7)
6 months	82.6 (74.5, 90.7)	70.9 (65.4, 76.5)
9 months	NE (NE, NE)	67.7 (61.3, 74.1)
12 months	NE (NE, NE)	59.2 (42.8, 75.7)
18 months	NE (NE, NE)	39.5 (6.0, 73.0)
Median Follow-up Time (months)	2.58	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	68 (17.2)
Number of Subjects Censored, n (%)	176 (95.7)	328 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.191 (0.376)
95% CI		(1.526, 6.673)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (92.2, 98.5)	84.4 (80.7, 88.2)
6 months	95.3 (92.2, 98.5)	79.9 (75.2, 84.7)
9 months	NE (NE, NE)	76.8 (70.6, 83.1)
12 months	NE (NE, NE)	76.8 (70.6, 83.1)
18 months	NE (NE, NE)	51.2 (10.0, 92.4)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	10 (2.5)
Number of Subjects Censored, n (%)	179 (97.3)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.790 (0.553)
95% CI		(0.267, 2.336)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.6, 99.6)	97.7 (96.1, 99.2)
6 months	97.1 (94.6, 99.6)	97.1 (95.3, 99.0)
9 months	NE (NE, NE)	97.1 (95.3, 99.0)
12 months	NE (NE, NE)	97.1 (95.3, 99.0)
18 months	NE (NE, NE)	97.1 (95.3, 99.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	20 (10.9)	81 (20.5)
Number of Subjects Censored, n (%)	164 (89.1)	315 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (5.78, NE)	6.28 (4.60, 7.92)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.286 (0.256)
95% CI		(0.778, 2.125)
Log-rank p-value		0.297

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (84.9, 94.1)	84.3 (80.5, 88.1)
6 months	74.7 (51.4, 97.9)	75.2 (69.6, 80.9)
9 months	NE (NE, NE)	65.0 (56.7, 73.4)
12 months	NE (NE, NE)	59.6 (46.9, 72.4)
18 months	NE (NE, NE)	59.6 (46.9, 72.4)
Median Follow-up Time (months)	2.78	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.3)	17 (4.3)
Number of Subjects Censored, n (%)	178 (96.7)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.493)
95% CI		(0.309, 2.137)
Log-rank p-value		0.854

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.5, 100.0)	96.8 (95.1, 98.6)
6 months	86.7 (73.6, 99.8)	95.4 (92.8, 98.1)
9 months	NE (NE, NE)	92.4 (88.1, 96.7)
12 months	NE (NE, NE)	92.4 (88.1, 96.7)
18 months	NE (NE, NE)	92.4 (88.1, 96.7)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	9 (2.3)
Number of Subjects Censored, n (%)	181 (98.4)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.766 (0.699)
95% CI		(0.195, 3.016)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.2, 100.0)	98.8 (97.7, 100.0)
6 months	98.2 (96.2, 100.0)	96.4 (93.8, 99.0)
9 months	NE (NE, NE)	96.4 (93.8, 99.0)
12 months	NE (NE, NE)	90.8 (79.7, 100.0)
18 months	NE (NE, NE)	90.8 (79.7, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	11 (2.8)
Number of Subjects Censored, n (%)	184 (100.0)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.3, 98.9)
6 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.7)
9 months	NE (NE, NE)	96.3 (94.0, 98.7)
12 months	NE (NE, NE)	96.3 (94.0, 98.7)
18 months	NE (NE, NE)	96.3 (94.0, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	30 (16.3)	61 (15.4)
Number of Subjects Censored, n (%)	154 (83.7)	335 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.756 (0.228)
95% CI		(0.483, 1.181)
Log-rank p-value		0.260

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.0, 87.9)	86.5 (83.0, 90.0)
6 months	82.0 (76.0, 87.9)	81.7 (77.0, 86.4)
9 months	NE (NE, NE)	78.7 (73.1, 84.4)
12 months	NE (NE, NE)	78.7 (73.1, 84.4)
18 months	NE (NE, NE)	78.7 (73.1, 84.4)
Median Follow-up Time (months)	2.58	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	21 (11.4)	32 (8.1)
Number of Subjects Censored, n (%)	163 (88.6)	364 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.515 (0.290)
95% CI		(0.292, 0.910)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.9 (81.6, 92.2)	93.9 (91.5, 96.4)
6 months	86.9 (81.6, 92.2)	89.1 (85.0, 93.2)
9 months	NE (NE, NE)	87.3 (82.6, 92.0)
12 months	NE (NE, NE)	87.3 (82.6, 92.0)
18 months	NE (NE, NE)	87.3 (82.6, 92.0)
Median Follow-up Time (months)	2.60	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	27 (6.8)
Number of Subjects Censored, n (%)	181 (98.4)	369 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.921 (0.609)
95% CI		(1.188, 12.944)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.3, 100.0)	92.8 (90.2, 95.4)
6 months	98.3 (96.3, 100.0)	92.8 (90.2, 95.4)
9 months	NE (NE, NE)	92.8 (90.2, 95.4)
12 months	NE (NE, NE)	92.8 (90.2, 95.4)
18 months	NE (NE, NE)	92.8 (90.2, 95.4)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	88 (22.2)
Number of Subjects Censored, n (%)	183 (99.5)	308 (77.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.71, 6.47)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		33.405 (1.007)
95% CI		(4.645, 240.245)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	81.8 (77.8, 85.7)
6 months	99.4 (98.3, 100.0)	70.7 (64.5, 76.8)
9 months	NE (NE, NE)	67.5 (60.6, 74.4)
12 months	NE (NE, NE)	64.6 (55.9, 73.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	82 (20.7)
Number of Subjects Censored, n (%)	183 (99.5)	314 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (3.91, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		30.357 (1.007)
95% CI		(4.216, 218.592)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	83.4 (79.6, 87.2)
6 months	99.4 (98.3, 100.0)	73.0 (67.1, 79.0)
9 months	NE (NE, NE)	68.4 (61.2, 75.6)
12 months	NE (NE, NE)	65.6 (56.8, 74.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	12 (6.5)	48 (12.1)
Number of Subjects Censored, n (%)	172 (93.5)	348 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.442 (0.327)
95% CI		(0.759, 2.739)
Log-rank p-value		0.264

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.5 (89.8, 97.3)	89.7 (86.5, 92.9)
6 months	91.4 (86.0, 96.9)	84.1 (79.5, 88.7)
9 months	NE (NE, NE)	83.1 (78.2, 88.0)
12 months	NE (NE, NE)	83.1 (78.2, 88.0)
18 months	NE (NE, NE)	83.1 (78.2, 88.0)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.8)	22 (5.6)
Number of Subjects Censored, n (%)	177 (96.2)	374 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.441)
95% CI		(0.450, 2.539)
Log-rank p-value		0.841

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (93.0, 98.9)	95.3 (93.0, 97.6)
6 months	96.0 (93.0, 98.9)	92.7 (89.5, 95.9)
9 months	NE (NE, NE)	91.7 (87.9, 95.4)
12 months	NE (NE, NE)	91.7 (87.9, 95.4)
18 months	NE (NE, NE)	91.7 (87.9, 95.4)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.5)
Number of Subjects Censored, n (%)	183 (99.5)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.879 (1.057)
95% CI		(0.488, 30.817)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.6, 99.1)
6 months	97.8 (93.5, 100.0)	96.7 (94.5, 98.9)
9 months	NE (NE, NE)	96.7 (94.5, 98.9)
12 months	NE (NE, NE)	96.7 (94.5, 98.9)
18 months	NE (NE, NE)	96.7 (94.5, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	182 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.024 (0.776)
95% CI		(0.442, 9.265)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	97.6 (96.0, 99.1)
6 months	98.7 (96.8, 100.0)	96.4 (94.1, 98.7)
9 months	NE (NE, NE)	96.4 (94.1, 98.7)
12 months	NE (NE, NE)	96.4 (94.1, 98.7)
18 months	NE (NE, NE)	96.4 (94.1, 98.7)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	20 (10.9)	42 (10.6)
Number of Subjects Censored, n (%)	164 (89.1)	354 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.759 (0.276)
95% CI		(0.442, 1.305)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (84.6, 93.8)	90.1 (87.0, 93.2)
6 months	87.1 (81.0, 93.2)	87.2 (83.3, 91.2)
9 months	NE (NE, NE)	87.2 (83.3, 91.2)
12 months	NE (NE, NE)	84.4 (77.8, 91.0)
18 months	NE (NE, NE)	84.4 (77.8, 91.0)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	17 (4.3)
Number of Subjects Censored, n (%)	182 (98.9)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.091 (0.753)
95% CI		(0.707, 13.512)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	95.7 (93.6, 97.9)
6 months	98.8 (97.1, 100.0)	95.2 (92.9, 97.6)
9 months	NE (NE, NE)	95.2 (92.9, 97.6)
12 months	NE (NE, NE)	92.2 (85.8, 98.5)
18 months	NE (NE, NE)	92.2 (85.8, 98.5)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	182 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.986 (0.777)
95% CI		(0.433, 9.099)
Log-rank p-value		0.375

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.6 (96.0, 99.1)
6 months	98.9 (97.4, 100.0)	96.3 (93.9, 98.7)
9 months	NE (NE, NE)	96.3 (93.9, 98.7)
12 months	NE (NE, NE)	96.3 (93.9, 98.7)
18 months	NE (NE, NE)	96.3 (93.9, 98.7)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	22 (52.4)	39 (65.0)
Number of Subjects Censored, n (%)	20 (47.6)	21 (35.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.03, 0.72)	0.69 (0.30, 0.69)
Median (95% CI)	2.23 (0.69, NE)	1.23 (0.69, 3.55)
75% percentile (95% CI)	NE (NE, NE)	NE (3.55, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Min, Max	0.0, 13.0*	0.1, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.104 (0.296)
95% CI		(0.618, 1.973)
Log-rank p-value		0.862

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	47.4 (32.2, 62.5)	38.0 (25.6, 50.4)
6 months	47.4 (32.2, 62.5)	33.7 (21.4, 46.1)
9 months	47.4 (32.2, 62.5)	33.7 (21.4, 46.1)
12 months	47.4 (32.2, 62.5)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.89	1.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (19.0)	22 (36.7)
Number of Subjects Censored, n (%)	34 (81.0)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	0.84 (0.69, 3.12)
Median (95% CI)	NE (NE, NE)	NE (3.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 10.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.980 (0.430)
95% CI		(0.853, 4.597)
Log-rank p-value		0.144

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (68.8, 92.8)	64.7 (52.6, 76.9)
6 months	80.8 (68.8, 92.8)	62.7 (50.2, 75.1)
9 months	80.8 (68.8, 92.8)	62.7 (50.2, 75.1)
12 months	80.8 (68.8, 92.8)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.20

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	10 (23.8)	10 (16.7)
Number of Subjects Censored, n (%)	32 (76.2)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.60 (0.72, NE)	NE (1.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.688 (0.531)
95% CI		(0.243, 1.945)
Log-rank p-value		0.490

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.9 (61.2, 88.5)	83.2 (73.7, 92.7)
6 months	74.9 (61.2, 88.5)	83.2 (73.7, 92.7)
9 months	74.9 (61.2, 88.5)	83.2 (73.7, 92.7)
12 months	74.9 (61.2, 88.5)	83.2 (73.7, 92.7)
18 months	NE (NE, NE)	83.2 (73.7, 92.7)
Median Follow-up Time (months)	2.81	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	7 (11.7)
Number of Subjects Censored, n (%)	36 (85.7)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.655 (0.668)
95% CI		(0.177, 2.425)
Log-rank p-value		0.524

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (74.8, 96.2)	91.3 (83.9, 98.6)
6 months	85.5 (74.8, 96.2)	89.0 (80.7, 97.4)
9 months	85.5 (74.8, 96.2)	84.6 (73.0, 96.2)
12 months	85.5 (74.8, 96.2)	84.6 (73.0, 96.2)
18 months	NE (NE, NE)	84.6 (73.0, 96.2)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	7 (11.7)
Number of Subjects Censored, n (%)	41 (97.6)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.739 (1.074)
95% CI		(0.577, 38.898)
Log-rank p-value		0.117

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	88.3 (80.2, 96.4)
6 months	97.6 (93.0, 100.0)	88.3 (80.2, 96.4)
9 months	97.6 (93.0, 100.0)	88.3 (80.2, 96.4)
12 months	97.6 (93.0, 100.0)	88.3 (80.2, 96.4)
18 months	NE (NE, NE)	88.3 (80.2, 96.4)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	1 (1.7)
Number of Subjects Censored, n (%)	39 (92.9)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.234 (1.179)
95% CI		(0.023, 2.366)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
6 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
9 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
12 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
18 months	NE (NE, NE)	98.1 (94.6, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	2 (3.3)
Number of Subjects Censored, n (%)	38 (90.5)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (0.886)
95% CI		(0.046, 1.486)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (81.6, 99.4)	96.7 (92.1, 100.0)
6 months	90.5 (81.6, 99.4)	96.7 (92.1, 100.0)
9 months	90.5 (81.6, 99.4)	96.7 (92.1, 100.0)
12 months	90.5 (81.6, 99.4)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
9 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
12 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
18 months	NE (NE, NE)	97.7 (93.3, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	42 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.343

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	19 (45.2)	42 (70.0)
Number of Subjects Censored, n (%)	23 (54.8)	18 (30.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.07, 1.61)	0.46 (0.26, 0.69)
Median (95% CI)	5.59 (1.38, NE)	0.99 (0.69, 3.58)
75% percentile (95% CI)	NE (5.59, NE)	NE (3.58, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.717 (0.307)
95% CI		(0.941, 3.131)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.5 (43.2, 73.7)	39.9 (27.4, 52.3)
6 months	NE (NE, NE)	28.7 (16.4, 41.0)
9 months	NE (NE, NE)	25.1 (12.5, 37.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	0.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	16 (26.7)
Number of Subjects Censored, n (%)	38 (90.5)	44 (73.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.895 (0.645)
95% CI		(1.101, 13.784)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (81.1, 99.3)	78.3 (67.9, 88.8)
6 months	90.2 (81.1, 99.3)	73.0 (60.8, 85.1)
9 months	90.2 (81.1, 99.3)	68.4 (54.1, 82.7)
12 months	90.2 (81.1, 99.3)	68.4 (54.1, 82.7)
18 months	NE (NE, NE)	68.4 (54.1, 82.7)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	7 (11.7)
Number of Subjects Censored, n (%)	38 (90.5)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.874 (0.716)
95% CI		(0.215, 3.557)
Log-rank p-value		0.720

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (81.5, 99.3)	89.5 (81.6, 97.5)
6 months	90.4 (81.5, 99.3)	87.3 (78.4, 96.2)
9 months	90.4 (81.5, 99.3)	87.3 (78.4, 96.2)
12 months	90.4 (81.5, 99.3)	87.3 (78.4, 96.2)
18 months	NE (NE, NE)	87.3 (78.4, 96.2)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	7 (16.7)	12 (20.0)
Number of Subjects Censored, n (%)	35 (83.3)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	6.41 (2.92, NE)
Median (95% CI)	NE (NE, NE)	12.25 (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.311 (0.565)
95% CI		(0.433, 3.970)
Log-rank p-value		0.714

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.7 (71.0, 94.4)	86.2 (77.2, 95.1)
6 months	82.7 (71.0, 94.4)	84.0 (74.3, 93.7)
9 months	82.7 (71.0, 94.4)	74.6 (59.7, 89.6)
12 months	82.7 (71.0, 94.4)	74.6 (59.7, 89.6)
18 months	NE (NE, NE)	37.3 (0.0, 89.6)
Median Follow-up Time (months)	2.83	4.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.9)	9 (15.0)
Number of Subjects Censored, n (%)	37 (88.1)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (2.92, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.083 (0.647)
95% CI		(0.305, 3.848)
Log-rank p-value		0.850

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (78.3, 97.9)	85.5 (76.2, 94.9)
6 months	88.1 (78.3, 97.9)	82.0 (70.7, 93.2)
9 months	88.1 (78.3, 97.9)	82.0 (70.7, 93.2)
12 months	88.1 (78.3, 97.9)	82.0 (70.7, 93.2)
18 months	NE (NE, NE)	82.0 (70.7, 93.2)
Median Follow-up Time (months)	2.83	3.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	9 (15.0)
Number of Subjects Censored, n (%)	41 (97.6)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.33, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.889 (1.061)
95% CI		(0.860, 55.159)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	84.9 (75.8, 94.0)
6 months	97.6 (92.8, 100.0)	84.9 (75.8, 94.0)
9 months	97.6 (92.8, 100.0)	84.9 (75.8, 94.0)
12 months	97.6 (92.8, 100.0)	84.9 (75.8, 94.0)
18 months	NE (NE, NE)	84.9 (75.8, 94.0)
Median Follow-up Time (months)	2.83	4.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	8 (13.3)
Number of Subjects Censored, n (%)	40 (95.2)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.884 (0.837)
95% CI		(0.559, 14.879)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	88.3 (80.2, 96.5)
6 months	95.1 (88.5, 100.0)	86.2 (77.3, 95.1)
9 months	95.1 (88.5, 100.0)	86.2 (77.3, 95.1)
12 months	95.1 (88.5, 100.0)	86.2 (77.3, 95.1)
18 months	NE (NE, NE)	86.2 (77.3, 95.1)
Median Follow-up Time (months)	2.83	4.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	4 (6.7)
Number of Subjects Censored, n (%)	39 (92.9)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	1.5*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.338 (0.898)
95% CI		(0.058, 1.964)
Log-rank p-value		0.182

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	94.7 (88.9, 100.0)
6 months	NE (NE, NE)	92.3 (85.0, 99.7)
9 months	NE (NE, NE)	92.3 (85.0, 99.7)
12 months	NE (NE, NE)	92.3 (85.0, 99.7)
18 months	NE (NE, NE)	92.3 (85.0, 99.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	42 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.426

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
18 months	NE (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	5 (8.3)
Number of Subjects Censored, n (%)	42 (100.0)	55 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.189

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
6 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
9 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
12 months	100.0 (100.0, 100.0)	91.6 (84.5, 98.6)
18 months	NE (NE, NE)	91.6 (84.5, 98.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	0
Number of Subjects Censored, n (%)	40 (95.2)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
6 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
9 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
12 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.584

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	14 (33.3)	22 (36.7)
Number of Subjects Censored, n (%)	28 (66.7)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.53, NE)	1.87 (0.72, 3.58)
Median (95% CI)	10.18 (NE, NE)	NE (3.58, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.3, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.890 (0.381)
95% CI		(0.422, 1.876)
Log-rank p-value		0.999

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.0 (55.1, 83.0)	65.4 (53.1, 77.8)
6 months	69.0 (55.1, 83.0)	61.3 (48.4, 74.1)
9 months	69.0 (55.1, 83.0)	61.3 (48.4, 74.1)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.66	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (19.0)	10 (16.7)
Number of Subjects Censored, n (%)	34 (81.0)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.560 (0.506)
95% CI		(0.208, 1.511)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (68.4, 92.7)	84.1 (74.6, 93.7)
6 months	80.6 (68.4, 92.7)	82.0 (71.8, 92.2)
9 months	80.6 (68.4, 92.7)	82.0 (71.8, 92.2)
12 months	80.6 (68.4, 92.7)	82.0 (71.8, 92.2)
18 months	NE (NE, NE)	82.0 (71.8, 92.2)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
18 months	NE (NE, NE)	94.8 (89.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	42 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.436

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
9 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
12 months	100.0 (100.0, 100.0)	96.6 (92.0, 100.0)
18 months	NE (NE, NE)	96.6 (92.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.176

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	85.9 (65.6, 100.0)
12 months	100.0 (100.0, 100.0)	85.9 (65.6, 100.0)
18 months	NE (NE, NE)	85.9 (65.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
9 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
12 months	100.0 (100.0, 100.0)	98.2 (94.7, 100.0)
18 months	NE (NE, NE)	98.2 (94.7, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
9 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
12 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
18 months	NE (NE, NE)	95.0 (89.4, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	2 (3.3)
Number of Subjects Censored, n (%)	41 (97.6)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.436

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	96.6 (92.0, 100.0)
6 months	97.6 (93.0, 100.0)	96.6 (92.0, 100.0)
9 months	97.6 (93.0, 100.0)	96.6 (92.0, 100.0)
12 months	97.6 (93.0, 100.0)	96.6 (92.0, 100.0)
18 months	NE (NE, NE)	96.6 (92.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	2 (3.3)
Number of Subjects Censored, n (%)	41 (97.6)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.033 (1.296)
95% CI		(0.082, 13.091)
Log-rank p-value		0.894

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	98.3 (95.1, 100.0)
6 months	97.6 (93.0, 100.0)	98.3 (95.1, 100.0)
9 months	97.6 (93.0, 100.0)	87.4 (67.0, 100.0)
12 months	97.6 (93.0, 100.0)	87.4 (67.0, 100.0)
18 months	NE (NE, NE)	87.4 (67.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	2 (3.3)
Number of Subjects Censored, n (%)	39 (92.9)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.7, 10.2	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.637 (1.078)
95% CI		(0.077, 5.269)
Log-rank p-value		0.788

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	96.5 (91.8, 100.0)
6 months	95.2 (88.8, 100.0)	96.5 (91.8, 100.0)
9 months	95.2 (88.8, 100.0)	96.5 (91.8, 100.0)
12 months	0.0 (NE, NE)	96.5 (91.8, 100.0)
18 months	0.0 (NE, NE)	96.5 (91.8, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	14 (33.3)	22 (36.7)
Number of Subjects Censored, n (%)	28 (66.7)	38 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.69, NE)	1.46 (0.69, 6.44)
Median (95% CI)	5.59 (5.59, NE)	16.79 (5.78, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (16.79, NE)
Min, Max	0.0, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.994 (0.402)
95% CI		(0.452, 2.186)
Log-rank p-value		0.963

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.0 (55.1, 83.0)	67.3 (55.1, 79.5)
6 months	NE (NE, NE)	63.1 (49.1, 77.0)
9 months	NE (NE, NE)	58.6 (43.1, 74.0)
12 months	NE (NE, NE)	58.6 (43.1, 74.0)
18 months	NE (NE, NE)	29.3 (0.0, 70.6)
Median Follow-up Time (months)	2.79	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.9)	7 (11.7)
Number of Subjects Censored, n (%)	37 (88.1)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (2.66, NE)	NE (6.87, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.556 (0.699)
95% CI		(0.141, 2.188)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (79.4, 99.4)	88.8 (80.3, 97.4)
6 months	NE (NE, NE)	88.8 (80.3, 97.4)
9 months	NE (NE, NE)	82.9 (69.2, 96.7)
12 months	NE (NE, NE)	82.9 (69.2, 96.7)
18 months	NE (NE, NE)	82.9 (69.2, 96.7)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	9 (15.0)
Number of Subjects Censored, n (%)	39 (92.9)	51 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (2.89, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.561 (0.854)
95% CI		(0.292, 8.331)
Log-rank p-value		0.533

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	86.0 (76.9, 95.1)
6 months	NE (NE, NE)	81.7 (69.7, 93.6)
9 months	NE (NE, NE)	81.7 (69.7, 93.6)
12 months	NE (NE, NE)	81.7 (69.7, 93.6)
18 months	NE (NE, NE)	81.7 (69.7, 93.6)
Median Follow-up Time (months)	2.83	4.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	6 (10.0)
Number of Subjects Censored, n (%)	39 (92.9)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.560 (0.870)
95% CI		(0.284, 8.577)
Log-rank p-value		0.622

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	89.5 (81.4, 97.5)
6 months	NE (NE, NE)	89.5 (81.4, 97.5)
9 months	NE (NE, NE)	89.5 (81.4, 97.5)
12 months	NE (NE, NE)	89.5 (81.4, 97.5)
18 months	NE (NE, NE)	89.5 (81.4, 97.5)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	4 (6.7)
Number of Subjects Censored, n (%)	39 (92.9)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.680 (0.847)
95% CI		(0.129, 3.572)
Log-rank p-value		0.694

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (85.1, 100.0)	93.1 (86.6, 99.6)
6 months	92.9 (85.1, 100.0)	93.1 (86.6, 99.6)
9 months	92.9 (85.1, 100.0)	93.1 (86.6, 99.6)
12 months	92.9 (85.1, 100.0)	93.1 (86.6, 99.6)
18 months	NE (NE, NE)	93.1 (86.6, 99.6)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	6 (10.0)
Number of Subjects Censored, n (%)	42 (100.0)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.4 (84.2, 98.6)
6 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
9 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
12 months	100.0 (100.0, 100.0)	87.9 (78.2, 97.6)
18 months	NE (NE, NE)	87.9 (78.2, 97.6)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	6 (10.0)
Number of Subjects Censored, n (%)	39 (92.9)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.319 (1.174)
95% CI		(0.232, 23.144)
Log-rank p-value		0.380

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.7 (84.8, 100.0)	93.2 (86.7, 99.6)
6 months	92.7 (84.8, 100.0)	86.1 (74.6, 97.6)
9 months	92.7 (84.8, 100.0)	86.1 (74.6, 97.6)
12 months	92.7 (84.8, 100.0)	86.1 (74.6, 97.6)
18 months	NE (NE, NE)	86.1 (74.6, 97.6)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	2 (3.3)
Number of Subjects Censored, n (%)	40 (95.2)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 7.4	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.256 (1.339)
95% CI		(0.019, 3.526)
Log-rank p-value		0.350

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	96.7 (92.1, 100.0)
6 months	97.6 (93.0, 100.0)	96.7 (92.1, 100.0)
9 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
12 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
18 months	0.0 (NE, NE)	96.7 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
6 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
9 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
12 months	100.0 (100.0, 100.0)	94.5 (88.4, 100.0)
18 months	NE (NE, NE)	94.5 (88.4, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	12 (28.6)	23 (38.3)
Number of Subjects Censored, n (%)	30 (71.4)	37 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.33, NE)	1.38 (0.72, 3.25)
Median (95% CI)	NE (NE, NE)	NE (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.178 (0.383)
95% CI		(0.556, 2.493)
Log-rank p-value		0.730

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (57.3, 84.9)	66.2 (54.2, 78.3)
6 months	71.1 (57.3, 84.9)	64.1 (51.7, 76.5)
9 months	71.1 (57.3, 84.9)	56.1 (41.1, 71.1)
12 months	71.1 (57.3, 84.9)	56.1 (41.1, 71.1)
18 months	NE (NE, NE)	56.1 (41.1, 71.1)
Median Follow-up Time (months)	2.79	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	7 (11.7)
Number of Subjects Censored, n (%)	38 (90.5)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.242 (0.645)
95% CI		(0.351, 4.399)
Log-rank p-value		0.727

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (81.2, 99.3)	88.2 (79.9, 96.4)
6 months	90.3 (81.2, 99.3)	88.2 (79.9, 96.4)
9 months	90.3 (81.2, 99.3)	88.2 (79.9, 96.4)
12 months	90.3 (81.2, 99.3)	88.2 (79.9, 96.4)
18 months	NE (NE, NE)	88.2 (79.9, 96.4)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	6 (10.0)
Number of Subjects Censored, n (%)	36 (85.7)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.05, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.545 (0.650)
95% CI		(0.152, 1.946)
Log-rank p-value		0.373

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (74.9, 96.3)	93.3 (87.0, 99.6)
6 months	85.6 (74.9, 96.3)	91.1 (83.6, 98.6)
9 months	85.6 (74.9, 96.3)	86.3 (74.8, 97.9)
12 months	85.6 (74.9, 96.3)	86.3 (74.8, 97.9)
18 months	NE (NE, NE)	86.3 (74.8, 97.9)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.9)	7 (11.7)
Number of Subjects Censored, n (%)	37 (88.1)	53 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.25, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.771 (0.618)
95% CI		(0.230, 2.588)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (78.3, 97.9)	90.0 (82.4, 97.6)
6 months	88.1 (78.3, 97.9)	90.0 (82.4, 97.6)
9 months	88.1 (78.3, 97.9)	85.2 (73.7, 96.8)
12 months	88.1 (78.3, 97.9)	85.2 (73.7, 96.8)
18 months	NE (NE, NE)	85.2 (73.7, 96.8)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.314

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
9 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
12 months	100.0 (100.0, 100.0)	94.8 (89.0, 100.0)
18 months	NE (NE, NE)	94.8 (89.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.1, 100.0)
18 months	NE (NE, NE)	98.3 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (19.0)	24 (40.0)
Number of Subjects Censored, n (%)	34 (81.0)	36 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.05, NE)	0.94 (0.53, 2.07)
Median (95% CI)	NE (NE, NE)	NE (2.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.490 (0.440)
95% CI		(1.051, 5.899)
Log-rank p-value		0.040

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.9 (69.0, 92.8)	59.2 (46.6, 71.8)
6 months	NE (NE, NE)	59.2 (46.6, 71.8)
9 months	NE (NE, NE)	59.2 (46.6, 71.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	23 (38.3)
Number of Subjects Censored, n (%)	36 (85.7)	37 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.41, NE)	1.30 (0.62, 2.50)
Median (95% CI)	NE (NE, NE)	NE (2.50, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.384 (0.503)
95% CI		(1.263, 9.069)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (74.7, 96.2)	60.6 (47.9, 73.2)
6 months	NE (NE, NE)	60.6 (47.9, 73.2)
9 months	NE (NE, NE)	60.6 (47.9, 73.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	10 (23.8)	28 (46.7)
Number of Subjects Censored, n (%)	32 (76.2)	32 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.35, NE)	0.99 (0.33, 1.77)
Median (95% CI)	5.59 (3.71, NE)	6.74 (1.77, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (9.76, NE)
Min, Max	0.0, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.963 (0.406)
95% CI		(0.885, 4.353)
Log-rank p-value		0.106

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.8 (67.2, 92.4)	57.7 (45.0, 70.3)
6 months	NE (NE, NE)	54.3 (40.7, 67.8)
9 months	NE (NE, NE)	49.3 (33.9, 64.7)
12 months	NE (NE, NE)	32.9 (4.6, 61.1)
18 months	NE (NE, NE)	32.9 (4.6, 61.1)
Median Follow-up Time (months)	2.83	2.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	8 (13.3)
Number of Subjects Censored, n (%)	40 (95.2)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.452 (1.091)
95% CI		(0.524, 37.816)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	89.9 (82.3, 97.6)
6 months	95.1 (88.5, 100.0)	86.7 (77.1, 96.3)
9 months	95.1 (88.5, 100.0)	81.9 (69.0, 94.8)
12 months	95.1 (88.5, 100.0)	81.9 (69.0, 94.8)
18 months	NE (NE, NE)	81.9 (69.0, 94.8)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	10 (16.7)
Number of Subjects Censored, n (%)	40 (95.2)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (2.79, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.693 (0.802)
95% CI		(0.560, 12.964)
Log-rank p-value		0.241

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	84.7 (75.4, 93.9)
6 months	NE (NE, NE)	84.7 (75.4, 93.9)
9 months	NE (NE, NE)	79.0 (65.3, 92.8)
12 months	NE (NE, NE)	79.0 (65.3, 92.8)
18 months	NE (NE, NE)	79.0 (65.3, 92.8)
Median Follow-up Time (months)	2.83	4.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	3 (5.0)
Number of Subjects Censored, n (%)	41 (97.6)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.332 (1.176)
95% CI		(0.233, 23.360)
Log-rank p-value		0.464

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.2, 100.0)
6 months	90.0 (71.4, 100.0)	94.8 (89.2, 100.0)
9 months	90.0 (71.4, 100.0)	94.8 (89.2, 100.0)
12 months	90.0 (71.4, 100.0)	94.8 (89.2, 100.0)
18 months	NE (NE, NE)	94.8 (89.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	4 (6.7)
Number of Subjects Censored, n (%)	41 (97.6)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.780 (1.133)
95% CI		(0.193, 16.408)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	93.1 (86.6, 99.6)
6 months	97.6 (92.8, 100.0)	93.1 (86.6, 99.6)
9 months	97.6 (92.8, 100.0)	93.1 (86.6, 99.6)
12 months	97.6 (92.8, 100.0)	93.1 (86.6, 99.6)
18 months	NE (NE, NE)	93.1 (86.6, 99.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	3 (5.0)
Number of Subjects Censored, n (%)	41 (97.6)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.617 (1.352)
95% CI		(0.044, 8.728)
Log-rank p-value		0.911

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	98.3 (94.9, 100.0)
6 months	97.6 (93.0, 100.0)	98.3 (94.9, 100.0)
9 months	97.6 (93.0, 100.0)	85.1 (67.5, 100.0)
12 months	97.6 (93.0, 100.0)	85.1 (67.5, 100.0)
18 months	NE (NE, NE)	85.1 (67.5, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	2 (3.3)
Number of Subjects Censored, n (%)	42 (100.0)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.343

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
12 months	100.0 (100.0, 100.0)	96.6 (92.1, 100.0)
18 months	NE (NE, NE)	96.6 (92.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	27 (45.0)
Number of Subjects Censored, n (%)	36 (85.7)	33 (55.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	1.05 (0.53, 1.61)
Median (95% CI)	NE (3.71, NE)	7.39 (1.61, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.39, NE)
Min, Max	0.7, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.051 (0.460)
95% CI		(1.239, 7.514)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (77.6, 97.8)	59.5 (47.0, 72.1)
6 months	75.2 (50.8, 99.5)	54.0 (40.5, 67.5)
9 months	75.2 (50.8, 99.5)	43.2 (21.4, 65.0)
12 months	75.2 (50.8, 99.5)	43.2 (21.4, 65.0)
18 months	NE (NE, NE)	43.2 (21.4, 65.0)
Median Follow-up Time (months)	2.83	2.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	20 (33.3)
Number of Subjects Censored, n (%)	41 (97.6)	40 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.66, 7.39)
Median (95% CI)	NE (NE, NE)	NE (5.19, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		12.010 (1.031)
95% CI		(1.592, 90.601)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.5, 100.0)	73.2 (62.0, 84.5)
6 months	97.4 (92.5, 100.0)	62.1 (46.4, 77.9)
9 months	97.4 (92.5, 100.0)	51.8 (29.1, 74.5)
12 months	97.4 (92.5, 100.0)	51.8 (29.1, 74.5)
18 months	NE (NE, NE)	51.8 (29.1, 74.5)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	0
Number of Subjects Censored, n (%)	41 (97.6)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.280

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
6 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
9 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
12 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	0
Number of Subjects Censored, n (%)	39 (92.9)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.4, 100.0)	100.0 (100.0, 100.0)
6 months	84.5 (64.1, 100.0)	100.0 (100.0, 100.0)
9 months	84.5 (64.1, 100.0)	100.0 (100.0, 100.0)
12 months	84.5 (64.1, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	9 (21.4)	14 (23.3)
Number of Subjects Censored, n (%)	33 (78.6)	46 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.976 (0.457)
95% CI		(0.398, 2.390)
Log-rank p-value		0.885

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.6 (66.2, 91.0)	78.2 (67.7, 88.7)
6 months	78.6 (66.2, 91.0)	75.2 (63.5, 86.8)
9 months	78.6 (66.2, 91.0)	75.2 (63.5, 86.8)
12 months	78.6 (66.2, 91.0)	75.2 (63.5, 86.8)
18 months	NE (NE, NE)	75.2 (63.5, 86.8)
Median Follow-up Time (months)	2.81	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	11 (18.3)
Number of Subjects Censored, n (%)	40 (95.2)	49 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.379 (1.060)
95% CI		(0.925, 58.861)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	83.3 (73.9, 92.8)
6 months	95.2 (88.8, 100.0)	80.4 (69.6, 91.1)
9 months	95.2 (88.8, 100.0)	80.4 (69.6, 91.1)
12 months	95.2 (88.8, 100.0)	80.4 (69.6, 91.1)
18 months	NE (NE, NE)	80.4 (69.6, 91.1)
Median Follow-up Time (months)	2.83	3.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	0
Number of Subjects Censored, n (%)	40 (95.2)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.073

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
6 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
9 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
12 months	95.2 (88.8, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	4 (6.7)
Number of Subjects Censored, n (%)	42 (100.0)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.194

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
6 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
9 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
12 months	100.0 (100.0, 100.0)	93.2 (86.7, 99.6)
18 months	NE (NE, NE)	93.2 (86.7, 99.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	14 (23.3)
Number of Subjects Censored, n (%)	38 (90.5)	46 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.025 (0.650)
95% CI		(0.845, 10.820)
Log-rank p-value		0.092

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (81.2, 99.3)	79.9 (69.7, 90.1)
6 months	90.3 (81.2, 99.3)	74.9 (63.3, 86.6)
9 months	90.3 (81.2, 99.3)	74.9 (63.3, 86.6)
12 months	90.3 (81.2, 99.3)	74.9 (63.3, 86.6)
18 months	NE (NE, NE)	74.9 (63.3, 86.6)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	11 (18.3)
Number of Subjects Censored, n (%)	39 (92.9)	49 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.847 (0.784)
95% CI		(0.827, 17.894)
Log-rank p-value		0.084

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.7 (84.7, 100.0)	84.8 (75.6, 94.0)
6 months	92.7 (84.7, 100.0)	79.9 (69.0, 90.8)
9 months	92.7 (84.7, 100.0)	79.9 (69.0, 90.8)
12 months	92.7 (84.7, 100.0)	79.9 (69.0, 90.8)
18 months	NE (NE, NE)	79.9 (69.0, 90.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	8 (19.0)	15 (25.0)
Number of Subjects Censored, n (%)	34 (81.0)	45 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.95, NE)	5.68 (1.87, 17.48)
Median (95% CI)	NE (3.71, NE)	17.48 (6.54, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.942 (0.505)
95% CI		(0.351, 2.533)
Log-rank p-value		0.820

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (74.5, 96.2)	84.9 (75.8, 94.0)
6 months	63.2 (35.1, 91.3)	71.2 (56.2, 86.3)
9 months	63.2 (35.1, 91.3)	65.7 (48.4, 83.0)
12 months	63.2 (35.1, 91.3)	65.7 (48.4, 83.0)
18 months	NE (NE, NE)	32.9 (0.0, 79.2)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	2 (3.3)
Number of Subjects Censored, n (%)	40 (95.2)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.141 (1.419)
95% CI		(0.009, 2.283)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	98.3 (95.0, 100.0)
6 months	87.9 (69.2, 100.0)	93.8 (84.7, 100.0)
9 months	87.9 (69.2, 100.0)	93.8 (84.7, 100.0)
12 months	87.9 (69.2, 100.0)	93.8 (84.7, 100.0)
18 months	NE (NE, NE)	93.8 (84.7, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	2 (4.8)	3 (5.0)
Number of Subjects Censored, n (%)	40 (95.2)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (6.54, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.915 (0.986)
95% CI		(0.132, 6.326)
Log-rank p-value		0.817

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	98.3 (95.1, 100.0)
6 months	85.4 (62.7, 100.0)	96.0 (90.6, 100.0)
9 months	85.4 (62.7, 100.0)	90.4 (78.5, 100.0)
12 months	85.4 (62.7, 100.0)	90.4 (78.5, 100.0)
18 months	NE (NE, NE)	90.4 (78.5, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	0
Number of Subjects Censored, n (%)	41 (97.6)	60 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.141

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
6 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
9 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
12 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	6 (10.0)
Number of Subjects Censored, n (%)	36 (85.7)	54 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.757 (0.597)
95% CI		(0.235, 2.442)
Log-rank p-value		0.619

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (72.3, 95.9)	89.9 (82.3, 97.6)
6 months	84.1 (72.3, 95.9)	89.9 (82.3, 97.6)
9 months	84.1 (72.3, 95.9)	89.9 (82.3, 97.6)
12 months	84.1 (72.3, 95.9)	89.9 (82.3, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	6 (14.3)	4 (6.7)
Number of Subjects Censored, n (%)	36 (85.7)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	1.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.728)
95% CI		(0.081, 1.411)
Log-rank p-value		0.110

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (72.3, 95.9)	94.9 (89.4, 100.0)
6 months	84.1 (72.3, 95.9)	94.9 (89.4, 100.0)
9 months	84.1 (72.3, 95.9)	94.9 (89.4, 100.0)
12 months	84.1 (72.3, 95.9)	94.9 (89.4, 100.0)
18 months	NE (NE, NE)	47.5 (0.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.122

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
9 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
12 months	100.0 (100.0, 100.0)	95.0 (89.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	12 (20.0)
Number of Subjects Censored, n (%)	42 (100.0)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.1 (74.5, 93.7)
6 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
9 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
12 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	12 (20.0)
Number of Subjects Censored, n (%)	42 (100.0)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.1 (74.5, 93.7)
6 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
9 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
12 months	100.0 (100.0, 100.0)	73.2 (58.5, 88.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	10 (16.7)
Number of Subjects Censored, n (%)	38 (90.5)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.129 (0.703)
95% CI		(0.285, 4.480)
Log-rank p-value		0.838

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (80.2, 99.3)	84.4 (75.0, 93.8)
6 months	89.8 (80.2, 99.3)	81.8 (71.3, 92.2)
9 months	89.8 (80.2, 99.3)	81.8 (71.3, 92.2)
12 months	89.8 (80.2, 99.3)	81.8 (71.3, 92.2)
18 months	NE (NE, NE)	81.8 (71.3, 92.2)
Median Follow-up Time (months)	2.83	3.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	4 (6.7)
Number of Subjects Censored, n (%)	38 (90.5)	56 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.230 (0.960)
95% CI		(0.035, 1.513)
Log-rank p-value		0.121

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (80.2, 99.3)	92.7 (85.7, 99.6)
6 months	89.8 (80.2, 99.3)	92.7 (85.7, 99.6)
9 months	89.8 (80.2, 99.3)	92.7 (85.7, 99.6)
12 months	89.8 (80.2, 99.3)	92.7 (85.7, 99.6)
18 months	NE (NE, NE)	92.7 (85.7, 99.6)
Median Follow-up Time (months)	2.83	4.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	1 (1.7)
Number of Subjects Censored, n (%)	42 (100.0)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.343

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (95.0, 100.0)
18 months	NE (NE, NE)	98.3 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	8 (13.3)
Number of Subjects Censored, n (%)	39 (92.9)	52 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.072 (0.741)
95% CI		(0.251, 4.582)
Log-rank p-value		0.927

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.7 (84.8, 100.0)	91.0 (83.4, 98.6)
6 months	92.7 (84.8, 100.0)	84.0 (72.1, 96.0)
9 months	92.7 (84.8, 100.0)	77.0 (59.9, 94.1)
12 months	92.7 (84.8, 100.0)	77.0 (59.9, 94.1)
18 months	NE (NE, NE)	77.0 (59.9, 94.1)
Median Follow-up Time (months)	2.83	4.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	2 (3.3)
Number of Subjects Censored, n (%)	41 (97.6)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.352 (1.418)
95% CI		(0.022, 5.661)
Log-rank p-value		0.478

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.5, 100.0)	97.8 (93.6, 100.0)
6 months	97.4 (92.5, 100.0)	93.4 (84.0, 100.0)
9 months	97.4 (92.5, 100.0)	93.4 (84.0, 100.0)
12 months	97.4 (92.5, 100.0)	93.4 (84.0, 100.0)
18 months	NE (NE, NE)	93.4 (84.0, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	0	3 (5.0)
Number of Subjects Censored, n (%)	42 (100.0)	57 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	96.7 (92.1, 100.0)
9 months	100.0 (100.0, 100.0)	89.2 (74.6, 100.0)
12 months	100.0 (100.0, 100.0)	89.2 (74.6, 100.0)
18 months	NE (NE, NE)	89.2 (74.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	107 (56.9)	276 (69.7)
Number of Subjects Censored, n (%)	81 (43.1)	120 (30.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.72)	0.36 (0.26, 0.49)
Median (95% CI)	1.87 (1.28, 2.76)	1.25 (0.92, 1.61)
75% percentile (95% CI)	NE (4.70, NE)	5.65 (4.47, 7.39)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.230 (0.115)
95% CI		(0.982, 1.542)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	42.6 (35.1, 50.1)	37.7 (32.9, 42.6)
6 months	31.2 (18.9, 43.5)	24.3 (19.0, 29.5)
9 months	NE (NE, NE)	17.5 (11.1, 23.9)
12 months	NE (NE, NE)	17.5 (11.1, 23.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.61	1.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	44 (23.4)	133 (33.6)
Number of Subjects Censored, n (%)	144 (76.6)	263 (66.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (1.28, NE)	1.41 (0.92, 2.53)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.334 (0.175)
95% CI		(0.946, 1.881)
Log-rank p-value		0.107

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.0 (69.6, 82.5)	68.2 (63.4, 72.9)
6 months	68.0 (55.1, 80.8)	63.9 (58.7, 69.1)
9 months	NE (NE, NE)	60.9 (54.4, 67.5)
12 months	NE (NE, NE)	60.9 (54.4, 67.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	27 (14.4)	81 (20.5)
Number of Subjects Censored, n (%)	161 (85.6)	315 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.284 (0.224)
95% CI		(0.827, 1.993)
Log-rank p-value		0.296

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.7 (79.4, 90.1)	81.2 (77.3, 85.1)
6 months	84.7 (79.4, 90.1)	77.5 (72.9, 82.2)
9 months	NE (NE, NE)	75.1 (69.5, 80.7)
12 months	NE (NE, NE)	75.1 (69.5, 80.7)
18 months	NE (NE, NE)	75.1 (69.5, 80.7)
Median Follow-up Time (months)	2.56	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	17 (9.0)	39 (9.8)
Number of Subjects Censored, n (%)	171 (91.0)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.919 (0.297)
95% CI		(0.514, 1.646)
Log-rank p-value		0.730

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (85.6, 94.9)	91.7 (88.9, 94.5)
6 months	84.2 (72.0, 96.4)	89.0 (85.4, 92.6)
9 months	NE (NE, NE)	88.1 (84.2, 92.1)
12 months	NE (NE, NE)	82.6 (71.5, 93.7)
18 months	NE (NE, NE)	82.6 (71.5, 93.7)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	55 (13.9)
Number of Subjects Censored, n (%)	183 (97.3)	341 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.678 (0.469)
95% CI		(1.866, 11.732)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.5, 99.6)	87.6 (84.3, 90.9)
6 months	97.1 (94.5, 99.6)	85.6 (81.8, 89.3)
9 months	NE (NE, NE)	82.9 (77.7, 88.1)
12 months	NE (NE, NE)	82.9 (77.7, 88.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	25 (13.3)	26 (6.6)
Number of Subjects Censored, n (%)	163 (86.7)	370 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.291)
95% CI		(0.192, 0.600)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (80.5, 91.3)	95.7 (93.7, 97.8)
6 months	81.5 (73.5, 89.4)	91.0 (87.4, 94.7)
9 months	NE (NE, NE)	91.0 (87.4, 94.7)
12 months	NE (NE, NE)	91.0 (87.4, 94.7)
18 months	NE (NE, NE)	83.4 (68.8, 98.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	13 (6.9)	20 (5.1)
Number of Subjects Censored, n (%)	175 (93.1)	376 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.590 (0.365)
95% CI		(0.288, 1.207)
Log-rank p-value		0.152

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (88.4, 96.5)	95.2 (93.0, 97.4)
6 months	92.5 (88.4, 96.5)	95.2 (93.0, 97.4)
9 months	NE (NE, NE)	92.9 (87.9, 97.9)
12 months	NE (NE, NE)	89.4 (81.3, 97.6)
18 months	NE (NE, NE)	89.4 (81.3, 97.6)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	15 (3.8)
Number of Subjects Censored, n (%)	183 (97.3)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.870 (0.547)
95% CI		(0.298, 2.543)
Log-rank p-value		0.733

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.6, 99.6)	97.9 (96.4, 99.3)
6 months	97.1 (94.6, 99.6)	96.3 (94.0, 98.6)
9 months	NE (NE, NE)	94.8 (91.1, 98.5)
12 months	NE (NE, NE)	86.2 (76.2, 96.2)
18 months	NE (NE, NE)	86.2 (76.2, 96.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	9 (2.3)
Number of Subjects Censored, n (%)	184 (97.9)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.653 (0.622)
95% CI		(0.193, 2.211)
Log-rank p-value		0.434

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.4, 100.0)	98.3 (96.9, 99.6)
6 months	97.2 (94.4, 100.0)	97.1 (95.1, 99.2)
9 months	NE (NE, NE)	95.6 (92.0, 99.2)
12 months	NE (NE, NE)	95.6 (92.0, 99.2)
18 months	NE (NE, NE)	95.6 (92.0, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	10 (2.5)
Number of Subjects Censored, n (%)	186 (98.9)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.843 (0.795)
95% CI		(0.388, 8.750)
Log-rank p-value		0.402

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	98.2 (96.9, 99.5)
6 months	98.9 (97.4, 100.0)	96.9 (94.6, 99.2)
9 months	NE (NE, NE)	94.7 (90.0, 99.5)
12 months	NE (NE, NE)	94.7 (90.0, 99.5)
18 months	NE (NE, NE)	94.7 (90.0, 99.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	112 (59.6)	267 (67.4)
Number of Subjects Censored, n (%)	76 (40.4)	129 (32.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.36, 0.69)	0.53 (0.46, 0.69)
Median (95% CI)	1.54 (0.95, 1.94)	1.58 (1.05, 1.91)
75% percentile (95% CI)	5.36 (3.75, NE)	5.95 (4.90, 7.79)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.967 (0.115)
95% CI		(0.772, 1.212)
Log-rank p-value		0.851

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	36.6 (28.6, 44.7)	38.4 (33.4, 43.3)
6 months	14.3 (0.0, 34.9)	24.4 (18.6, 30.2)
9 months	NE (NE, NE)	17.0 (10.1, 23.8)
12 months	NE (NE, NE)	13.6 (5.5, 21.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.22	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	20 (10.6)	94 (23.7)
Number of Subjects Censored, n (%)	168 (89.4)	302 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.89, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.941 (0.249)
95% CI		(1.191, 3.163)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.1 (84.5, 93.6)	79.2 (75.1, 83.3)
6 months	89.1 (84.5, 93.6)	72.1 (66.4, 77.7)
9 months	NE (NE, NE)	68.5 (61.9, 75.2)
12 months	NE (NE, NE)	62.3 (49.2, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	38 (20.2)	72 (18.2)
Number of Subjects Censored, n (%)	150 (79.8)	324 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.87, NE)	9.00 (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.635 (0.207)
95% CI		(0.423, 0.952)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.2 (73.1, 85.2)	84.5 (80.7, 88.2)
6 months	74.5 (64.0, 85.0)	78.4 (73.3, 83.5)
9 months	NE (NE, NE)	75.0 (68.8, 81.3)
12 months	NE (NE, NE)	70.6 (62.3, 79.0)
18 months	NE (NE, NE)	70.6 (62.3, 79.0)
Median Follow-up Time (months)	2.51	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	30 (16.0)	71 (17.9)
Number of Subjects Censored, n (%)	158 (84.0)	325 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	9.23 (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.868 (0.223)
95% CI		(0.561, 1.345)
Log-rank p-value		0.624

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (75.5, 88.5)	84.7 (80.9, 88.4)
6 months	77.4 (66.8, 88.1)	79.2 (74.4, 84.1)
9 months	NE (NE, NE)	75.3 (68.9, 81.7)
12 months	NE (NE, NE)	69.5 (59.6, 79.4)
18 months	NE (NE, NE)	69.5 (59.6, 79.4)
Median Follow-up Time (months)	2.61	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	17 (9.0)	69 (17.4)
Number of Subjects Censored, n (%)	171 (91.0)	327 (82.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.514 (0.276)
95% CI		(0.882, 2.599)
Log-rank p-value		0.135

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (83.8, 95.0)	85.3 (81.7, 89.0)
6 months	87.3 (80.5, 94.1)	79.4 (74.5, 84.3)
9 months	NE (NE, NE)	75.8 (69.6, 81.9)
12 months	NE (NE, NE)	73.3 (65.6, 80.9)
18 months	NE (NE, NE)	73.3 (65.6, 80.9)
Median Follow-up Time (months)	2.76	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	27 (14.4)	57 (14.4)
Number of Subjects Censored, n (%)	161 (85.6)	339 (85.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	10.18 (7.10, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.684 (0.243)
95% CI		(0.425, 1.101)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (80.2, 90.8)	89.5 (86.4, 92.7)
6 months	77.0 (64.1, 90.0)	83.3 (78.6, 88.0)
9 months	NE (NE, NE)	79.0 (73.0, 85.1)
12 months	NE (NE, NE)	73.5 (64.1, 82.9)
18 months	NE (NE, NE)	73.5 (64.1, 82.9)
Median Follow-up Time (months)	2.76	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.2)	59 (14.9)
Number of Subjects Censored, n (%)	182 (96.8)	337 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.584 (0.430)
95% CI		(1.972, 10.655)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (93.6, 99.2)	86.3 (82.8, 89.7)
6 months	96.4 (93.6, 99.2)	84.0 (80.0, 88.0)
9 months	NE (NE, NE)	81.4 (76.1, 86.7)
12 months	NE (NE, NE)	81.4 (76.1, 86.7)
18 months	NE (NE, NE)	81.4 (76.1, 86.7)
Median Follow-up Time (months)	2.79	3.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	30 (7.6)
Number of Subjects Censored, n (%)	183 (97.3)	366 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.328 (0.488)
95% CI		(0.894, 6.061)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.7, 99.6)	93.7 (91.2, 96.1)
6 months	97.2 (94.7, 99.6)	90.8 (87.4, 94.3)
9 months	NE (NE, NE)	89.3 (84.7, 93.8)
12 months	NE (NE, NE)	89.3 (84.7, 93.8)
18 months	NE (NE, NE)	89.3 (84.7, 93.8)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	14 (3.5)
Number of Subjects Censored, n (%)	184 (97.9)	382 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.251 (0.579)
95% CI		(0.402, 3.893)
Log-rank p-value		0.736

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.5, 99.9)	97.2 (95.5, 98.8)
6 months	97.7 (95.5, 99.9)	95.9 (93.4, 98.3)
9 months	NE (NE, NE)	94.4 (90.6, 98.1)
12 months	NE (NE, NE)	94.4 (90.6, 98.1)
18 months	NE (NE, NE)	94.4 (90.6, 98.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	6 (1.5)
Number of Subjects Censored, n (%)	184 (97.9)	390 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.623 (0.651)
95% CI		(0.174, 2.230)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.1, 100.0)	98.3 (97.0, 99.7)
6 months	97.5 (95.1, 100.0)	98.3 (97.0, 99.7)
9 months	NE (NE, NE)	98.3 (97.0, 99.7)
12 months	NE (NE, NE)	98.3 (97.0, 99.7)
18 months	NE (NE, NE)	98.3 (97.0, 99.7)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	9 (4.8)	3 (0.8)
Number of Subjects Censored, n (%)	179 (95.2)	393 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.110 (0.698)
95% CI		(0.028, 0.432)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (91.2, 98.1)	99.5 (98.7, 100.0)
6 months	94.6 (91.2, 98.1)	98.6 (96.8, 100.0)
9 months	NE (NE, NE)	98.6 (96.8, 100.0)
12 months	NE (NE, NE)	98.6 (96.8, 100.0)
18 months	NE (NE, NE)	98.6 (96.8, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	12 (3.0)
Number of Subjects Censored, n (%)	188 (100.0)	384 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.3, 98.8)
6 months	100.0 (100.0, 100.0)	97.0 (95.3, 98.8)
9 months	NE (NE, NE)	95.4 (91.8, 99.0)
12 months	NE (NE, NE)	95.4 (91.8, 99.0)
18 months	NE (NE, NE)	95.4 (91.8, 99.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	49 (26.1)	174 (43.9)
Number of Subjects Censored, n (%)	139 (73.9)	222 (56.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (1.02, NE)	1.08 (0.92, 1.61)
Median (95% CI)	NE (NE, NE)	6.24 (4.63, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.528 (0.163)
95% CI		(1.110, 2.105)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.3 (66.7, 80.0)	59.5 (54.5, 64.5)
6 months	66.7 (55.6, 77.8)	51.9 (46.0, 57.7)
9 months	NE (NE, NE)	46.4 (39.6, 53.2)
12 months	NE (NE, NE)	43.6 (35.4, 51.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	32 (17.0)	114 (28.8)
Number of Subjects Censored, n (%)	156 (83.0)	282 (71.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.73 (1.68, 3.94)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.533 (0.202)
95% CI		(1.032, 2.278)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.4 (76.7, 88.1)	72.7 (68.1, 77.3)
6 months	78.0 (68.2, 87.9)	68.5 (63.3, 73.7)
9 months	NE (NE, NE)	65.7 (59.7, 71.6)
12 months	NE (NE, NE)	63.0 (55.4, 70.6)
18 months	NE (NE, NE)	63.0 (55.4, 70.6)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	25 (6.3)
Number of Subjects Censored, n (%)	184 (97.9)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.412 (0.543)
95% CI		(0.832, 6.994)
Log-rank p-value		0.081

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.8, 99.9)	93.8 (91.3, 96.4)
6 months	97.8 (95.8, 99.9)	92.8 (90.0, 95.7)
9 months	NE (NE, NE)	91.4 (87.3, 95.4)
12 months	NE (NE, NE)	91.4 (87.3, 95.4)
18 months	NE (NE, NE)	91.4 (87.3, 95.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	18 (4.5)
Number of Subjects Censored, n (%)	183 (97.3)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.226 (0.519)
95% CI		(0.443, 3.391)
Log-rank p-value		0.682

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	96.5 (94.6, 98.4)
6 months	95.5 (90.7, 100.0)	94.0 (91.0, 97.1)
9 months	NE (NE, NE)	92.7 (88.7, 96.7)
12 months	NE (NE, NE)	92.7 (88.7, 96.7)
18 months	NE (NE, NE)	92.7 (88.7, 96.7)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	11 (2.8)
Number of Subjects Censored, n (%)	184 (97.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.198 (0.589)
95% CI		(0.378, 3.798)
Log-rank p-value		0.721

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.2, 100.0)	97.3 (95.6, 98.9)
6 months	97.6 (95.2, 100.0)	96.8 (94.9, 98.7)
9 months	NE (NE, NE)	96.8 (94.9, 98.7)
12 months	NE (NE, NE)	96.8 (94.9, 98.7)
18 months	NE (NE, NE)	96.8 (94.9, 98.7)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	14 (3.5)
Number of Subjects Censored, n (%)	185 (98.4)	382 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.818 (0.645)
95% CI		(0.513, 6.440)
Log-rank p-value		0.359

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.5, 100.0)	96.7 (94.9, 98.6)
6 months	98.4 (96.5, 100.0)	96.0 (93.7, 98.3)
9 months	NE (NE, NE)	94.6 (91.2, 98.1)
12 months	NE (NE, NE)	94.6 (91.2, 98.1)
18 months	NE (NE, NE)	94.6 (91.2, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	15 (3.8)
Number of Subjects Censored, n (%)	188 (100.0)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.8)
6 months	100.0 (100.0, 100.0)	95.2 (92.4, 97.9)
9 months	NE (NE, NE)	93.9 (90.1, 97.6)
12 months	NE (NE, NE)	93.9 (90.1, 97.6)
18 months	NE (NE, NE)	93.9 (90.1, 97.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	186 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.068 (0.776)
95% CI		(0.452, 9.453)
Log-rank p-value		0.353

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.0, 100.0)	97.3 (95.6, 98.9)
6 months	98.4 (96.0, 100.0)	97.3 (95.6, 98.9)
9 months	NE (NE, NE)	96.4 (94.0, 98.8)
12 months	NE (NE, NE)	96.4 (94.0, 98.8)
18 months	NE (NE, NE)	96.4 (94.0, 98.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.8)
Number of Subjects Censored, n (%)	187 (99.5)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.856 (1.053)
95% CI		(0.489, 30.391)
Log-rank p-value		0.164

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	97.8 (96.3, 99.3)
6 months	99.5 (98.4, 100.0)	96.6 (94.4, 98.9)
9 months	NE (NE, NE)	95.8 (92.9, 98.6)
12 months	NE (NE, NE)	95.8 (92.9, 98.6)
18 months	NE (NE, NE)	95.8 (92.9, 98.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	9 (2.3)
Number of Subjects Censored, n (%)	188 (100.0)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (96.1, 99.2)
6 months	100.0 (100.0, 100.0)	97.6 (96.1, 99.2)
9 months	NE (NE, NE)	97.6 (96.1, 99.2)
12 months	NE (NE, NE)	97.6 (96.1, 99.2)
18 months	NE (NE, NE)	97.6 (96.1, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.5)
Number of Subjects Censored, n (%)	187 (99.5)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.390 (1.072)
95% CI		(0.292, 19.551)
Log-rank p-value		0.466

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.8 (97.6, 100.0)
6 months	99.4 (98.2, 100.0)	95.1 (91.9, 98.3)
9 months	NE (NE, NE)	95.1 (91.9, 98.3)
12 months	NE (NE, NE)	95.1 (91.9, 98.3)
18 months	NE (NE, NE)	95.1 (91.9, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	49 (26.1)	164 (41.4)
Number of Subjects Censored, n (%)	139 (73.9)	232 (58.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.73 (1.35, 5.82)	1.58 (0.95, 1.68)
Median (95% CI)	NE (5.82, NE)	6.90 (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.421 (0.165)
95% CI		(1.028, 1.963)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.4 (66.6, 80.1)	62.5 (57.5, 67.4)
6 months	58.1 (38.7, 77.6)	54.6 (48.7, 60.4)
9 months	NE (NE, NE)	46.8 (39.6, 54.0)
12 months	NE (NE, NE)	46.8 (39.6, 54.0)
18 months	NE (NE, NE)	46.8 (39.6, 54.0)
Median Follow-up Time (months)	2.58	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	16 (8.5)	49 (12.4)
Number of Subjects Censored, n (%)	172 (91.5)	347 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.198 (0.294)
95% CI		(0.674, 2.130)
Log-rank p-value		0.563

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (84.8, 94.8)	89.4 (86.3, 92.5)
6 months	78.6 (57.5, 99.6)	85.1 (80.8, 89.5)
9 months	NE (NE, NE)	82.8 (77.5, 88.2)
12 months	NE (NE, NE)	82.8 (77.5, 88.2)
18 months	NE (NE, NE)	82.8 (77.5, 88.2)
Median Follow-up Time (months)	2.78	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	39 (9.8)
Number of Subjects Censored, n (%)	180 (95.7)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.847 (0.394)
95% CI		(0.854, 3.997)
Log-rank p-value		0.118

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.5, 98.6)	91.6 (88.7, 94.5)
6 months	95.6 (92.5, 98.6)	88.9 (85.3, 92.6)
9 months	NE (NE, NE)	85.7 (80.7, 90.8)
12 months	NE (NE, NE)	85.7 (80.7, 90.8)
18 months	NE (NE, NE)	85.7 (80.7, 90.8)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.2)	41 (10.4)
Number of Subjects Censored, n (%)	182 (96.8)	355 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.505 (0.443)
95% CI		(1.052, 5.964)
Log-rank p-value		0.031

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.1, 99.3)	91.7 (88.9, 94.5)
6 months	96.7 (94.1, 99.3)	88.4 (84.7, 92.2)
9 months	NE (NE, NE)	84.3 (78.8, 89.7)
12 months	NE (NE, NE)	84.3 (78.8, 89.7)
18 months	NE (NE, NE)	84.3 (78.8, 89.7)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	32 (8.1)
Number of Subjects Censored, n (%)	180 (95.7)	364 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.402)
95% CI		(0.632, 3.054)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.7, 98.6)	93.8 (91.3, 96.3)
6 months	95.6 (92.7, 98.6)	90.1 (86.6, 93.7)
9 months	NE (NE, NE)	87.8 (83.1, 92.5)
12 months	NE (NE, NE)	87.8 (83.1, 92.5)
18 months	NE (NE, NE)	87.8 (83.1, 92.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	26 (6.6)
Number of Subjects Censored, n (%)	185 (98.4)	370 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.401 (0.616)
95% CI		(1.016, 11.379)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	94.0 (91.5, 96.4)
6 months	95.7 (89.6, 100.0)	93.2 (90.2, 96.1)
9 months	NE (NE, NE)	89.4 (84.1, 94.8)
12 months	NE (NE, NE)	89.4 (84.1, 94.8)
18 months	NE (NE, NE)	89.4 (84.1, 94.8)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.7)	18 (4.5)
Number of Subjects Censored, n (%)	181 (96.3)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.058 (0.453)
95% CI		(0.436, 2.570)
Log-rank p-value		0.920

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.4, 98.9)	95.7 (93.6, 97.8)
6 months	95.6 (92.4, 98.9)	95.0 (92.6, 97.5)
9 months	NE (NE, NE)	94.1 (91.2, 97.1)
12 months	NE (NE, NE)	94.1 (91.2, 97.1)
18 months	NE (NE, NE)	94.1 (91.2, 97.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	25 (6.3)
Number of Subjects Censored, n (%)	188 (100.0)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.0 (91.6, 96.5)
6 months	100.0 (100.0, 100.0)	92.4 (89.3, 95.4)
9 months	NE (NE, NE)	92.4 (89.3, 95.4)
12 months	NE (NE, NE)	92.4 (89.3, 95.4)
18 months	NE (NE, NE)	92.4 (89.3, 95.4)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	17 (4.3)
Number of Subjects Censored, n (%)	183 (97.3)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.120 (0.518)
95% CI		(0.406, 3.089)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.8, 100.0)	96.4 (94.5, 98.4)
6 months	94.5 (88.4, 100.0)	94.6 (91.9, 97.4)
9 months	NE (NE, NE)	93.8 (90.6, 97.0)
12 months	NE (NE, NE)	93.8 (90.6, 97.0)
18 months	NE (NE, NE)	93.8 (90.6, 97.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	12 (3.0)
Number of Subjects Censored, n (%)	187 (99.5)	384 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.386 (1.048)
95% CI		(0.562, 34.229)
Log-rank p-value		0.123

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.4, 100.0)	97.1 (95.3, 98.9)
6 months	99.4 (98.4, 100.0)	96.5 (94.4, 98.6)
9 months	NE (NE, NE)	95.3 (92.2, 98.4)
12 months	NE (NE, NE)	95.3 (92.2, 98.4)
18 months	NE (NE, NE)	95.3 (92.2, 98.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	186 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.261 (0.775)
95% CI		(0.495, 10.325)
Log-rank p-value		0.275

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.2 (95.5, 98.9)
6 months	98.9 (97.4, 100.0)	97.2 (95.5, 98.9)
9 months	NE (NE, NE)	96.0 (93.2, 98.9)
12 months	NE (NE, NE)	96.0 (93.2, 98.9)
18 months	NE (NE, NE)	96.0 (93.2, 98.9)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	45 (23.9)	152 (38.4)
Number of Subjects Censored, n (%)	143 (76.1)	244 (61.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (1.48, NE)	0.72 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.577 (0.172)
95% CI		(1.126, 2.209)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.8 (67.1, 80.6)	65.0 (60.3, 69.8)
6 months	73.8 (67.1, 80.6)	58.9 (53.3, 64.5)
9 months	NE (NE, NE)	56.6 (50.3, 62.8)
12 months	NE (NE, NE)	46.9 (35.1, 58.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	67 (16.9)
Number of Subjects Censored, n (%)	180 (95.7)	329 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.303 (0.376)
95% CI		(2.060, 8.987)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (92.0, 98.5)	83.1 (79.3, 86.8)
6 months	95.3 (92.0, 98.5)	82.6 (78.8, 86.4)
9 months	NE (NE, NE)	82.6 (78.8, 86.4)
12 months	NE (NE, NE)	82.6 (78.8, 86.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	16 (8.5)	37 (9.3)
Number of Subjects Censored, n (%)	172 (91.5)	359 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.837 (0.307)
95% CI		(0.459, 1.527)
Log-rank p-value		0.573

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (86.7, 95.2)	92.3 (89.5, 95.0)
6 months	90.9 (86.7, 95.2)	89.4 (85.8, 93.1)
9 months	NE (NE, NE)	88.6 (84.7, 92.6)
12 months	NE (NE, NE)	84.8 (76.5, 93.1)
18 months	NE (NE, NE)	63.6 (27.1, 100.0)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	16 (8.5)	31 (7.8)
Number of Subjects Censored, n (%)	172 (91.5)	365 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.801 (0.313)
95% CI		(0.434, 1.479)
Log-rank p-value		0.524

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (86.3, 95.1)	92.6 (90.0, 95.3)
6 months	90.7 (86.3, 95.1)	91.6 (88.6, 94.6)
9 months	NE (NE, NE)	91.6 (88.6, 94.6)
12 months	NE (NE, NE)	85.8 (74.6, 97.1)
18 months	NE (NE, NE)	85.8 (74.6, 97.1)
Median Follow-up Time (months)	2.61	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	15 (3.8)
Number of Subjects Censored, n (%)	185 (98.4)	381 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.247 (0.634)
95% CI		(0.649, 7.779)
Log-rank p-value		0.202

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.6, 100.0)	96.0 (94.1, 98.0)
6 months	98.4 (96.6, 100.0)	96.0 (94.1, 98.0)
9 months	NE (NE, NE)	96.0 (94.1, 98.0)
12 months	NE (NE, NE)	96.0 (94.1, 98.0)
18 months	NE (NE, NE)	96.0 (94.1, 98.0)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	9 (2.3)
Number of Subjects Censored, n (%)	186 (98.9)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.548 (0.806)
95% CI		(0.319, 7.516)
Log-rank p-value		0.633

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	98.5 (97.3, 99.7)
6 months	98.8 (97.1, 100.0)	97.8 (96.0, 99.6)
9 months	NE (NE, NE)	95.7 (92.2, 99.1)
12 months	NE (NE, NE)	95.7 (92.2, 99.1)
18 months	NE (NE, NE)	95.7 (92.2, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	26 (13.8)	155 (39.1)
Number of Subjects Censored, n (%)	162 (86.2)	241 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.880 (0.213)
95% CI		(1.897, 4.371)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (80.1, 90.8)	62.2 (57.3, 67.2)
6 months	82.1 (74.0, 90.3)	57.9 (52.3, 63.5)
9 months	NE (NE, NE)	52.5 (45.4, 59.7)
12 months	NE (NE, NE)	52.5 (45.4, 59.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	14 (7.4)	145 (36.6)
Number of Subjects Censored, n (%)	174 (92.6)	251 (63.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.72, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.122 (0.281)
95% CI		(2.956, 8.878)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (87.4, 95.9)	64.7 (59.8, 69.5)
6 months	91.7 (87.4, 95.9)	61.8 (56.5, 67.0)
9 months	NE (NE, NE)	55.0 (47.7, 62.4)
12 months	NE (NE, NE)	55.0 (47.7, 62.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	38 (20.2)	125 (31.6)
Number of Subjects Censored, n (%)	150 (79.8)	271 (68.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	1.84 (1.22, 2.76)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.398 (0.187)
95% CI		(0.969, 2.017)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.7 (72.5, 85.0)	70.0 (65.3, 74.6)
6 months	75.7 (67.4, 84.1)	64.9 (59.3, 70.4)
9 months	NE (NE, NE)	59.6 (51.8, 67.5)
12 months	NE (NE, NE)	59.6 (51.8, 67.5)
18 months	NE (NE, NE)	59.6 (51.8, 67.5)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	15 (8.0)	39 (9.8)
Number of Subjects Censored, n (%)	173 (92.0)	357 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.979 (0.307)
95% CI		(0.536, 1.789)
Log-rank p-value		0.961

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (87.7, 95.7)	90.7 (87.7, 93.7)
6 months	91.7 (87.7, 95.7)	88.0 (84.3, 91.8)
9 months	NE (NE, NE)	88.0 (84.3, 91.8)
12 months	NE (NE, NE)	88.0 (84.3, 91.8)
18 months	NE (NE, NE)	88.0 (84.3, 91.8)
Median Follow-up Time (months)	2.78	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	40 (10.1)
Number of Subjects Censored, n (%)	180 (95.7)	356 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.967 (0.392)
95% CI		(0.913, 4.241)
Log-rank p-value		0.081

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.4, 98.5)	91.3 (88.4, 94.1)
6 months	95.5 (92.4, 98.5)	88.2 (84.3, 92.1)
9 months	NE (NE, NE)	85.1 (79.5, 90.8)
12 months	NE (NE, NE)	85.1 (79.5, 90.8)
18 months	NE (NE, NE)	85.1 (79.5, 90.8)
Median Follow-up Time (months)	2.79	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	23 (5.8)
Number of Subjects Censored, n (%)	184 (97.9)	373 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.390 (0.545)
95% CI		(0.821, 6.959)
Log-rank p-value		0.093

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.2, 100.0)	94.5 (92.2, 96.8)
6 months	95.3 (89.2, 100.0)	93.0 (90.0, 96.1)
9 months	NE (NE, NE)	93.0 (90.0, 96.1)
12 months	NE (NE, NE)	93.0 (90.0, 96.1)
18 months	NE (NE, NE)	93.0 (90.0, 96.1)
Median Follow-up Time (months)	2.81	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	10 (2.5)
Number of Subjects Censored, n (%)	184 (97.9)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.041 (0.601)
95% CI		(0.320, 3.381)
Log-rank p-value		0.981

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	97.6 (96.1, 99.2)
6 months	97.8 (95.7, 99.9)	96.8 (94.5, 99.0)
9 months	NE (NE, NE)	96.8 (94.5, 99.0)
12 months	NE (NE, NE)	96.8 (94.5, 99.0)
18 months	NE (NE, NE)	96.8 (94.5, 99.0)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	9 (2.3)
Number of Subjects Censored, n (%)	187 (99.5)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.154 (1.066)
95% CI		(0.390, 25.505)
Log-rank p-value		0.262

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	98.2 (96.9, 99.5)
6 months	99.5 (98.4, 100.0)	97.4 (95.4, 99.4)
9 months	NE (NE, NE)	95.2 (90.5, 99.9)
12 months	NE (NE, NE)	95.2 (90.5, 99.9)
18 months	NE (NE, NE)	95.2 (90.5, 99.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	9 (2.3)
Number of Subjects Censored, n (%)	188 (100.0)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
6 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
9 months	NE (NE, NE)	97.5 (95.9, 99.1)
12 months	NE (NE, NE)	97.5 (95.9, 99.1)
18 months	NE (NE, NE)	97.5 (95.9, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	21 (11.2)	130 (32.8)
Number of Subjects Censored, n (%)	167 (88.8)	266 (67.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (1.02, 2.10)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.011 (0.236)
95% CI		(1.895, 4.785)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (83.9, 93.1)	68.6 (63.9, 73.3)
6 months	88.5 (83.9, 93.1)	63.7 (58.2, 69.2)
9 months	NE (NE, NE)	62.7 (56.9, 68.5)
12 months	NE (NE, NE)	62.7 (56.9, 68.5)
18 months	NE (NE, NE)	31.4 (0.0, 74.9)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	68 (17.2)
Number of Subjects Censored, n (%)	183 (97.3)	328 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.386 (0.464)
95% CI		(2.570, 15.865)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (95.0, 99.6)	83.8 (80.1, 87.5)
6 months	97.3 (95.0, 99.6)	80.3 (75.8, 84.8)
9 months	NE (NE, NE)	80.3 (75.8, 84.8)
12 months	NE (NE, NE)	80.3 (75.8, 84.8)
18 months	NE (NE, NE)	80.3 (75.8, 84.8)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	7 (3.7)	18 (4.5)
Number of Subjects Censored, n (%)	181 (96.3)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.190 (0.447)
95% CI		(0.495, 2.857)
Log-rank p-value		0.716

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.4, 99.0)	95.2 (93.1, 97.4)
6 months	96.2 (93.4, 99.0)	95.2 (93.1, 97.4)
9 months	NE (NE, NE)	95.2 (93.1, 97.4)
12 months	NE (NE, NE)	95.2 (93.1, 97.4)
18 months	NE (NE, NE)	95.2 (93.1, 97.4)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	13 (3.3)
Number of Subjects Censored, n (%)	188 (100.0)	383 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (95.0, 98.6)
6 months	100.0 (100.0, 100.0)	96.3 (94.3, 98.3)
9 months	NE (NE, NE)	96.3 (94.3, 98.3)
12 months	NE (NE, NE)	96.3 (94.3, 98.3)
18 months	NE (NE, NE)	96.3 (94.3, 98.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	28 (14.9)	101 (25.5)
Number of Subjects Censored, n (%)	160 (85.1)	295 (74.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.01 (2.27, 6.21)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.505 (0.216)
95% CI		(0.985, 2.298)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (77.7, 89.1)	77.4 (73.1, 81.6)
6 months	83.4 (77.7, 89.1)	70.9 (65.5, 76.3)
9 months	NE (NE, NE)	69.1 (63.4, 74.9)
12 months	NE (NE, NE)	65.5 (56.7, 74.4)
18 months	NE (NE, NE)	65.5 (56.7, 74.4)
Median Follow-up Time (months)	2.58	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	9 (4.8)	30 (7.6)
Number of Subjects Censored, n (%)	179 (95.2)	366 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.353 (0.385)
95% CI		(0.636, 2.878)
Log-rank p-value		0.437

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.9, 98.1)	93.3 (90.8, 95.8)
6 months	94.5 (90.9, 98.1)	92.7 (90.0, 95.4)
9 months	NE (NE, NE)	91.0 (87.4, 94.6)
12 months	NE (NE, NE)	91.0 (87.4, 94.6)
18 months	NE (NE, NE)	91.0 (87.4, 94.6)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	10 (2.5)
Number of Subjects Censored, n (%)	183 (97.3)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.893 (0.550)
95% CI		(0.304, 2.621)
Log-rank p-value		0.789

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.9, 99.6)	97.3 (95.7, 99.0)
6 months	97.3 (94.9, 99.6)	97.3 (95.7, 99.0)
9 months	NE (NE, NE)	97.3 (95.7, 99.0)
12 months	NE (NE, NE)	97.3 (95.7, 99.0)
18 months	NE (NE, NE)	97.3 (95.7, 99.0)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	8 (2.0)
Number of Subjects Censored, n (%)	184 (97.9)	388 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.836 (0.613)
95% CI		(0.251, 2.780)
Log-rank p-value		0.722

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.4, 99.9)	97.9 (96.5, 99.4)
6 months	97.7 (95.4, 99.9)	97.9 (96.5, 99.4)
9 months	NE (NE, NE)	97.9 (96.5, 99.4)
12 months	NE (NE, NE)	97.9 (96.5, 99.4)
18 months	NE (NE, NE)	97.9 (96.5, 99.4)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	26 (13.8)	98 (24.7)
Number of Subjects Censored, n (%)	162 (86.2)	298 (75.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (2.83, 6.54)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.224)
95% CI		(0.911, 2.191)
Log-rank p-value		0.153

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.0 (79.5, 90.6)	78.5 (74.3, 82.7)
6 months	81.9 (73.8, 90.0)	70.9 (65.4, 76.5)
9 months	NE (NE, NE)	67.7 (61.3, 74.1)
12 months	NE (NE, NE)	59.2 (42.8, 75.7)
18 months	NE (NE, NE)	39.5 (6.0, 73.0)
Median Follow-up Time (months)	2.58	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	9 (4.8)	68 (17.2)
Number of Subjects Censored, n (%)	179 (95.2)	328 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.896 (0.357)
95% CI		(1.438, 5.835)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.6, 98.2)	84.4 (80.7, 88.2)
6 months	94.9 (91.6, 98.2)	79.9 (75.2, 84.7)
9 months	NE (NE, NE)	76.8 (70.6, 83.1)
12 months	NE (NE, NE)	76.8 (70.6, 83.1)
18 months	NE (NE, NE)	51.2 (10.0, 92.4)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	5 (2.7)	10 (2.5)
Number of Subjects Censored, n (%)	183 (97.3)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.817 (0.553)
95% CI		(0.276, 2.412)
Log-rank p-value		0.679

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.7, 99.6)	97.7 (96.1, 99.2)
6 months	97.2 (94.7, 99.6)	97.1 (95.3, 99.0)
9 months	NE (NE, NE)	97.1 (95.3, 99.0)
12 months	NE (NE, NE)	97.1 (95.3, 99.0)
18 months	NE (NE, NE)	97.1 (95.3, 99.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	21 (11.2)	81 (20.5)
Number of Subjects Censored, n (%)	167 (88.8)	315 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (5.78, NE)	6.28 (4.60, 7.92)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.253 (0.252)
95% CI		(0.765, 2.052)
Log-rank p-value		0.336

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (84.2, 93.7)	84.3 (80.5, 88.1)
6 months	74.3 (51.2, 97.4)	75.2 (69.6, 80.9)
9 months	NE (NE, NE)	65.0 (56.7, 73.4)
12 months	NE (NE, NE)	59.6 (46.9, 72.4)
18 months	NE (NE, NE)	59.6 (46.9, 72.4)
Median Follow-up Time (months)	2.78	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	6 (3.2)	17 (4.3)
Number of Subjects Censored, n (%)	182 (96.8)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.829 (0.493)
95% CI		(0.315, 2.181)
Log-rank p-value		0.882

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.6, 100.0)	96.8 (95.1, 98.6)
6 months	87.0 (74.1, 99.8)	95.4 (92.8, 98.1)
9 months	NE (NE, NE)	92.4 (88.1, 96.7)
12 months	NE (NE, NE)	92.4 (88.1, 96.7)
18 months	NE (NE, NE)	92.4 (88.1, 96.7)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	4 (2.1)	9 (2.3)
Number of Subjects Censored, n (%)	184 (97.9)	387 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.578 (0.634)
95% CI		(0.167, 2.003)
Log-rank p-value		0.346

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.0, 100.0)	98.8 (97.7, 100.0)
6 months	97.5 (95.0, 100.0)	96.4 (93.8, 99.0)
9 months	NE (NE, NE)	96.4 (93.8, 99.0)
12 months	NE (NE, NE)	90.8 (79.7, 100.0)
18 months	NE (NE, NE)	90.8 (79.7, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	0	11 (2.8)
Number of Subjects Censored, n (%)	188 (100.0)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.041

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.3, 98.9)
6 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.7)
9 months	NE (NE, NE)	96.3 (94.0, 98.7)
12 months	NE (NE, NE)	96.3 (94.0, 98.7)
18 months	NE (NE, NE)	96.3 (94.0, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	31 (16.5)	61 (15.4)
Number of Subjects Censored, n (%)	157 (83.5)	335 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.747 (0.225)
95% CI		(0.480, 1.161)
Log-rank p-value		0.232

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (76.0, 87.7)	86.5 (83.0, 90.0)
6 months	81.9 (76.0, 87.7)	81.7 (77.0, 86.4)
9 months	NE (NE, NE)	78.7 (73.1, 84.4)
12 months	NE (NE, NE)	78.7 (73.1, 84.4)
18 months	NE (NE, NE)	78.7 (73.1, 84.4)
Median Follow-up Time (months)	2.60	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	22 (11.7)	32 (8.1)
Number of Subjects Censored, n (%)	166 (88.3)	364 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.502 (0.286)
95% CI		(0.286, 0.879)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.7 (81.4, 92.0)	93.9 (91.5, 96.4)
6 months	86.7 (81.4, 92.0)	89.1 (85.0, 93.2)
9 months	NE (NE, NE)	87.3 (82.6, 92.0)
12 months	NE (NE, NE)	87.3 (82.6, 92.0)
18 months	NE (NE, NE)	87.3 (82.6, 92.0)
Median Follow-up Time (months)	2.61	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	3 (1.6)	27 (6.8)
Number of Subjects Censored, n (%)	185 (98.4)	369 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.032 (0.609)
95% CI		(1.222, 13.306)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.4, 100.0)	92.8 (90.2, 95.4)
6 months	98.3 (96.4, 100.0)	92.8 (90.2, 95.4)
9 months	NE (NE, NE)	92.8 (90.2, 95.4)
12 months	NE (NE, NE)	92.8 (90.2, 95.4)
18 months	NE (NE, NE)	92.8 (90.2, 95.4)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	88 (22.2)
Number of Subjects Censored, n (%)	187 (99.5)	308 (77.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.71, 6.47)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		34.142 (1.007)
95% CI		(4.748, 245.535)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	81.8 (77.8, 85.7)
6 months	99.5 (98.4, 100.0)	70.7 (64.5, 76.8)
9 months	NE (NE, NE)	67.5 (60.6, 74.4)
12 months	NE (NE, NE)	64.6 (55.9, 73.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	1 (0.5)	82 (20.7)
Number of Subjects Censored, n (%)	187 (99.5)	314 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (3.91, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		30.985 (1.007)
95% CI		(4.303, 223.102)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	83.4 (79.6, 87.2)
6 months	99.5 (98.4, 100.0)	73.0 (67.1, 79.0)
9 months	NE (NE, NE)	68.4 (61.2, 75.6)
12 months	NE (NE, NE)	65.6 (56.8, 74.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	13 (6.9)	48 (12.1)
Number of Subjects Censored, n (%)	175 (93.1)	348 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.358 (0.317)
95% CI		(0.729, 2.529)
Log-rank p-value		0.339

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (89.3, 96.9)	89.7 (86.5, 92.9)
6 months	91.1 (85.7, 96.5)	84.1 (79.5, 88.7)
9 months	NE (NE, NE)	83.1 (78.2, 88.0)
12 months	NE (NE, NE)	83.1 (78.2, 88.0)
18 months	NE (NE, NE)	83.1 (78.2, 88.0)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	8 (4.3)	22 (5.6)
Number of Subjects Censored, n (%)	180 (95.7)	374 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.956 (0.420)
95% CI		(0.419, 2.179)
Log-rank p-value		0.944

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.5, 98.6)	95.3 (93.0, 97.6)
6 months	95.5 (92.5, 98.6)	92.7 (89.5, 95.9)
9 months	NE (NE, NE)	91.7 (87.9, 95.4)
12 months	NE (NE, NE)	91.7 (87.9, 95.4)
18 months	NE (NE, NE)	91.7 (87.9, 95.4)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	10 (2.5)
Number of Subjects Censored, n (%)	186 (98.9)	386 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.942 (0.784)
95% CI		(0.418, 9.027)
Log-rank p-value		0.461

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	97.4 (95.6, 99.1)
6 months	97.2 (92.9, 100.0)	96.7 (94.5, 98.9)
9 months	NE (NE, NE)	96.7 (94.5, 98.9)
12 months	NE (NE, NE)	96.7 (94.5, 98.9)
18 months	NE (NE, NE)	96.7 (94.5, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	186 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.070 (0.776)
95% CI		(0.452, 9.471)
Log-rank p-value		0.350

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	97.6 (96.0, 99.1)
6 months	98.7 (96.9, 100.0)	96.4 (94.1, 98.7)
9 months	NE (NE, NE)	96.4 (94.1, 98.7)
12 months	NE (NE, NE)	96.4 (94.1, 98.7)
18 months	NE (NE, NE)	96.4 (94.1, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	21 (11.2)	42 (10.6)
Number of Subjects Censored, n (%)	167 (88.8)	354 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.741 (0.272)
95% CI		(0.435, 1.263)
Log-rank p-value		0.273

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (84.3, 93.5)	90.1 (87.0, 93.2)
6 months	86.9 (80.9, 92.8)	87.2 (83.3, 91.2)
9 months	NE (NE, NE)	87.2 (83.3, 91.2)
12 months	NE (NE, NE)	84.4 (77.8, 91.0)
18 months	NE (NE, NE)	84.4 (77.8, 91.0)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	17 (4.3)
Number of Subjects Censored, n (%)	186 (98.9)	379 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.160 (0.752)
95% CI		(0.723, 13.808)
Log-rank p-value		0.109

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.2, 100.0)	95.7 (93.6, 97.9)
6 months	98.8 (97.2, 100.0)	95.2 (92.9, 97.6)
9 months	NE (NE, NE)	95.2 (92.9, 97.6)
12 months	NE (NE, NE)	92.2 (85.8, 98.5)
18 months	NE (NE, NE)	92.2 (85.8, 98.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.8)
Number of Subjects Censored, n (%)	186 (98.9)	385 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.042 (0.776)
95% CI		(0.446, 9.352)
Log-rank p-value		0.354

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.6 (96.0, 99.1)
6 months	98.9 (97.4, 100.0)	96.3 (93.9, 98.7)
9 months	NE (NE, NE)	96.3 (93.9, 98.7)
12 months	NE (NE, NE)	96.3 (93.9, 98.7)
18 months	NE (NE, NE)	96.3 (93.9, 98.7)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	7 (50.0)	18 (90.0)
Number of Subjects Censored, n (%)	7 (50.0)	2 (10.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.49 (0.16, 3.22)	0.44 (0.07, 0.69)
Median (95% CI)	3.22 (0.39, NE)	0.82 (0.43, 1.61)
75% percentile (95% CI)	NE (3.22, NE)	1.66 (0.95, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Min, Max	0.2, 3.7*	0.1, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.965 (0.484)
95% CI		(0.761, 5.072)
Log-rank p-value		0.184

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.1 (27.9, 82.3)	20.0 (2.5, 37.5)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.91	0.82

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	8 (40.0)
Number of Subjects Censored, n (%)	12 (85.7)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.16, NE)	1.02 (0.30, 3.68)
Median (95% CI)	3.22 (3.22, NE)	NE (0.99, NE)
75% percentile (95% CI)	NE (3.22, NE)	NE (3.68, NE)
Min, Max	0.2, 3.7*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.684 (0.803)
95% CI		(0.556, 12.960)
Log-rank p-value		0.112

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	64.2 (42.7, 85.6)
6 months	NE (NE, NE)	51.3 (23.1, 79.6)
9 months	NE (NE, NE)	51.3 (23.1, 79.6)
12 months	NE (NE, NE)	51.3 (23.1, 79.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	2 (10.0)
Number of Subjects Censored, n (%)	12 (85.7)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.646 (1.019)
95% CI		(0.088, 4.760)
Log-rank p-value		0.842

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (66.0, 100.0)	88.8 (74.2, 100.0)
6 months	NE (NE, NE)	88.8 (74.2, 100.0)
9 months	NE (NE, NE)	88.8 (74.2, 100.0)
12 months	NE (NE, NE)	88.8 (74.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	NE (0.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 4.1*	0.1, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.355 (1.166)
95% CI		(0.239, 23.173)
Log-rank p-value		0.516

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	85.0 (69.4, 100.0)
6 months	NE (NE, NE)	85.0 (69.4, 100.0)
9 months	NE (NE, NE)	85.0 (69.4, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	4 (20.0)
Number of Subjects Censored, n (%)	14 (100.0)	16 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.55 (0.30, NE)
Median (95% CI)	NE (NE, NE)	NE (3.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.095

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.0 (69.4, 100.0)
6 months	NE (NE, NE)	74.4 (50.6, 98.2)
9 months	NE (NE, NE)	74.4 (50.6, 98.2)
12 months	NE (NE, NE)	74.4 (50.6, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	4 (20.0)
Number of Subjects Censored, n (%)	12 (85.7)	16 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	5.03 (1.51, NE)
Median (95% CI)	NE (1.94, NE)	NE (5.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.462 (1.006)
95% CI		(0.064, 3.314)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.5 (60.0, 100.0)	82.1 (63.6, 100.0)
6 months	NE (NE, NE)	70.4 (43.8, 96.9)
9 months	NE (NE, NE)	70.4 (43.8, 96.9)
12 months	NE (NE, NE)	70.4 (43.8, 96.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.264

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	9.82 (1.35, NE)
Median (95% CI)	NE (NE, NE)	9.82 (4.83, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Min, Max	0.4, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.532 (1.424)
95% CI		(0.033, 8.675)
Log-rank p-value		0.592

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	81.2 (55.2, 100.0)
9 months	NE (NE, NE)	81.2 (55.2, 100.0)
12 months	NE (NE, NE)	40.6 (0.0, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.57, NE)
Median (95% CI)	NE (NE, NE)	NE (8.57, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.57, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	75.0 (32.6, 100.0)
12 months	NE (NE, NE)	75.0 (32.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	7 (50.0)	15 (75.0)
Number of Subjects Censored, n (%)	7 (50.0)	5 (25.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.03, 1.61)	0.39 (0.03, 1.87)
Median (95% CI)	1.61 (0.43, NE)	2.20 (0.30, 2.99)
75% percentile (95% CI)	NE (1.61, NE)	4.40 (2.53, NE)
Min, Max	0.0, 4.1*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.214 (0.522)
95% CI		(0.436, 3.377)
Log-rank p-value		0.967

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	48.2 (21.3, 75.2)	26.5 (3.8, 49.2)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.31	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	6 (30.0)
Number of Subjects Censored, n (%)	13 (92.9)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	1.87 (0.26, NE)
Median (95% CI)	NE (NE, NE)	NE (1.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 4.1*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.337 (1.095)
95% CI		(0.507, 37.113)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	68.4 (47.3, 89.6)
6 months	NE (NE, NE)	68.4 (47.3, 89.6)
9 months	NE (NE, NE)	68.4 (47.3, 89.6)
12 months	NE (NE, NE)	68.4 (47.3, 89.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	5.55 (1.38, NE)
Median (95% CI)	NE (NE, NE)	NE (5.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.254 (1.547)
95% CI		(0.012, 5.272)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	88.0 (72.2, 100.0)
6 months	NE (NE, NE)	70.4 (37.0, 100.0)
9 months	NE (NE, NE)	70.4 (37.0, 100.0)
12 months	NE (NE, NE)	70.4 (37.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (1.25, NE)
Median (95% CI)	NE (1.91, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	4 (20.0)
Number of Subjects Censored, n (%)	12 (85.7)	16 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	2.99 (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (2.99, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.1*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.076 (1.141)
95% CI		(0.222, 19.444)
Log-rank p-value		0.516

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	71.4 (46.0, 96.7)
6 months	NE (NE, NE)	71.4 (46.0, 96.7)
9 months	NE (NE, NE)	71.4 (46.0, 96.7)
12 months	NE (NE, NE)	71.4 (46.0, 96.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	3 (15.0)
Number of Subjects Censored, n (%)	14 (100.0)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (4.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.4 (73.2, 100.0)
6 months	NE (NE, NE)	75.8 (49.4, 100.0)
9 months	NE (NE, NE)	75.8 (49.4, 100.0)
12 months	NE (NE, NE)	75.8 (49.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (0.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.524 (1.237)
95% CI		(0.135, 17.234)
Log-rank p-value		0.833

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	84.7 (68.8, 100.0)
6 months	NE (NE, NE)	84.7 (68.8, 100.0)
9 months	NE (NE, NE)	84.7 (68.8, 100.0)
12 months	NE (NE, NE)	84.7 (68.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
6 months	NE (NE, NE)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	95.0 (85.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.264

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.05, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	3 (21.4)	9 (45.0)
Number of Subjects Censored, n (%)	11 (78.6)	11 (55.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	0.95 (0.49, 2.56)
Median (95% CI)	NE (0.69, NE)	NE (0.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.1*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.392 (0.691)
95% CI		(0.359, 5.394)
Log-rank p-value		0.752

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.6 (57.1, 100.0)	50.8 (27.6, 74.1)
6 months	NE (NE, NE)	50.8 (27.6, 74.1)
9 months	NE (NE, NE)	50.8 (27.6, 74.1)
12 months	NE (NE, NE)	50.8 (27.6, 74.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	6 (30.0)
Number of Subjects Censored, n (%)	13 (92.9)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.33, NE)	1.84 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (1.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.009 (1.083)
95% CI		(0.480, 33.483)
Log-rank p-value		0.199

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	65.6 (43.0, 88.2)
6 months	NE (NE, NE)	65.6 (43.0, 88.2)
9 months	NE (NE, NE)	65.6 (43.0, 88.2)
12 months	NE (NE, NE)	65.6 (43.0, 88.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.2 (72.9, 100.0)
6 months	NE (NE, NE)	88.2 (72.9, 100.0)
9 months	NE (NE, NE)	88.2 (72.9, 100.0)
12 months	NE (NE, NE)	88.2 (72.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.49, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
6 months	NE (NE, NE)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	95.0 (85.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	4 (28.6)	8 (40.0)
Number of Subjects Censored, n (%)	10 (71.4)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.68 (0.39, NE)	0.72 (0.46, NE)
Median (95% CI)	NE (0.95, NE)	NE (0.72, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 3.7*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.426 (0.642)
95% CI		(0.406, 5.016)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.7 (46.5, 95.0)	57.0 (34.2, 79.8)
6 months	NE (NE, NE)	57.0 (34.2, 79.8)
9 months	NE (NE, NE)	57.0 (34.2, 79.8)
12 months	NE (NE, NE)	57.0 (34.2, 79.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.95

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.763 (1.245)
95% CI		(0.154, 20.228)
Log-rank p-value		0.695

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	84.2 (67.8, 100.0)
6 months	NE (NE, NE)	84.2 (67.8, 100.0)
9 months	NE (NE, NE)	84.2 (67.8, 100.0)
12 months	NE (NE, NE)	84.2 (67.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.763 (1.245)
95% CI		(0.154, 20.228)
Log-rank p-value		0.695

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	84.2 (67.8, 100.0)
6 months	NE (NE, NE)	84.2 (67.8, 100.0)
9 months	NE (NE, NE)	84.2 (67.8, 100.0)
12 months	NE (NE, NE)	84.2 (67.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	2 (10.0)
Number of Subjects Censored, n (%)	13 (92.9)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.631 (1.244)
95% CI		(0.142, 18.663)
Log-rank p-value		0.695

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	89.5 (75.7, 100.0)
6 months	NE (NE, NE)	89.5 (75.7, 100.0)
9 months	NE (NE, NE)	89.5 (75.7, 100.0)
12 months	NE (NE, NE)	89.5 (75.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.7 (76.2, 100.0)
6 months	NE (NE, NE)	89.7 (76.2, 100.0)
9 months	NE (NE, NE)	89.7 (76.2, 100.0)
12 months	NE (NE, NE)	89.7 (76.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	4 (28.6)	8 (40.0)
Number of Subjects Censored, n (%)	10 (71.4)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.03, NE)	1.84 (0.72, 6.34)
Median (95% CI)	NE (1.61, NE)	6.34 (1.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.34, NE)
Min, Max	0.0, 3.7*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.871 (0.690)
95% CI		(0.225, 3.366)
Log-rank p-value		0.808

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.8 (44.8, 94.8)	71.6 (50.4, 92.8)
6 months	NE (NE, NE)	59.6 (31.9, 87.4)
9 months	NE (NE, NE)	47.7 (17.2, 78.2)
12 months	NE (NE, NE)	31.8 (0.0, 64.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.596 (1.425)
95% CI		(0.037, 9.723)
Log-rank p-value		0.592

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (4.67, NE)
Median (95% CI)	NE (NE, NE)	NE (4.67, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 3.7*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	87.5 (64.6, 100.0)
9 months	NE (NE, NE)	87.5 (64.6, 100.0)
12 months	NE (NE, NE)	87.5 (64.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.604 (1.514)
95% CI		(0.031, 11.744)
Log-rank p-value		0.919

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.34, NE)
Median (95% CI)	NE (NE, NE)	NE (6.34, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	83.3 (53.5, 100.0)
12 months	NE (NE, NE)	83.3 (53.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	8 (40.0)
Number of Subjects Censored, n (%)	12 (85.7)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.02 (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (1.02, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.0, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.914 (0.810)
95% CI		(0.595, 14.267)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (66.0, 100.0)	55.8 (32.3, 79.3)
6 months	NE (NE, NE)	55.8 (32.3, 79.3)
9 months	NE (NE, NE)	55.8 (32.3, 79.3)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.77

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	8 (40.0)
Number of Subjects Censored, n (%)	12 (85.7)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.02 (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (1.02, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.0, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.914 (0.810)
95% CI		(0.595, 14.267)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (66.0, 100.0)	55.8 (32.3, 79.3)
6 months	NE (NE, NE)	55.8 (32.3, 79.3)
9 months	NE (NE, NE)	55.8 (32.3, 79.3)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.77

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	5 (25.0)
Number of Subjects Censored, n (%)	14 (100.0)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.77 (0.16, NE)
Median (95% CI)	NE (NE, NE)	NE (1.77, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.2, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	72.4 (51.6, 93.2)
6 months	NE (NE, NE)	72.4 (51.6, 93.2)
9 months	NE (NE, NE)	72.4 (51.6, 93.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (82.9, 100.0)
6 months	NE (NE, NE)	94.1 (82.9, 100.0)
9 months	NE (NE, NE)	94.1 (82.9, 100.0)
12 months	NE (NE, NE)	94.1 (82.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.199

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.7 (76.2, 100.0)
6 months	NE (NE, NE)	89.7 (76.2, 100.0)
9 months	NE (NE, NE)	89.7 (76.2, 100.0)
12 months	NE (NE, NE)	89.7 (76.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.38, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.45, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	3 (21.4)	6 (30.0)
Number of Subjects Censored, n (%)	11 (78.6)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.05 (0.23, NE)
Median (95% CI)	NE (1.61, NE)	NE (1.05, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.2, 9.7*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.140 (0.754)
95% CI		(0.260, 4.997)
Log-rank p-value		0.744

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.9 (55.8, 100.0)	68.7 (47.7, 89.6)
6 months	NE (NE, NE)	68.7 (47.7, 89.6)
9 months	NE (NE, NE)	68.7 (47.7, 89.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	2.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	3 (15.0)
Number of Subjects Censored, n (%)	13 (92.9)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (0.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.3, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.038 (1.277)
95% CI		(0.085, 12.684)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	84.4 (68.1, 100.0)
6 months	NE (NE, NE)	84.4 (68.1, 100.0)
9 months	NE (NE, NE)	84.4 (68.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.89, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.5 (75.7, 100.0)
6 months	NE (NE, NE)	89.5 (75.7, 100.0)
9 months	NE (NE, NE)	89.5 (75.7, 100.0)
12 months	NE (NE, NE)	89.5 (75.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	7 (35.0)
Number of Subjects Censored, n (%)	12 (85.7)	13 (65.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.20, NE)	1.02 (0.10, NE)
Median (95% CI)	NE (NE, NE)	NE (1.02, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.1*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.868 (0.837)
95% CI		(0.556, 14.784)
Log-rank p-value		0.250

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	62.4 (40.1, 84.6)
6 months	NE (NE, NE)	62.4 (40.1, 84.6)
9 months	NE (NE, NE)	62.4 (40.1, 84.6)
12 months	NE (NE, NE)	62.4 (40.1, 84.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.8 (74.2, 100.0)
6 months	NE (NE, NE)	88.8 (74.2, 100.0)
9 months	NE (NE, NE)	88.8 (74.2, 100.0)
12 months	NE (NE, NE)	88.8 (74.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	2 (10.0)
Number of Subjects Censored, n (%)	14 (100.0)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.199

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.5 (75.7, 100.0)
6 months	NE (NE, NE)	89.5 (75.7, 100.0)
9 months	NE (NE, NE)	89.5 (75.7, 100.0)
12 months	NE (NE, NE)	89.5 (75.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.38, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	5 (25.0)
Number of Subjects Censored, n (%)	13 (92.9)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	5.06 (0.36, NE)
Median (95% CI)	NE (NE, NE)	NE (5.06, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 3.7*	0.4, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.644 (1.182)
95% CI		(0.360, 36.928)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	79.2 (61.0, 97.4)
6 months	NE (NE, NE)	63.3 (32.0, 94.7)
9 months	NE (NE, NE)	63.3 (32.0, 94.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	5 (25.0)
Number of Subjects Censored, n (%)	13 (92.9)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	5.06 (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (5.06, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 3.7*	0.5, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.644 (1.182)
95% CI		(0.360, 36.928)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	79.2 (61.0, 97.4)
6 months	NE (NE, NE)	63.3 (32.0, 94.7)
9 months	NE (NE, NE)	63.3 (32.0, 94.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	2 (10.0)
Number of Subjects Censored, n (%)	13 (92.9)	18 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (0.36, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 3.7*	0.4, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.015 (1.420)
95% CI		(0.063, 16.404)
Log-rank p-value		0.982

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	89.7 (76.2, 100.0)
6 months	NE (NE, NE)	89.7 (76.2, 100.0)
9 months	NE (NE, NE)	89.7 (76.2, 100.0)
12 months	NE (NE, NE)	89.7 (76.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	6 (30.0)
Number of Subjects Censored, n (%)	13 (92.9)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	7.69 (0.72, 7.92)
Median (95% CI)	NE (NE, NE)	7.92 (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	8.21 (7.69, NE)
Min, Max	0.0, 3.7*	0.6*, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.905 (1.167)
95% CI		(0.194, 18.754)
Log-rank p-value		0.426

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	79.5 (57.4, 100.0)
6 months	NE (NE, NE)	79.5 (57.4, 100.0)
9 months	NE (NE, NE)	19.9 (0.0, 54.1)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	90.0 (71.4, 100.0)
6 months	NE (NE, NE)	90.0 (71.4, 100.0)
9 months	NE (NE, NE)	90.0 (71.4, 100.0)
12 months	NE (NE, NE)	90.0 (71.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	5 (25.0)
Number of Subjects Censored, n (%)	14 (100.0)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.55 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (3.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.077

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	78.2 (59.2, 97.2)
6 months	NE (NE, NE)	65.2 (37.0, 93.3)
9 months	NE (NE, NE)	65.2 (37.0, 93.3)
12 months	NE (NE, NE)	65.2 (37.0, 93.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	3 (15.0)
Number of Subjects Censored, n (%)	14 (100.0)	17 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (3.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.5 (75.7, 100.0)
6 months	NE (NE, NE)	76.7 (50.7, 100.0)
9 months	NE (NE, NE)	76.7 (50.7, 100.0)
12 months	NE (NE, NE)	76.7 (50.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	6 (30.0)
Number of Subjects Censored, n (%)	14 (100.0)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.84 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (1.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.47, NE)
Min, Max	0.9*, 4.1*	0.6*, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	71.6 (50.4, 92.8)
6 months	NE (NE, NE)	71.6 (50.4, 92.8)
9 months	NE (NE, NE)	53.7 (19.4, 88.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	5 (25.0)
Number of Subjects Censored, n (%)	14 (100.0)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.47 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (1.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 10.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	77.0 (57.1, 96.8)
6 months	NE (NE, NE)	77.0 (57.1, 96.8)
9 months	NE (NE, NE)	61.6 (30.3, 92.9)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (1.15, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.577 (1.418)
95% CI		(0.036, 9.297)
Log-rank p-value		0.695

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	1 (5.0)
Number of Subjects Censored, n (%)	13 (92.9)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (1.15, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.577 (1.418)
95% CI		(0.036, 9.297)
Log-rank p-value		0.695

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	1 (5.0)
Number of Subjects Censored, n (%)	14 (100.0)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.25, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (84.7, 100.0)
6 months	NE (NE, NE)	94.7 (84.7, 100.0)
9 months	NE (NE, NE)	94.7 (84.7, 100.0)
12 months	NE (NE, NE)	94.7 (84.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	1 (5.0)
Number of Subjects Censored, n (%)	12 (85.7)	19 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.205 (1.341)
95% CI		(0.015, 2.833)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (65.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	93.3 (80.7, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	0
Number of Subjects Censored, n (%)	13 (92.9)	20 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9*, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	39 (51.3)	96 (68.6)
Number of Subjects Censored, n (%)	37 (48.7)	44 (31.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 1.22)	0.44 (0.23, 0.69)
Median (95% CI)	2.76 (1.35, NE)	1.25 (0.72, 1.74)
75% percentile (95% CI)	NE (4.70, NE)	6.93 (3.65, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.480 (0.195)
95% CI		(1.010, 2.169)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.6 (34.6, 58.6)	37.9 (29.8, 46.1)
6 months	40.0 (24.1, 55.8)	25.9 (17.3, 34.5)
9 months	NE (NE, NE)	22.2 (12.2, 32.2)
12 months	NE (NE, NE)	22.2 (12.2, 32.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.76	1.18

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	13 (17.1)	47 (33.6)
Number of Subjects Censored, n (%)	63 (82.9)	93 (66.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.70 (1.35, NE)	1.61 (0.72, 3.06)
Median (95% CI)	NE (4.70, NE)	NE (8.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.921 (0.319)
95% CI		(1.027, 3.593)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (73.8, 91.9)	68.7 (60.8, 76.7)
6 months	73.7 (54.9, 92.5)	63.2 (54.2, 72.3)
9 months	NE (NE, NE)	55.3 (38.8, 71.8)
12 months	NE (NE, NE)	55.3 (38.8, 71.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	15 (19.7)	29 (20.7)
Number of Subjects Censored, n (%)	61 (80.3)	111 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.960 (0.326)
95% CI		(0.507, 1.819)
Log-rank p-value		0.924

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.8 (69.1, 88.4)	81.3 (74.7, 88.0)
6 months	78.8 (69.1, 88.4)	75.8 (67.7, 83.9)
9 months	NE (NE, NE)	75.8 (67.7, 83.9)
12 months	NE (NE, NE)	75.8 (67.7, 83.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.43	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	6 (7.9)	19 (13.6)
Number of Subjects Censored, n (%)	70 (92.1)	121 (86.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	11.53 (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.495 (0.485)
95% CI		(0.578, 3.866)
Log-rank p-value		0.402

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (84.9, 99.0)	88.3 (82.9, 93.7)
6 months	81.7 (61.9, 100.0)	84.8 (77.7, 91.9)
9 months	NE (NE, NE)	84.8 (77.7, 91.9)
12 months	NE (NE, NE)	70.7 (44.7, 96.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	16 (11.4)
Number of Subjects Censored, n (%)	74 (97.4)	124 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (7.26, NE)
Median (95% CI)	NE (NE, NE)	13.24 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.24 (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 13.2
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.858 (0.759)
95% CI		(0.871, 17.085)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.2, 100.0)	89.9 (84.9, 94.9)
6 months	97.1 (93.2, 100.0)	89.9 (84.9, 94.9)
9 months	NE (NE, NE)	85.2 (74.9, 95.4)
12 months	NE (NE, NE)	85.2 (74.9, 95.4)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	9 (11.8)	12 (8.6)
Number of Subjects Censored, n (%)	67 (88.2)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.60, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.534 (0.472)
95% CI		(0.212, 1.345)
Log-rank p-value		0.267

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.5 (75.0, 94.0)	94.8 (91.0, 98.5)
6 months	84.5 (75.0, 94.0)	88.3 (81.0, 95.6)
9 months	NE (NE, NE)	88.3 (81.0, 95.6)
12 months	NE (NE, NE)	88.3 (81.0, 95.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	5 (6.6)	10 (7.1)
Number of Subjects Censored, n (%)	71 (93.4)	130 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.865 (0.565)
95% CI		(0.286, 2.619)
Log-rank p-value		0.797

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (87.5, 99.0)	93.0 (88.6, 97.5)
6 months	93.2 (87.5, 99.0)	93.0 (88.6, 97.5)
9 months	NE (NE, NE)	93.0 (88.6, 97.5)
12 months	NE (NE, NE)	82.7 (63.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	5 (3.6)
Number of Subjects Censored, n (%)	75 (98.7)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.786 (1.140)
95% CI		(0.191, 16.668)
Log-rank p-value		0.661

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	97.7 (95.2, 100.0)
6 months	98.6 (96.0, 100.0)	96.3 (92.4, 100.0)
9 months	NE (NE, NE)	90.9 (80.1, 100.0)
12 months	NE (NE, NE)	90.9 (80.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	2 (1.4)
Number of Subjects Censored, n (%)	73 (96.1)	138 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.251 (0.995)
95% CI		(0.036, 1.767)
Log-rank p-value		0.108

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (91.1, 100.0)	99.0 (97.1, 100.0)
6 months	95.8 (91.1, 100.0)	99.0 (97.1, 100.0)
9 months	NE (NE, NE)	93.8 (83.7, 100.0)
12 months	NE (NE, NE)	93.8 (83.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	5 (3.6)
Number of Subjects Censored, n (%)	76 (100.0)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.132

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (93.3, 99.5)
6 months	100.0 (100.0, 100.0)	96.4 (93.3, 99.5)
9 months	NE (NE, NE)	96.4 (93.3, 99.5)
12 months	NE (NE, NE)	96.4 (93.3, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	46 (60.5)	103 (73.6)
Number of Subjects Censored, n (%)	30 (39.5)	37 (26.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.30, 0.69)	0.46 (0.26, 0.53)
Median (95% CI)	1.41 (0.72, 2.79)	0.92 (0.69, 1.64)
75% percentile (95% CI)	NE (3.75, NE)	3.71 (3.02, 7.75)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.188 (0.182)
95% CI		(0.831, 1.698)
Log-rank p-value		0.275

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	38.2 (26.5, 49.8)	32.9 (24.9, 40.9)
6 months	25.4 (9.1, 41.8)	20.4 (12.0, 28.9)
9 months	NE (NE, NE)	7.7 (0.0, 19.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.30	0.90

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	12 (15.8)	30 (21.4)
Number of Subjects Censored, n (%)	64 (84.2)	110 (78.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	6.70 (2.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.132 (0.351)
95% CI		(0.569, 2.252)
Log-rank p-value		0.803

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (74.8, 92.0)	80.4 (73.5, 87.2)
6 months	83.4 (74.8, 92.0)	75.7 (67.3, 84.1)
9 months	NE (NE, NE)	72.1 (61.5, 82.6)
12 months	NE (NE, NE)	72.1 (61.5, 82.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	16 (21.1)	26 (18.6)
Number of Subjects Censored, n (%)	60 (78.9)	114 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.61, NE)	8.31 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (9.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.694 (0.333)
95% CI		(0.361, 1.334)
Log-rank p-value		0.409

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.2 (68.3, 88.2)	83.0 (76.4, 89.6)
6 months	71.7 (56.5, 87.0)	81.4 (74.3, 88.6)
9 months	NE (NE, NE)	73.2 (60.2, 86.2)
12 months	NE (NE, NE)	65.1 (46.1, 84.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.68	2.87

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	11 (14.5)	15 (10.7)
Number of Subjects Censored, n (%)	65 (85.5)	125 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	9.23 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (9.23, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.373 (0.444)
95% CI		(0.156, 0.892)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.5 (76.1, 93.0)	91.9 (86.8, 97.1)
6 months	84.5 (76.1, 93.0)	88.0 (81.5, 94.6)
9 months	NE (NE, NE)	80.4 (68.1, 92.6)
12 months	NE (NE, NE)	72.3 (53.7, 90.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.68	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	34 (24.3)
Number of Subjects Censored, n (%)	72 (94.7)	106 (75.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.68 (2.89, 7.10)
Median (95% CI)	NE (NE, NE)	NE (7.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.319 (0.538)
95% CI		(1.157, 9.520)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (88.3, 99.8)	80.9 (73.9, 87.9)
6 months	94.0 (88.3, 99.8)	68.9 (58.8, 79.0)
9 months	NE (NE, NE)	60.7 (46.8, 74.6)
12 months	NE (NE, NE)	60.7 (46.8, 74.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.87

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	12 (15.8)	14 (10.0)
Number of Subjects Censored, n (%)	64 (84.2)	126 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.77, NE)	10.18 (9.20, NE)
Median (95% CI)	NE (NE, NE)	NE (10.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.462 (0.427)
95% CI		(0.200, 1.066)
Log-rank p-value		0.107

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (74.7, 92.0)	91.9 (87.2, 96.5)
6 months	83.3 (74.7, 92.0)	91.9 (87.2, 96.5)
9 months	NE (NE, NE)	88.9 (81.6, 96.2)
12 months	NE (NE, NE)	70.7 (47.2, 94.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	29 (20.7)
Number of Subjects Censored, n (%)	73 (96.1)	111 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.64, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.635 (0.611)
95% CI		(1.700, 18.681)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (91.0, 100.0)	80.3 (73.6, 87.0)
6 months	95.7 (91.0, 100.0)	77.5 (70.1, 85.0)
9 months	NE (NE, NE)	77.5 (70.1, 85.0)
12 months	NE (NE, NE)	77.5 (70.1, 85.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	8 (5.7)
Number of Subjects Censored, n (%)	74 (97.4)	132 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.870 (0.796)
95% CI		(0.393, 8.903)
Log-rank p-value		0.445

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.7, 100.0)	94.8 (91.0, 98.6)
6 months	97.3 (93.7, 100.0)	93.4 (88.9, 98.0)
9 months	NE (NE, NE)	93.4 (88.9, 98.0)
12 months	NE (NE, NE)	93.4 (88.9, 98.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	8 (5.7)
Number of Subjects Censored, n (%)	76 (100.0)	132 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.6 (92.1, 99.0)
6 months	100.0 (100.0, 100.0)	91.7 (85.4, 98.0)
9 months	NE (NE, NE)	91.7 (85.4, 98.0)
12 months	NE (NE, NE)	91.7 (85.4, 98.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	6 (4.3)
Number of Subjects Censored, n (%)	74 (97.4)	134 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.334 (0.857)
95% CI		(0.249, 7.163)
Log-rank p-value		0.640

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	95.1 (91.2, 99.0)
6 months	96.9 (92.6, 100.0)	95.1 (91.2, 99.0)
9 months	NE (NE, NE)	95.1 (91.2, 99.0)
12 months	NE (NE, NE)	95.1 (91.2, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	5 (6.6)	1 (0.7)
Number of Subjects Censored, n (%)	71 (93.4)	139 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.060 (1.210)
95% CI		(0.006, 0.647)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (86.4, 98.9)	100.0 (100.0, 100.0)
6 months	92.6 (86.4, 98.9)	97.4 (92.3, 100.0)
9 months	NE (NE, NE)	97.4 (92.3, 100.0)
12 months	NE (NE, NE)	97.4 (92.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	3 (2.1)
Number of Subjects Censored, n (%)	76 (100.0)	137 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.31, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.231

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.4, 100.0)
6 months	100.0 (100.0, 100.0)	98.5 (96.4, 100.0)
9 months	NE (NE, NE)	92.7 (81.5, 100.0)
12 months	NE (NE, NE)	92.7 (81.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	24 (31.6)	62 (44.3)
Number of Subjects Censored, n (%)	52 (68.4)	78 (55.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.54 (0.72, 4.27)	0.95 (0.69, 1.68)
Median (95% CI)	NE (4.27, NE)	6.24 (3.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.02, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.241 (0.247)
95% CI		(0.765, 2.013)
Log-rank p-value		0.423

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.0 (55.7, 78.3)	59.8 (51.3, 68.2)
6 months	60.9 (45.6, 76.3)	53.0 (43.1, 62.8)
9 months	NE (NE, NE)	38.2 (22.7, 53.7)
12 months	NE (NE, NE)	38.2 (22.7, 53.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	2.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	16 (21.1)	44 (31.4)
Number of Subjects Censored, n (%)	60 (78.9)	96 (68.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (1.22, NE)	1.91 (0.99, 4.73)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.433 (0.298)
95% CI		(0.799, 2.570)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.3 (69.9, 88.7)	68.9 (60.8, 76.9)
6 months	73.2 (58.8, 87.6)	67.2 (58.7, 75.7)
9 months	NE (NE, NE)	61.3 (50.4, 72.3)
12 months	NE (NE, NE)	61.3 (50.4, 72.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	12 (8.6)
Number of Subjects Censored, n (%)	75 (98.7)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.951 (1.061)
95% CI		(0.619, 39.595)
Log-rank p-value		0.124

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	90.8 (85.6, 96.1)
6 months	98.7 (96.1, 100.0)	90.8 (85.6, 96.1)
9 months	NE (NE, NE)	85.5 (74.2, 96.8)
12 months	NE (NE, NE)	85.5 (74.2, 96.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	8 (5.7)
Number of Subjects Censored, n (%)	75 (98.7)	132 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.040 (1.081)
95% CI		(0.365, 25.297)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	95.5 (92.0, 99.0)
6 months	98.6 (96.0, 100.0)	93.0 (86.9, 99.0)
9 months	NE (NE, NE)	88.7 (78.8, 98.7)
12 months	NE (NE, NE)	88.7 (78.8, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	2 (1.4)
Number of Subjects Censored, n (%)	73 (96.1)	138 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.225 (0.953)
95% CI		(0.035, 1.454)
Log-rank p-value		0.101

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (90.5, 100.0)	98.6 (96.6, 100.0)
6 months	95.5 (90.5, 100.0)	98.6 (96.6, 100.0)
9 months	NE (NE, NE)	98.6 (96.6, 100.0)
12 months	NE (NE, NE)	98.6 (96.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	9 (6.4)
Number of Subjects Censored, n (%)	76 (100.0)	131 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (89.6, 98.0)
6 months	100.0 (100.0, 100.0)	91.7 (85.9, 97.5)
9 months	NE (NE, NE)	91.7 (85.9, 97.5)
12 months	NE (NE, NE)	91.7 (85.9, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	4 (2.9)
Number of Subjects Censored, n (%)	76 (100.0)	136 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (94.9, 100.0)
6 months	100.0 (100.0, 100.0)	96.2 (92.4, 100.0)
9 months	NE (NE, NE)	96.2 (92.4, 100.0)
12 months	NE (NE, NE)	96.2 (92.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	4 (2.9)
Number of Subjects Censored, n (%)	74 (97.4)	136 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.912 (0.872)
95% CI		(0.165, 5.038)
Log-rank p-value		0.946

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (90.5, 100.0)	97.0 (94.0, 99.9)
6 months	96.0 (90.5, 100.0)	97.0 (94.0, 99.9)
9 months	NE (NE, NE)	97.0 (94.0, 99.9)
12 months	NE (NE, NE)	97.0 (94.0, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	2 (1.4)
Number of Subjects Censored, n (%)	76 (100.0)	138 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.286

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.2, 100.0)
6 months	100.0 (100.0, 100.0)	97.8 (94.7, 100.0)
9 months	NE (NE, NE)	97.8 (94.7, 100.0)
12 months	NE (NE, NE)	97.8 (94.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	2 (1.4)
Number of Subjects Censored, n (%)	75 (98.7)	138 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.213 (1.239)
95% CI		(0.107, 13.752)
Log-rank p-value		0.886

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	98.4 (96.2, 100.0)
6 months	98.6 (96.0, 100.0)	98.4 (96.2, 100.0)
9 months	NE (NE, NE)	98.4 (96.2, 100.0)
12 months	NE (NE, NE)	98.4 (96.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	4 (2.9)
Number of Subjects Censored, n (%)	75 (98.7)	136 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.708 (1.196)
95% CI		(0.068, 7.379)
Log-rank p-value		0.902

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	98.1 (95.3, 100.0)
6 months	98.5 (95.5, 100.0)	93.8 (87.3, 100.0)
9 months	NE (NE, NE)	93.8 (87.3, 100.0)
12 months	NE (NE, NE)	93.8 (87.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	19 (25.0)	53 (37.9)
Number of Subjects Censored, n (%)	57 (75.0)	87 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.92, NE)	1.61 (0.95, 2.53)
Median (95% CI)	NE (NE, NE)	7.16 (5.49, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.366 (0.277)
95% CI		(0.795, 2.349)
Log-rank p-value		0.245

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.6 (63.3, 83.8)	66.2 (58.1, 74.3)
6 months	73.6 (63.3, 83.8)	58.5 (48.8, 68.2)
9 months	NE (NE, NE)	49.3 (36.6, 62.1)
12 months	NE (NE, NE)	49.3 (36.6, 62.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.51	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	8 (10.5)	18 (12.9)
Number of Subjects Censored, n (%)	68 (89.5)	122 (87.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.153 (0.439)
95% CI		(0.488, 2.725)
Log-rank p-value		0.786

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (79.4, 95.8)	88.2 (82.8, 93.6)
6 months	87.6 (79.4, 95.8)	84.9 (78.0, 91.8)
9 months	NE (NE, NE)	84.9 (78.0, 91.8)
12 months	NE (NE, NE)	84.9 (78.0, 91.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	13 (9.3)
Number of Subjects Censored, n (%)	72 (94.7)	127 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.540 (0.582)
95% CI		(0.492, 4.817)
Log-rank p-value		0.449

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (89.5, 99.7)	90.8 (85.7, 95.8)
6 months	94.6 (89.5, 99.7)	90.8 (85.7, 95.8)
9 months	NE (NE, NE)	87.7 (79.9, 95.4)
12 months	NE (NE, NE)	87.7 (79.9, 95.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	13 (9.3)
Number of Subjects Censored, n (%)	73 (96.1)	127 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.897 (0.653)
95% CI		(0.528, 6.818)
Log-rank p-value		0.382

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (91.5, 100.0)	92.4 (87.9, 97.0)
6 months	95.9 (91.5, 100.0)	89.5 (83.5, 95.4)
9 months	NE (NE, NE)	86.4 (78.1, 94.7)
12 months	NE (NE, NE)	86.4 (78.1, 94.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	12 (8.6)
Number of Subjects Censored, n (%)	75 (98.7)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.67, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.663 (1.049)
95% CI		(0.597, 36.429)
Log-rank p-value		0.132

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	93.8 (89.6, 98.0)
6 months	98.6 (96.0, 100.0)	89.2 (82.7, 95.7)
9 months	NE (NE, NE)	86.1 (77.5, 94.7)
12 months	NE (NE, NE)	86.1 (77.5, 94.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	12 (8.6)
Number of Subjects Censored, n (%)	74 (97.4)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.361 (0.792)
95% CI		(0.500, 11.142)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (94.7, 100.0)	92.2 (87.5, 96.9)
6 months	92.1 (80.0, 100.0)	90.4 (84.6, 96.2)
9 months	NE (NE, NE)	87.7 (80.1, 95.3)
12 months	NE (NE, NE)	87.7 (80.1, 95.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	6 (7.9)	5 (3.6)
Number of Subjects Censored, n (%)	70 (92.1)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.380 (0.627)
95% CI		(0.111, 1.301)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (83.0, 97.9)	96.6 (93.3, 100.0)
6 months	90.4 (83.0, 97.9)	95.2 (90.9, 99.5)
9 months	NE (NE, NE)	95.2 (90.9, 99.5)
12 months	NE (NE, NE)	95.2 (90.9, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	11 (7.9)
Number of Subjects Censored, n (%)	76 (100.0)	129 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.6 (86.8, 96.4)
6 months	100.0 (100.0, 100.0)	91.6 (86.8, 96.4)
9 months	NE (NE, NE)	91.6 (86.8, 96.4)
12 months	NE (NE, NE)	91.6 (86.8, 96.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	8 (5.7)
Number of Subjects Censored, n (%)	72 (94.7)	132 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.967 (0.627)
95% CI		(0.283, 3.303)
Log-rank p-value		0.997

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (87.8, 99.7)	94.5 (90.5, 98.5)
6 months	93.8 (87.8, 99.7)	92.3 (86.6, 98.1)
9 months	NE (NE, NE)	92.3 (86.6, 98.1)
12 months	NE (NE, NE)	92.3 (86.6, 98.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	5 (3.6)
Number of Subjects Censored, n (%)	76 (100.0)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.180

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.5 (91.6, 99.4)
6 months	100.0 (100.0, 100.0)	95.5 (91.6, 99.4)
9 months	NE (NE, NE)	95.5 (91.6, 99.4)
12 months	NE (NE, NE)	95.5 (91.6, 99.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	5 (3.6)
Number of Subjects Censored, n (%)	75 (98.7)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.226 (1.105)
95% CI		(0.255, 19.398)
Log-rank p-value		0.436

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.1 (92.8, 99.5)
6 months	98.6 (96.0, 100.0)	96.1 (92.8, 99.5)
9 months	NE (NE, NE)	96.1 (92.8, 99.5)
12 months	NE (NE, NE)	96.1 (92.8, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	16 (21.1)	59 (42.1)
Number of Subjects Censored, n (%)	60 (78.9)	81 (57.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.15, NE)	0.69 (0.46, 0.72)
Median (95% CI)	NE (NE, NE)	11.53 (2.83, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.165 (0.288)
95% CI		(1.231, 3.806)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.3 (67.4, 87.3)	58.4 (50.0, 66.7)
6 months	77.3 (67.4, 87.3)	56.9 (48.2, 65.5)
9 months	NE (NE, NE)	56.9 (48.2, 65.5)
12 months	NE (NE, NE)	42.6 (17.7, 67.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	26 (18.6)
Number of Subjects Censored, n (%)	73 (96.1)	114 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.229 (0.617)
95% CI		(1.560, 17.526)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (91.5, 100.0)	81.3 (74.7, 87.8)
6 months	95.9 (91.5, 100.0)	81.3 (74.7, 87.8)
9 months	NE (NE, NE)	81.3 (74.7, 87.8)
12 months	NE (NE, NE)	81.3 (74.7, 87.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	7 (9.2)	15 (10.7)
Number of Subjects Censored, n (%)	69 (90.8)	125 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (NE, NE)
Median (95% CI)	NE (NE, NE)	14.32 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	14.32 (NE, NE)
Min, Max	0.0, 8.4*	0.2, 14.3
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.926 (0.483)
95% CI		(0.360, 2.384)
Log-rank p-value		0.937

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (83.6, 97.2)	89.8 (84.4, 95.1)
6 months	90.4 (83.6, 97.2)	89.8 (84.4, 95.1)
9 months	NE (NE, NE)	87.1 (79.7, 94.4)
12 months	NE (NE, NE)	87.1 (79.7, 94.4)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.74	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	8 (10.5)	14 (10.0)
Number of Subjects Censored, n (%)	68 (89.5)	126 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.739 (0.466)
95% CI		(0.297, 1.841)
Log-rank p-value		0.544

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (80.7, 96.1)	90.0 (84.8, 95.3)
6 months	88.4 (80.7, 96.1)	90.0 (84.8, 95.3)
9 months	NE (NE, NE)	90.0 (84.8, 95.3)
12 months	NE (NE, NE)	75.0 (47.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	11 (7.9)
Number of Subjects Censored, n (%)	75 (98.7)	129 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		10.917 (1.146)
95% CI		(1.154, 103.242)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	91.8 (87.1, 96.4)
6 months	98.6 (96.0, 100.0)	91.8 (87.1, 96.4)
9 months	NE (NE, NE)	91.8 (87.1, 96.4)
12 months	NE (NE, NE)	91.8 (87.1, 96.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	1 (0.7)
Number of Subjects Censored, n (%)	76 (100.0)	139 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.3 (97.9, 100.0)
6 months	100.0 (100.0, 100.0)	99.3 (97.9, 100.0)
9 months	NE (NE, NE)	99.3 (97.9, 100.0)
12 months	NE (NE, NE)	99.3 (97.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	12 (15.8)	56 (40.0)
Number of Subjects Censored, n (%)	64 (84.2)	84 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	0.89 (0.66, 1.77)
Median (95% CI)	NE (NE, NE)	NE (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.147 (0.322)
95% CI		(1.673, 5.920)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (73.5, 91.7)	59.0 (50.4, 67.6)
6 months	82.6 (73.5, 91.7)	57.4 (48.4, 66.3)
9 months	NE (NE, NE)	53.3 (41.9, 64.6)
12 months	NE (NE, NE)	53.3 (41.9, 64.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	2.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	53 (37.9)
Number of Subjects Censored, n (%)	72 (94.7)	87 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.89 (0.69, 1.94)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.071 (0.522)
95% CI		(3.258, 25.255)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.5 (87.2, 99.8)	61.7 (53.3, 70.1)
6 months	93.5 (87.2, 99.8)	60.0 (51.2, 68.8)
9 months	NE (NE, NE)	55.7 (44.2, 67.2)
12 months	NE (NE, NE)	55.7 (44.2, 67.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	9 (11.8)	42 (30.0)
Number of Subjects Censored, n (%)	67 (88.2)	98 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.53 (0.95, 7.20)
Median (95% CI)	NE (NE, NE)	9.76 (7.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.676 (0.381)
95% CI		(1.269, 5.642)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (80.3, 95.3)	72.0 (64.2, 79.7)
6 months	87.8 (80.3, 95.3)	69.9 (61.3, 78.4)
9 months	NE (NE, NE)	56.5 (40.5, 72.5)
12 months	NE (NE, NE)	48.4 (28.4, 68.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	13 (9.3)
Number of Subjects Censored, n (%)	72 (94.7)	127 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.655 (0.585)
95% CI		(0.526, 5.212)
Log-rank p-value		0.252

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (89.0, 99.8)	90.5 (85.3, 95.6)
6 months	94.4 (89.0, 99.8)	88.3 (81.6, 94.9)
9 months	NE (NE, NE)	88.3 (81.6, 94.9)
12 months	NE (NE, NE)	88.3 (81.6, 94.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	15 (10.7)
Number of Subjects Censored, n (%)	75 (98.7)	125 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.586 (1.057)
95% CI		(1.082, 68.130)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	90.2 (85.1, 95.3)
6 months	98.7 (96.1, 100.0)	90.2 (85.1, 95.3)
9 months	NE (NE, NE)	82.4 (70.9, 93.8)
12 months	NE (NE, NE)	82.4 (70.9, 93.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	5 (3.6)
Number of Subjects Censored, n (%)	74 (97.4)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.4, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.662 (0.845)
95% CI		(0.317, 8.699)
Log-rank p-value		0.543

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.7, 100.0)	97.1 (94.4, 99.9)
6 months	97.4 (93.7, 100.0)	95.0 (90.0, 100.0)
9 months	NE (NE, NE)	95.0 (90.0, 100.0)
12 months	NE (NE, NE)	95.0 (90.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	6 (4.3)
Number of Subjects Censored, n (%)	75 (98.7)	134 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.165 (1.100)
95% CI		(0.251, 18.690)
Log-rank p-value		0.477

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	95.5 (91.9, 99.0)
6 months	98.6 (96.0, 100.0)	95.5 (91.9, 99.0)
9 months	NE (NE, NE)	95.5 (91.9, 99.0)
12 months	NE (NE, NE)	95.5 (91.9, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	3 (2.1)
Number of Subjects Censored, n (%)	76 (100.0)	137 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.64, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.299

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
9 months	NE (NE, NE)	92.0 (79.4, 100.0)
12 months	NE (NE, NE)	92.0 (79.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	2 (1.4)
Number of Subjects Censored, n (%)	76 (100.0)	138 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.670

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (95.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.2 (95.7, 100.0)
9 months	NE (NE, NE)	98.2 (95.7, 100.0)
12 months	NE (NE, NE)	98.2 (95.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	10 (13.2)	56 (40.0)
Number of Subjects Censored, n (%)	66 (86.8)	84 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (4.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.996 (0.346)
95% CI		(1.521, 5.904)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (78.6, 94.3)	60.3 (51.8, 68.8)
6 months	86.5 (78.6, 94.3)	55.0 (44.5, 65.5)
9 months	NE (NE, NE)	50.4 (37.5, 63.3)
12 months	NE (NE, NE)	50.4 (37.5, 63.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.51

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	32 (22.9)
Number of Subjects Censored, n (%)	74 (97.4)	108 (77.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.86 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.247 (0.731)
95% CI		(1.968, 34.560)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.7, 100.0)	76.9 (69.7, 84.1)
6 months	97.3 (93.7, 100.0)	74.4 (66.0, 82.8)
9 months	NE (NE, NE)	74.4 (66.0, 82.8)
12 months	NE (NE, NE)	74.4 (66.0, 82.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	4 (2.9)
Number of Subjects Censored, n (%)	74 (97.4)	136 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (0.889)
95% CI		(0.183, 5.965)
Log-rank p-value		0.979

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.7, 100.0)	96.5 (93.1, 100.0)
6 months	97.3 (93.7, 100.0)	96.5 (93.1, 100.0)
9 months	NE (NE, NE)	96.5 (93.1, 100.0)
12 months	NE (NE, NE)	96.5 (93.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	6 (4.3)
Number of Subjects Censored, n (%)	75 (98.7)	134 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.807 (1.090)
95% CI		(0.332, 23.753)
Log-rank p-value		0.332

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.0)
6 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.0)
9 months	NE (NE, NE)	95.6 (92.2, 99.0)
12 months	NE (NE, NE)	95.6 (92.2, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	12 (15.8)	37 (26.4)
Number of Subjects Censored, n (%)	64 (84.2)	103 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.50, NE)	2.37 (1.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.639 (0.339)
95% CI		(0.844, 3.183)
Log-rank p-value		0.178

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (72.8, 91.6)	74.0 (66.5, 81.5)
6 months	82.2 (72.8, 91.6)	72.4 (64.5, 80.3)
9 months	NE (NE, NE)	69.5 (60.1, 78.9)
12 months	NE (NE, NE)	69.5 (60.1, 78.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	15 (10.7)
Number of Subjects Censored, n (%)	74 (97.4)	125 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.647 (0.758)
95% CI		(0.826, 16.105)
Log-rank p-value		0.069

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.4, 100.0)	89.8 (84.7, 94.9)
6 months	97.2 (93.4, 100.0)	89.8 (84.7, 94.9)
9 months	NE (NE, NE)	86.9 (79.5, 94.3)
12 months	NE (NE, NE)	86.9 (79.5, 94.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	5 (6.6)	1 (0.7)
Number of Subjects Censored, n (%)	71 (93.4)	139 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.093 (1.102)
95% CI		(0.011, 0.807)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (87.6, 99.0)	99.2 (97.7, 100.0)
6 months	93.3 (87.6, 99.0)	99.2 (97.7, 100.0)
9 months	NE (NE, NE)	99.2 (97.7, 100.0)
12 months	NE (NE, NE)	99.2 (97.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	5 (3.6)
Number of Subjects Censored, n (%)	75 (98.7)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.567 (1.123)
95% CI		(0.284, 23.198)
Log-rank p-value		0.470

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	96.2 (93.0, 99.5)
6 months	98.6 (96.0, 100.0)	96.2 (93.0, 99.5)
9 months	NE (NE, NE)	96.2 (93.0, 99.5)
12 months	NE (NE, NE)	96.2 (93.0, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	9 (11.8)	37 (26.4)
Number of Subjects Censored, n (%)	67 (88.2)	103 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	3.91 (2.53, 5.78)
Median (95% CI)	NE (NE, NE)	11.96 (6.54, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.948 (0.381)
95% CI		(0.924, 4.106)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (79.6, 96.0)	78.2 (71.0, 85.4)
6 months	81.9 (68.5, 95.4)	65.1 (54.1, 76.2)
9 months	NE (NE, NE)	61.5 (49.0, 74.0)
12 months	NE (NE, NE)	41.0 (7.1, 74.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	4 (5.3)	25 (17.9)
Number of Subjects Censored, n (%)	72 (94.7)	115 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.38 (3.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.5, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.151 (0.546)
95% CI		(1.080, 9.192)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (89.4, 99.7)	84.2 (77.8, 90.6)
6 months	94.6 (89.4, 99.7)	76.6 (66.9, 86.2)
9 months	NE (NE, NE)	69.6 (53.9, 85.3)
12 months	NE (NE, NE)	69.6 (53.9, 85.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	3 (2.1)
Number of Subjects Censored, n (%)	75 (98.7)	137 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.978 (1.216)
95% CI		(0.090, 10.606)
Log-rank p-value		0.735

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	98.5 (96.4, 100.0)
6 months	98.6 (96.0, 100.0)	97.0 (93.4, 100.0)
9 months	NE (NE, NE)	97.0 (93.4, 100.0)
12 months	NE (NE, NE)	97.0 (93.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	11 (14.5)	23 (16.4)
Number of Subjects Censored, n (%)	65 (85.5)	117 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	11.53 (3.71, NE)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (5.78, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.831 (0.395)
95% CI		(0.383, 1.801)
Log-rank p-value		0.742

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.3 (79.5, 95.1)	87.7 (81.9, 93.4)
6 months	59.5 (23.7, 95.4)	77.7 (68.1, 87.2)
9 months	NE (NE, NE)	77.7 (68.1, 87.2)
12 months	NE (NE, NE)	62.1 (33.8, 90.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	6 (4.3)
Number of Subjects Censored, n (%)	73 (96.1)	134 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.111 (0.726)
95% CI		(0.268, 4.613)
Log-rank p-value		0.853

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.8, 100.0)	95.5 (92.0, 99.0)
6 months	89.9 (75.4, 100.0)	95.5 (92.0, 99.0)
9 months	NE (NE, NE)	95.5 (92.0, 99.0)
12 months	NE (NE, NE)	95.5 (92.0, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	3 (2.1)
Number of Subjects Censored, n (%)	75 (98.7)	137 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (11.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.046 (1.246)
95% CI		(0.091, 12.012)
Log-rank p-value		0.797

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.2, 100.0)
6 months	92.3 (77.8, 100.0)	98.4 (96.2, 100.0)
9 months	NE (NE, NE)	98.4 (96.2, 100.0)
12 months	NE (NE, NE)	82.0 (52.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	6 (4.3)
Number of Subjects Censored, n (%)	76 (100.0)	134 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (92.3, 99.5)
6 months	100.0 (100.0, 100.0)	93.6 (88.0, 99.3)
9 months	NE (NE, NE)	93.6 (88.0, 99.3)
12 months	NE (NE, NE)	93.6 (88.0, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	7 (9.2)	25 (17.9)
Number of Subjects Censored, n (%)	69 (90.8)	115 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.77 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.553 (0.440)
95% CI		(0.655, 3.682)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (81.7, 97.1)	84.8 (78.7, 91.0)
6 months	89.4 (81.7, 97.1)	77.1 (67.8, 86.4)
9 months	NE (NE, NE)	73.5 (62.2, 84.8)
12 months	NE (NE, NE)	73.5 (62.2, 84.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	12 (8.6)
Number of Subjects Censored, n (%)	73 (96.1)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.660 (0.676)
95% CI		(0.441, 6.249)
Log-rank p-value		0.406

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (88.5, 100.0)	92.9 (88.4, 97.4)
6 months	94.7 (88.5, 100.0)	87.0 (79.1, 94.9)
9 months	NE (NE, NE)	87.0 (79.1, 94.9)
12 months	NE (NE, NE)	87.0 (79.1, 94.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	11 (7.9)
Number of Subjects Censored, n (%)	76 (100.0)	129 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (87.2, 96.5)
6 months	100.0 (100.0, 100.0)	91.8 (87.2, 96.5)
9 months	NE (NE, NE)	91.8 (87.2, 96.5)
12 months	NE (NE, NE)	91.8 (87.2, 96.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	29 (20.7)
Number of Subjects Censored, n (%)	76 (100.0)	111 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.1 (75.5, 88.8)
6 months	100.0 (100.0, 100.0)	72.4 (62.2, 82.5)
9 months	NE (NE, NE)	68.6 (56.5, 80.6)
12 months	NE (NE, NE)	68.6 (56.5, 80.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	29 (20.7)
Number of Subjects Censored, n (%)	76 (100.0)	111 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.1 (75.5, 88.8)
6 months	100.0 (100.0, 100.0)	72.4 (62.2, 82.5)
9 months	NE (NE, NE)	68.6 (56.5, 80.6)
12 months	NE (NE, NE)	68.6 (56.5, 80.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	5 (6.6)	20 (14.3)
Number of Subjects Censored, n (%)	71 (93.4)	120 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.74, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.776 (0.520)
95% CI		(0.641, 4.916)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (86.1, 98.9)	86.0 (79.7, 92.3)
6 months	92.5 (86.1, 98.9)	83.5 (76.5, 90.5)
9 months	NE (NE, NE)	80.1 (70.8, 89.4)
12 months	NE (NE, NE)	80.1 (70.8, 89.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	3 (3.9)	10 (7.1)
Number of Subjects Censored, n (%)	73 (96.1)	130 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.333 (0.691)
95% CI		(0.344, 5.164)
Log-rank p-value		0.677

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (90.5, 100.0)	92.8 (87.8, 97.7)
6 months	95.5 (90.5, 100.0)	91.4 (85.9, 97.0)
9 months	NE (NE, NE)	88.0 (79.6, 96.4)
12 months	NE (NE, NE)	88.0 (79.6, 96.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	0	5 (3.6)
Number of Subjects Censored, n (%)	76 (100.0)	135 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.099

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (92.1, 99.5)
6 months	100.0 (100.0, 100.0)	95.8 (92.1, 99.5)
9 months	NE (NE, NE)	95.8 (92.1, 99.5)
12 months	NE (NE, NE)	95.8 (92.1, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	4 (2.9)
Number of Subjects Censored, n (%)	75 (98.7)	136 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.558 (1.167)
95% CI		(0.260, 25.186)
Log-rank p-value		0.390

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (94.7, 100.0)	96.9 (94.0, 99.9)
6 months	98.2 (94.7, 100.0)	96.9 (94.0, 99.9)
9 months	NE (NE, NE)	96.9 (94.0, 99.9)
12 months	NE (NE, NE)	96.9 (94.0, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	8 (10.5)	17 (12.1)
Number of Subjects Censored, n (%)	68 (89.5)	123 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.740 (0.448)
95% CI		(0.308, 1.779)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.7 (81.4, 96.1)	89.5 (84.1, 94.9)
6 months	88.7 (81.4, 96.1)	84.0 (75.9, 92.1)
9 months	NE (NE, NE)	84.0 (75.9, 92.1)
12 months	NE (NE, NE)	75.6 (58.3, 92.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	2 (2.6)	9 (6.4)
Number of Subjects Censored, n (%)	74 (97.4)	131 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.553 (0.802)
95% CI		(0.322, 7.484)
Log-rank p-value		0.660

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.7, 100.0)	94.0 (89.7, 98.3)
6 months	96.9 (92.7, 100.0)	92.5 (87.4, 97.7)
9 months	NE (NE, NE)	92.5 (87.4, 97.7)
12 months	NE (NE, NE)	83.3 (65.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	1 (1.3)	3 (2.1)
Number of Subjects Censored, n (%)	75 (98.7)	137 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.420 (1.174)
95% CI		(0.142, 14.189)
Log-rank p-value		0.761

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	97.8 (95.2, 100.0)
6 months	98.7 (96.1, 100.0)	97.8 (95.2, 100.0)
9 months	NE (NE, NE)	97.8 (95.2, 100.0)
12 months	NE (NE, NE)	97.8 (95.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	81 (60.0)	193 (67.7)
Number of Subjects Censored, n (%)	54 (40.0)	92 (32.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.36, 0.72)	0.43 (0.30, 0.66)
Median (95% CI)	1.48 (0.95, 2.56)	1.41 (0.95, 2.17)
75% percentile (95% CI)	NE (3.71, NE)	7.29 (4.96, NE)
Min, Max	0.0, 13.0*	0.0, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.082 (0.135)
95% CI		(0.830, 1.412)
Log-rank p-value		0.567

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.1 (31.5, 48.6)	39.1 (33.3, 44.8)
6 months	34.9 (24.7, 45.0)	27.7 (21.5, 33.8)
9 months	34.9 (24.7, 45.0)	21.5 (14.2, 28.8)
12 months	34.9 (24.7, 45.0)	21.5 (14.2, 28.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.35	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	36 (26.7)	98 (34.4)
Number of Subjects Censored, n (%)	99 (73.3)	187 (65.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.72, NE)	0.99 (0.69, 2.43)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.243 (0.197)
95% CI		(0.845, 1.829)
Log-rank p-value		0.298

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.0 (64.1, 79.9)	67.0 (61.4, 72.5)
6 months	72.0 (64.1, 79.9)	64.0 (58.1, 70.0)
9 months	72.0 (64.1, 79.9)	63.0 (56.8, 69.1)
12 months	72.0 (64.1, 79.9)	63.0 (56.8, 69.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	19 (14.1)	56 (19.6)
Number of Subjects Censored, n (%)	116 (85.9)	229 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.325 (0.270)
95% CI		(0.781, 2.247)
Log-rank p-value		0.298

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (78.5, 91.2)	81.3 (76.7, 85.9)
6 months	84.9 (78.5, 91.2)	79.8 (74.8, 84.8)
9 months	84.9 (78.5, 91.2)	76.7 (70.4, 83.1)
12 months	84.9 (78.5, 91.2)	76.7 (70.4, 83.1)
18 months	NE (NE, NE)	76.7 (70.4, 83.1)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	16 (11.9)	22 (7.7)
Number of Subjects Censored, n (%)	119 (88.1)	263 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.481 (0.346)
95% CI		(0.244, 0.947)
Log-rank p-value		0.031

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (81.2, 93.1)	94.1 (91.4, 96.9)
6 months	87.1 (81.2, 93.1)	91.7 (88.0, 95.3)
9 months	87.1 (81.2, 93.1)	89.6 (85.0, 94.1)
12 months	87.1 (81.2, 93.1)	89.6 (85.0, 94.1)
18 months	NE (NE, NE)	89.6 (85.0, 94.1)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	4 (3.0)	41 (14.4)
Number of Subjects Censored, n (%)	131 (97.0)	244 (85.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.747 (0.526)
95% CI		(1.693, 13.313)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (93.7, 99.9)	86.7 (82.7, 90.7)
6 months	96.8 (93.7, 99.9)	84.8 (80.3, 89.3)
9 months	96.8 (93.7, 99.9)	83.3 (78.1, 88.6)
12 months	96.8 (93.7, 99.9)	83.3 (78.1, 88.6)
18 months	NE (NE, NE)	83.3 (78.1, 88.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	16 (11.9)	11 (3.9)
Number of Subjects Censored, n (%)	119 (88.1)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.235 (0.409)
95% CI		(0.106, 0.524)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (83.8, 94.6)	97.4 (95.6, 99.3)
6 months	83.0 (73.2, 92.9)	95.0 (91.9, 98.0)
9 months	83.0 (73.2, 92.9)	95.0 (91.9, 98.0)
12 months	83.0 (73.2, 92.9)	95.0 (91.9, 98.0)
18 months	NE (NE, NE)	95.0 (91.9, 98.0)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	11 (8.1)	11 (3.9)
Number of Subjects Censored, n (%)	124 (91.9)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.393 (0.438)
95% CI		(0.167, 0.927)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (86.1, 96.2)	96.4 (94.2, 98.6)
6 months	91.2 (86.1, 96.2)	96.4 (94.2, 98.6)
9 months	91.2 (86.1, 96.2)	93.4 (87.2, 99.6)
12 months	91.2 (86.1, 96.2)	93.4 (87.2, 99.6)
18 months	NE (NE, NE)	93.4 (87.2, 99.6)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	8 (2.8)
Number of Subjects Censored, n (%)	132 (97.8)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (0.711)
95% CI		(0.196, 3.193)
Log-rank p-value		0.646

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.7, 100.0)	98.6 (97.1, 100.0)
6 months	97.5 (94.7, 100.0)	97.5 (95.4, 99.5)
9 months	97.5 (94.7, 100.0)	97.5 (95.4, 99.5)
12 months	97.5 (94.7, 100.0)	90.3 (80.4, 100.0)
18 months	NE (NE, NE)	90.3 (80.4, 100.0)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	134 (99.3)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.060 (1.086)
95% CI		(0.245, 17.321)
Log-rank p-value		0.515

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	98.1 (96.5, 99.8)
6 months	98.6 (96.0, 100.0)	96.7 (94.2, 99.2)
9 months	98.6 (96.0, 100.0)	96.7 (94.2, 99.2)
12 months	98.6 (96.0, 100.0)	96.7 (94.2, 99.2)
18 months	NE (NE, NE)	96.7 (94.2, 99.2)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	3 (1.1)
Number of Subjects Censored, n (%)	133 (98.5)	282 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.394 (1.003)
95% CI		(0.055, 2.808)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	99.6 (98.9, 100.0)
6 months	98.5 (96.5, 100.0)	98.0 (95.5, 100.0)
9 months	98.5 (96.5, 100.0)	98.0 (95.5, 100.0)
12 months	98.5 (96.5, 100.0)	98.0 (95.5, 100.0)
18 months	NE (NE, NE)	98.0 (95.5, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	74 (54.8)	184 (64.6)
Number of Subjects Censored, n (%)	61 (45.2)	101 (35.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.53 (0.26, 0.69)	0.66 (0.46, 0.69)
Median (95% CI)	1.94 (1.22, 5.36)	1.61 (1.08, 2.37)
75% percentile (95% CI)	5.59 (5.36, NE)	7.79 (5.19, NE)
Min, Max	0.0, 5.6*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.026 (0.142)
95% CI		(0.777, 1.354)
Log-rank p-value		0.851

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	42.9 (33.3, 52.4)	42.4 (36.5, 48.2)
6 months	NE (NE, NE)	29.1 (22.4, 35.8)
9 months	NE (NE, NE)	23.7 (16.4, 31.0)
12 months	NE (NE, NE)	19.8 (10.4, 29.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.54

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	10 (7.4)	70 (24.6)
Number of Subjects Censored, n (%)	125 (92.6)	215 (75.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.53, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.069 (0.342)
95% CI		(1.570, 5.999)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (87.8, 96.9)	79.9 (75.2, 84.7)
6 months	92.4 (87.8, 96.9)	71.7 (65.1, 78.3)
9 months	92.4 (87.8, 96.9)	67.8 (60.1, 75.4)
12 months	92.4 (87.8, 96.9)	58.1 (39.3, 76.8)
18 months	NE (NE, NE)	58.1 (39.3, 76.8)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	24 (17.8)	49 (17.2)
Number of Subjects Censored, n (%)	111 (82.2)	236 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.705 (0.260)
95% CI		(0.424, 1.174)
Log-rank p-value		0.183

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (75.5, 88.5)	85.9 (81.6, 90.1)
6 months	82.0 (75.5, 88.5)	79.2 (73.3, 85.0)
9 months	82.0 (75.5, 88.5)	78.0 (71.9, 84.2)
12 months	82.0 (75.5, 88.5)	75.1 (67.0, 83.3)
18 months	NE (NE, NE)	75.1 (67.0, 83.3)
Median Follow-up Time (months)	2.63	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	22 (16.3)	63 (22.1)
Number of Subjects Censored, n (%)	113 (83.7)	222 (77.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	6.18 (3.68, 12.25)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.097 (0.254)
95% CI		(0.666, 1.806)
Log-rank p-value		0.739

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (74.1, 89.4)	81.7 (77.1, 86.3)
6 months	75.9 (62.8, 89.1)	75.8 (69.9, 81.7)
9 months	75.9 (62.8, 89.1)	71.8 (64.6, 79.0)
12 months	75.9 (62.8, 89.1)	67.6 (57.1, 78.1)
18 months	NE (NE, NE)	56.3 (34.4, 78.3)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	15 (11.1)	38 (13.3)
Number of Subjects Censored, n (%)	120 (88.9)	247 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.012 (0.311)
95% CI		(0.550, 1.862)
Log-rank p-value		0.919

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (80.6, 94.4)	87.9 (84.0, 91.8)
6 months	84.9 (76.6, 93.3)	84.6 (79.7, 89.6)
9 months	84.9 (76.6, 93.3)	83.2 (77.6, 88.8)
12 months	84.9 (76.6, 93.3)	83.2 (77.6, 88.8)
18 months	NE (NE, NE)	83.2 (77.6, 88.8)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	16 (11.9)	49 (17.2)
Number of Subjects Censored, n (%)	119 (88.1)	236 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	18.04 (5.22, NE)
Median (95% CI)	NE (5.36, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.005 (0.300)
95% CI		(0.559, 1.808)
Log-rank p-value		0.935

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (83.0, 94.3)	87.2 (83.2, 91.2)
6 months	75.4 (56.1, 94.6)	79.9 (74.1, 85.7)
9 months	75.4 (56.1, 94.6)	75.8 (68.6, 82.9)
12 months	75.4 (56.1, 94.6)	75.8 (68.6, 82.9)
18 months	NE (NE, NE)	75.8 (68.6, 82.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	4 (3.0)	34 (11.9)
Number of Subjects Censored, n (%)	131 (97.0)	251 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.656 (0.533)
95% CI		(1.285, 10.401)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (93.7, 99.9)	89.3 (85.6, 92.9)
6 months	96.8 (93.7, 99.9)	87.8 (83.7, 91.9)
9 months	96.8 (93.7, 99.9)	84.6 (78.7, 90.5)
12 months	96.8 (93.7, 99.9)	84.6 (78.7, 90.5)
18 months	NE (NE, NE)	84.6 (78.7, 90.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	25 (8.8)
Number of Subjects Censored, n (%)	130 (96.3)	260 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.880 (0.502)
95% CI		(0.703, 5.028)
Log-rank p-value		0.223

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.9, 99.9)	93.1 (90.0, 96.1)
6 months	86.1 (66.1, 100.0)	89.4 (85.1, 93.7)
9 months	NE (NE, NE)	87.5 (81.9, 93.1)
12 months	NE (NE, NE)	87.5 (81.9, 93.1)
18 months	NE (NE, NE)	87.5 (81.9, 93.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	4 (3.0)	8 (2.8)
Number of Subjects Censored, n (%)	131 (97.0)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.788 (0.631)
95% CI		(0.229, 2.714)
Log-rank p-value		0.693

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (93.8, 99.9)	97.5 (95.7, 99.3)
6 months	96.8 (93.8, 99.9)	97.5 (95.7, 99.3)
9 months	96.8 (93.8, 99.9)	95.7 (91.8, 99.7)
12 months	96.8 (93.8, 99.9)	95.7 (91.8, 99.7)
18 months	NE (NE, NE)	95.7 (91.8, 99.7)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	5 (1.8)
Number of Subjects Censored, n (%)	134 (99.3)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.258 (1.096)
95% CI		(0.263, 19.350)
Log-rank p-value		0.449

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	98.2 (96.7, 99.8)
6 months	99.1 (97.5, 100.0)	98.2 (96.7, 99.8)
9 months	99.1 (97.5, 100.0)	98.2 (96.7, 99.8)
12 months	99.1 (97.5, 100.0)	98.2 (96.7, 99.8)
18 months	NE (NE, NE)	98.2 (96.7, 99.8)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	2 (0.7)
Number of Subjects Censored, n (%)	130 (96.3)	283 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.145 (0.858)
95% CI		(0.027, 0.776)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.7, 99.5)	99.3 (98.2, 100.0)
6 months	96.1 (92.7, 99.5)	99.3 (98.2, 100.0)
9 months	96.1 (92.7, 99.5)	99.3 (98.2, 100.0)
12 months	96.1 (92.7, 99.5)	99.3 (98.2, 100.0)
18 months	NE (NE, NE)	99.3 (98.2, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	0	10 (3.5)
Number of Subjects Censored, n (%)	135 (100.0)	275 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.6)
6 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.6)
9 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.6)
12 months	100.0 (100.0, 100.0)	96.3 (94.0, 98.6)
18 months	NE (NE, NE)	96.3 (94.0, 98.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	34 (25.2)	122 (42.8)
Number of Subjects Censored, n (%)	101 (74.8)	163 (57.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.85, NE)	1.45 (0.95, 1.81)
Median (95% CI)	10.18 (NE, NE)	9.43 (3.94, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.542 (0.198)
95% CI		(1.046, 2.272)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.7 (68.3, 83.0)	60.7 (54.8, 66.6)
6 months	72.6 (63.5, 81.8)	53.0 (46.3, 59.6)
9 months	72.6 (63.5, 81.8)	51.1 (44.1, 58.0)
12 months	0.0 (NE, NE)	47.7 (38.5, 56.8)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	21 (15.6)	72 (25.3)
Number of Subjects Censored, n (%)	114 (84.4)	213 (74.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.58 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.464 (0.252)
95% CI		(0.893, 2.400)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (76.8, 89.9)	77.1 (72.0, 82.1)
6 months	83.4 (76.8, 89.9)	72.1 (66.2, 77.9)
9 months	83.4 (76.8, 89.9)	70.7 (64.4, 77.0)
12 months	83.4 (76.8, 89.9)	67.8 (59.5, 76.1)
18 months	NE (NE, NE)	67.8 (59.5, 76.1)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	14 (4.9)
Number of Subjects Censored, n (%)	133 (98.5)	271 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.646 (0.764)
95% CI		(0.592, 11.818)
Log-rank p-value		0.184

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	95.5 (93.1, 98.0)
6 months	98.5 (96.5, 100.0)	94.2 (91.2, 97.3)
9 months	98.5 (96.5, 100.0)	94.2 (91.2, 97.3)
12 months	98.5 (96.5, 100.0)	94.2 (91.2, 97.3)
18 months	NE (NE, NE)	94.2 (91.2, 97.3)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	4 (3.0)	11 (3.9)
Number of Subjects Censored, n (%)	131 (97.0)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.928 (0.602)
95% CI		(0.285, 3.023)
Log-rank p-value		0.954

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	97.0 (94.9, 99.0)
6 months	94.9 (88.8, 100.0)	94.9 (91.8, 98.0)
9 months	94.9 (88.8, 100.0)	94.9 (91.8, 98.0)
12 months	94.9 (88.8, 100.0)	94.9 (91.8, 98.0)
18 months	NE (NE, NE)	94.9 (91.8, 98.0)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	11 (3.9)
Number of Subjects Censored, n (%)	134 (99.3)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.985 (1.055)
95% CI		(0.504, 31.501)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.8, 100.0)	96.6 (94.4, 98.8)
6 months	99.2 (97.8, 100.0)	96.0 (93.6, 98.5)
9 months	99.2 (97.8, 100.0)	93.3 (87.5, 99.1)
12 months	99.2 (97.8, 100.0)	93.3 (87.5, 99.1)
18 months	NE (NE, NE)	93.3 (87.5, 99.1)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	5 (1.8)
Number of Subjects Censored, n (%)	132 (97.8)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.623 (0.759)
95% CI		(0.141, 2.758)
Log-rank p-value		0.541

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	98.5 (97.0, 100.0)
6 months	97.7 (95.2, 100.0)	98.5 (97.0, 100.0)
9 months	97.7 (95.2, 100.0)	96.7 (92.9, 100.0)
12 months	97.7 (95.2, 100.0)	96.7 (92.9, 100.0)
18 months	NE (NE, NE)	96.7 (92.9, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	0	14 (4.9)
Number of Subjects Censored, n (%)	135 (100.0)	271 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (93.7, 98.3)
6 months	100.0 (100.0, 100.0)	94.3 (90.9, 97.6)
9 months	100.0 (100.0, 100.0)	92.7 (88.2, 97.2)
12 months	100.0 (100.0, 100.0)	92.7 (88.2, 97.2)
18 months	NE (NE, NE)	92.7 (88.2, 97.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	134 (99.3)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.311 (1.086)
95% CI		(0.275, 19.415)
Log-rank p-value		0.385

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.8, 100.0)	97.7 (95.9, 99.5)
6 months	99.2 (97.8, 100.0)	97.7 (95.9, 99.5)
9 months	99.2 (97.8, 100.0)	96.6 (93.9, 99.4)
12 months	99.2 (97.8, 100.0)	96.6 (93.9, 99.4)
18 months	NE (NE, NE)	96.6 (93.9, 99.4)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	10 (3.5)
Number of Subjects Censored, n (%)	133 (98.5)	275 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.824 (0.795)
95% CI		(0.384, 8.665)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	97.5 (95.7, 99.3)
6 months	98.5 (96.4, 100.0)	96.5 (93.9, 99.2)
9 months	98.5 (96.4, 100.0)	92.9 (86.9, 98.8)
12 months	98.5 (96.4, 100.0)	92.9 (86.9, 98.8)
18 months	NE (NE, NE)	92.9 (86.9, 98.8)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	9 (3.2)
Number of Subjects Censored, n (%)	133 (98.5)	276 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 10.2	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.570 (0.798)
95% CI		(0.329, 7.501)
Log-rank p-value		0.583

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.8, 100.0)	96.7 (94.6, 98.8)
6 months	99.2 (97.8, 100.0)	96.7 (94.6, 98.8)
9 months	99.2 (97.8, 100.0)	96.7 (94.6, 98.8)
12 months	0.0 (NE, NE)	96.7 (94.6, 98.8)
18 months	0.0 (NE, NE)	96.7 (94.6, 98.8)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	0	6 (2.1)
Number of Subjects Censored, n (%)	135 (100.0)	279 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.285

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (97.6, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (93.7, 99.5)
9 months	100.0 (100.0, 100.0)	96.6 (93.7, 99.5)
12 months	100.0 (100.0, 100.0)	96.6 (93.7, 99.5)
18 months	NE (NE, NE)	96.6 (93.7, 99.5)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	39 (28.9)	119 (41.8)
Number of Subjects Censored, n (%)	96 (71.1)	166 (58.2)
Time to first TEAE (months)		
25% percentile (95% CI)	2.17 (0.95, 5.59)	1.58 (0.95, 1.84)
Median (95% CI)	5.82 (5.59, NE)	7.85 (5.78, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (16.79, NE)
Min, Max	0.0, 6.5*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.223 (0.189)
95% CI		(0.844, 1.772)
Log-rank p-value		0.300

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.3 (64.3, 80.2)	62.9 (57.1, 68.6)
6 months	37.0 (4.6, 69.3)	55.3 (48.5, 62.1)
9 months	NE (NE, NE)	48.4 (40.3, 56.4)
12 months	NE (NE, NE)	48.4 (40.3, 56.4)
18 months	NE (NE, NE)	36.3 (14.9, 57.6)
Median Follow-up Time (months)	2.76	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	13 (9.6)	34 (11.9)
Number of Subjects Censored, n (%)	122 (90.4)	251 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 6.5*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.922 (0.339)
95% CI		(0.474, 1.793)
Log-rank p-value		0.759

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (83.9, 95.6)	89.8 (86.2, 93.5)
6 months	53.2 (8.8, 97.6)	86.7 (82.0, 91.4)
9 months	NE (NE, NE)	82.5 (75.9, 89.0)
12 months	NE (NE, NE)	82.5 (75.9, 89.0)
18 months	NE (NE, NE)	82.5 (75.9, 89.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	6 (4.4)	31 (10.9)
Number of Subjects Censored, n (%)	129 (95.6)	254 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.922 (0.455)
95% CI		(0.788, 4.690)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.8, 99.5)	91.0 (87.5, 94.5)
6 months	85.4 (65.5, 100.0)	87.1 (82.4, 91.9)
9 months	NE (NE, NE)	84.4 (78.4, 90.4)
12 months	NE (NE, NE)	84.4 (78.4, 90.4)
18 months	NE (NE, NE)	84.4 (78.4, 90.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	30 (10.5)
Number of Subjects Censored, n (%)	130 (96.3)	255 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.143 (0.492)
95% CI		(0.817, 5.625)
Log-rank p-value		0.101

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.0, 99.9)	91.1 (87.6, 94.5)
6 months	86.2 (66.1, 100.0)	88.8 (84.6, 93.1)
9 months	NE (NE, NE)	84.9 (78.9, 90.9)
12 months	NE (NE, NE)	84.9 (78.9, 90.9)
18 months	NE (NE, NE)	84.9 (78.9, 90.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	10 (7.4)	20 (7.0)
Number of Subjects Censored, n (%)	125 (92.6)	265 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.717 (0.399)
95% CI		(0.328, 1.567)
Log-rank p-value		0.333

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (88.0, 97.0)	94.1 (91.3, 96.9)
6 months	92.5 (88.0, 97.0)	92.3 (88.8, 95.7)
9 months	92.5 (88.0, 97.0)	90.6 (86.0, 95.3)
12 months	92.5 (88.0, 97.0)	90.6 (86.0, 95.3)
18 months	NE (NE, NE)	90.6 (86.0, 95.3)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	19 (6.7)
Number of Subjects Censored, n (%)	134 (99.3)	266 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.694 (1.030)
95% CI		(1.155, 65.457)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	93.7 (90.8, 96.6)
6 months	99.2 (97.7, 100.0)	92.6 (89.1, 96.2)
9 months	99.2 (97.7, 100.0)	89.9 (83.6, 96.2)
12 months	99.2 (97.7, 100.0)	89.9 (83.6, 96.2)
18 months	NE (NE, NE)	89.9 (83.6, 96.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	17 (6.0)
Number of Subjects Censored, n (%)	132 (97.8)	268 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.209 (0.636)
95% CI		(0.635, 7.684)
Log-rank p-value		0.223

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	94.9 (92.3, 97.5)
6 months	97.7 (95.2, 100.0)	93.1 (89.5, 96.7)
9 months	97.7 (95.2, 100.0)	92.0 (87.9, 96.1)
12 months	97.7 (95.2, 100.0)	92.0 (87.9, 96.1)
18 months	NE (NE, NE)	92.0 (87.9, 96.1)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	12 (4.2)
Number of Subjects Censored, n (%)	133 (98.5)	273 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 7.4	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.661 (0.784)
95% CI		(0.357, 7.724)
Log-rank p-value		0.517

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.6 (94.4, 98.8)
6 months	99.3 (97.8, 100.0)	94.4 (91.2, 97.7)
9 months	0.0 (NE, NE)	94.4 (91.2, 97.7)
12 months	0.0 (NE, NE)	94.4 (91.2, 97.7)
18 months	0.0 (NE, NE)	94.4 (91.2, 97.7)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	11 (3.9)
Number of Subjects Censored, n (%)	134 (99.3)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.270 (1.059)
95% CI		(0.410, 26.044)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.9, 99.1)
6 months	95.7 (87.3, 100.0)	95.6 (92.8, 98.4)
9 months	95.7 (87.3, 100.0)	94.5 (91.1, 98.0)
12 months	95.7 (87.3, 100.0)	94.5 (91.1, 98.0)
18 months	NE (NE, NE)	94.5 (91.1, 98.0)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	134 (99.3)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.442 (1.089)
95% CI		(0.289, 20.658)
Log-rank p-value		0.388

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.1 (96.5, 99.8)
6 months	99.2 (97.7, 100.0)	97.4 (95.2, 99.6)
9 months	99.2 (97.7, 100.0)	95.9 (92.3, 99.5)
12 months	99.2 (97.7, 100.0)	95.9 (92.3, 99.5)
18 months	NE (NE, NE)	95.9 (92.3, 99.5)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	5 (1.8)
Number of Subjects Censored, n (%)	134 (99.3)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.675 (1.121)
95% CI		(0.186, 15.063)
Log-rank p-value		0.635

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.5 (96.9, 100.0)
6 months	99.2 (97.7, 100.0)	98.5 (96.9, 100.0)
9 months	99.2 (97.7, 100.0)	97.0 (93.7, 100.0)
12 months	99.2 (97.7, 100.0)	97.0 (93.7, 100.0)
18 months	NE (NE, NE)	97.0 (93.7, 100.0)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	35 (25.9)	105 (36.8)
Number of Subjects Censored, n (%)	100 (74.1)	180 (63.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.85, NE)	0.99 (0.69, 1.84)
Median (95% CI)	NE (NE, NE)	NE (7.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.409 (0.198)
95% CI		(0.955, 2.080)
Log-rank p-value		0.082

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.8 (65.0, 80.6)	67.3 (61.8, 72.8)
6 months	72.8 (65.0, 80.6)	60.9 (54.4, 67.4)
9 months	72.8 (65.0, 80.6)	57.1 (49.7, 64.5)
12 months	72.8 (65.0, 80.6)	54.4 (45.6, 63.2)
18 months	NE (NE, NE)	54.4 (45.6, 63.2)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	8 (5.9)	46 (16.1)
Number of Subjects Censored, n (%)	127 (94.1)	239 (83.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.976 (0.385)
95% CI		(1.400, 6.327)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (89.2, 97.9)	84.0 (79.7, 88.3)
6 months	93.6 (89.2, 97.9)	83.4 (79.0, 87.8)
9 months	93.6 (89.2, 97.9)	83.4 (79.0, 87.8)
12 months	93.6 (89.2, 97.9)	83.4 (79.0, 87.8)
18 months	NE (NE, NE)	83.4 (79.0, 87.8)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	13 (9.6)	27 (9.5)
Number of Subjects Censored, n (%)	122 (90.4)	258 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.745 (0.348)
95% CI		(0.376, 1.474)
Log-rank p-value		0.381

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (84.5, 95.1)	93.2 (90.2, 96.1)
6 months	89.8 (84.5, 95.1)	89.0 (84.6, 93.4)
9 months	89.8 (84.5, 95.1)	88.0 (83.2, 92.7)
12 months	89.8 (84.5, 95.1)	82.8 (72.0, 93.6)
18 months	NE (NE, NE)	82.8 (72.0, 93.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	12 (8.9)	23 (8.1)
Number of Subjects Censored, n (%)	123 (91.1)	262 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.363)
95% CI		(0.416, 1.728)
Log-rank p-value		0.652

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (85.9, 95.8)	92.5 (89.4, 95.6)
6 months	90.8 (85.9, 95.8)	91.9 (88.6, 95.2)
9 months	90.8 (85.9, 95.8)	90.8 (87.0, 94.7)
12 months	90.8 (85.9, 95.8)	90.8 (87.0, 94.7)
18 months	NE (NE, NE)	90.8 (87.0, 94.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	6 (2.1)
Number of Subjects Censored, n (%)	134 (99.3)	279 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.863 (1.084)
95% CI		(0.342, 23.948)
Log-rank p-value		0.330

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.8 (96.0, 99.5)
6 months	99.3 (97.8, 100.0)	97.8 (96.0, 99.5)
9 months	99.3 (97.8, 100.0)	97.8 (96.0, 99.5)
12 months	99.3 (97.8, 100.0)	97.8 (96.0, 99.5)
18 months	NE (NE, NE)	97.8 (96.0, 99.5)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	8 (2.8)
Number of Subjects Censored, n (%)	133 (98.5)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.574 (0.810)
95% CI		(0.322, 7.692)
Log-rank p-value		0.620

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	97.9 (96.2, 99.6)
6 months	98.3 (96.0, 100.0)	97.0 (94.6, 99.4)
9 months	98.3 (96.0, 100.0)	95.5 (91.7, 99.3)
12 months	98.3 (96.0, 100.0)	95.5 (91.7, 99.3)
18 months	NE (NE, NE)	95.5 (91.7, 99.3)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	19 (14.1)	113 (39.6)
Number of Subjects Censored, n (%)	116 (85.9)	172 (60.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.92 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.879 (0.250)
95% CI		(1.763, 4.702)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (79.7, 91.9)	62.6 (56.9, 68.4)
6 months	81.0 (70.3, 91.8)	58.0 (51.5, 64.4)
9 months	NE (NE, NE)	53.1 (45.1, 61.1)
12 months	NE (NE, NE)	53.1 (45.1, 61.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	13 (9.6)	105 (36.8)
Number of Subjects Censored, n (%)	122 (90.4)	180 (63.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.69, 1.64)
Median (95% CI)	NE (NE, NE)	NE (7.13, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.953 (0.296)
95% CI		(2.213, 7.062)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (84.5, 95.1)	65.0 (59.4, 70.7)
6 months	89.8 (84.5, 95.1)	62.2 (56.1, 68.3)
9 months	NE (NE, NE)	55.6 (47.3, 63.8)
12 months	NE (NE, NE)	55.6 (47.3, 63.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	38 (28.1)	101 (35.4)
Number of Subjects Censored, n (%)	97 (71.9)	184 (64.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (0.99, 3.71)	1.58 (0.92, 1.87)
Median (95% CI)	5.59 (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.087 (0.195)
95% CI		(0.742, 1.593)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.5 (63.2, 79.7)	66.4 (60.8, 72.0)
6 months	46.9 (18.5, 75.4)	60.5 (53.9, 67.2)
9 months	NE (NE, NE)	58.4 (50.8, 66.0)
12 months	NE (NE, NE)	58.4 (50.8, 66.0)
18 months	NE (NE, NE)	58.4 (50.8, 66.0)
Median Follow-up Time (months)	2.33	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	13 (9.6)	31 (10.9)
Number of Subjects Censored, n (%)	122 (90.4)	254 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.932 (0.339)
95% CI		(0.480, 1.811)
Log-rank p-value		0.809

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (84.9, 95.2)	90.4 (86.8, 93.9)
6 months	90.1 (84.9, 95.2)	87.8 (83.5, 92.1)
9 months	90.1 (84.9, 95.2)	86.7 (82.0, 91.4)
12 months	90.1 (84.9, 95.2)	86.7 (82.0, 91.4)
18 months	NE (NE, NE)	86.7 (82.0, 91.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	9 (6.7)	34 (11.9)
Number of Subjects Censored, n (%)	126 (93.3)	251 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.537 (0.384)
95% CI		(0.724, 3.261)
Log-rank p-value		0.282

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (89.5, 97.9)	89.8 (86.3, 93.4)
6 months	83.3 (63.7, 100.0)	85.9 (81.0, 90.8)
9 months	NE (NE, NE)	83.9 (77.6, 90.1)
12 months	NE (NE, NE)	83.9 (77.6, 90.1)
18 months	NE (NE, NE)	83.9 (77.6, 90.1)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	19 (6.7)
Number of Subjects Censored, n (%)	133 (98.5)	266 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.495 (0.750)
95% CI		(0.804, 15.187)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.4 (90.5, 96.4)
6 months	91.3 (79.8, 100.0)	92.5 (89.1, 95.9)
9 months	91.3 (79.8, 100.0)	92.5 (89.1, 95.9)
12 months	91.3 (79.8, 100.0)	92.5 (89.1, 95.9)
18 months	NE (NE, NE)	92.5 (89.1, 95.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	4 (3.0)	7 (2.5)
Number of Subjects Censored, n (%)	131 (97.0)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.638 (0.660)
95% CI		(0.175, 2.330)
Log-rank p-value		0.570

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (94.0, 99.9)	97.8 (96.0, 99.5)
6 months	96.9 (94.0, 99.9)	96.7 (94.1, 99.4)
9 months	96.9 (94.0, 99.9)	96.7 (94.1, 99.4)
12 months	96.9 (94.0, 99.9)	96.7 (94.1, 99.4)
18 months	NE (NE, NE)	96.7 (94.1, 99.4)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	8 (2.8)
Number of Subjects Censored, n (%)	133 (98.5)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.271 (0.817)
95% CI		(0.256, 6.306)
Log-rank p-value		0.853

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	98.2 (96.6, 99.8)
6 months	98.5 (96.4, 100.0)	97.2 (94.7, 99.7)
9 months	98.5 (96.4, 100.0)	94.0 (89.0, 99.0)
12 months	98.5 (96.4, 100.0)	94.0 (89.0, 99.0)
18 months	NE (NE, NE)	94.0 (89.0, 99.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	0	7 (2.5)
Number of Subjects Censored, n (%)	135 (100.0)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.5, 99.3)
6 months	100.0 (100.0, 100.0)	97.4 (95.5, 99.3)
9 months	100.0 (100.0, 100.0)	97.4 (95.5, 99.3)
12 months	100.0 (100.0, 100.0)	97.4 (95.5, 99.3)
18 months	NE (NE, NE)	97.4 (95.5, 99.3)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	14 (10.4)	95 (33.3)
Number of Subjects Censored, n (%)	121 (89.6)	190 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.58 (1.12, 2.56)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.137 (0.288)
95% CI		(1.783, 5.520)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (84.9, 95.2)	69.5 (64.0, 74.9)
6 months	85.6 (75.7, 95.4)	63.9 (57.6, 70.1)
9 months	85.6 (75.7, 95.4)	62.0 (55.0, 69.1)
12 months	85.6 (75.7, 95.4)	62.0 (55.0, 69.1)
18 months	NE (NE, NE)	46.5 (19.7, 73.4)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	53 (18.6)
Number of Subjects Censored, n (%)	132 (97.8)	232 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.168 (0.596)
95% CI		(2.229, 23.058)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.3, 100.0)	84.3 (80.0, 88.5)
6 months	97.8 (95.3, 100.0)	78.4 (72.7, 84.1)
9 months	97.8 (95.3, 100.0)	76.6 (70.0, 83.1)
12 months	97.8 (95.3, 100.0)	76.6 (70.0, 83.1)
18 months	NE (NE, NE)	76.6 (70.0, 83.1)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	14 (4.9)
Number of Subjects Censored, n (%)	130 (96.3)	271 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.367 (0.524)
95% CI		(0.490, 3.815)
Log-rank p-value		0.559

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.0, 99.5)	95.0 (92.5, 97.6)
6 months	96.2 (93.0, 99.5)	95.0 (92.5, 97.6)
9 months	96.2 (93.0, 99.5)	95.0 (92.5, 97.6)
12 months	96.2 (93.0, 99.5)	95.0 (92.5, 97.6)
18 months	NE (NE, NE)	95.0 (92.5, 97.6)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	5 (1.8)
Number of Subjects Censored, n (%)	133 (98.5)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.852 (0.872)
95% CI		(0.154, 4.707)
Log-rank p-value		0.818

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.5 (97.0, 100.0)
6 months	94.9 (86.5, 100.0)	97.9 (95.9, 99.8)
9 months	94.9 (86.5, 100.0)	97.9 (95.9, 99.8)
12 months	94.9 (86.5, 100.0)	97.9 (95.9, 99.8)
18 months	NE (NE, NE)	97.9 (95.9, 99.8)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	23 (17.0)	70 (24.6)
Number of Subjects Censored, n (%)	112 (83.0)	215 (75.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	4.86 (2.99, 18.04)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.195 (0.246)
95% CI		(0.738, 1.935)
Log-rank p-value		0.522

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (75.2, 88.6)	79.7 (75.0, 84.5)
6 months	81.9 (75.2, 88.6)	71.1 (64.6, 77.7)
9 months	81.9 (75.2, 88.6)	70.0 (63.2, 76.8)
12 months	81.9 (75.2, 88.6)	64.2 (51.6, 76.8)
18 months	NE (NE, NE)	64.2 (51.6, 76.8)
Median Follow-up Time (months)	2.69	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	9 (6.7)	24 (8.4)
Number of Subjects Censored, n (%)	126 (93.3)	261 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.024 (0.401)
95% CI		(0.467, 2.249)
Log-rank p-value		0.936

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (87.8, 97.3)	92.9 (89.9, 95.9)
6 months	92.5 (87.8, 97.3)	91.4 (87.8, 95.0)
9 months	92.5 (87.8, 97.3)	90.3 (86.1, 94.5)
12 months	92.5 (87.8, 97.3)	90.3 (86.1, 94.5)
18 months	NE (NE, NE)	90.3 (86.1, 94.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	7 (2.5)
Number of Subjects Censored, n (%)	133 (98.5)	278 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.323 (0.812)
95% CI		(0.269, 6.498)
Log-rank p-value		0.856

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	97.5 (95.6, 99.3)
6 months	98.5 (96.4, 100.0)	97.5 (95.6, 99.3)
9 months	98.5 (96.4, 100.0)	97.5 (95.6, 99.3)
12 months	98.5 (96.4, 100.0)	97.5 (95.6, 99.3)
18 months	NE (NE, NE)	97.5 (95.6, 99.3)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	6 (2.1)
Number of Subjects Censored, n (%)	132 (97.8)	279 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.939 (0.708)
95% CI		(0.235, 3.762)
Log-rank p-value		0.949

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.8, 100.0)	97.9 (96.2, 99.6)
6 months	97.6 (94.8, 100.0)	97.9 (96.2, 99.6)
9 months	97.6 (94.8, 100.0)	97.9 (96.2, 99.6)
12 months	97.6 (94.8, 100.0)	97.9 (96.2, 99.6)
18 months	NE (NE, NE)	97.9 (96.2, 99.6)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	20 (14.8)	68 (23.9)
Number of Subjects Censored, n (%)	115 (85.2)	217 (76.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.76, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.346 (0.259)
95% CI		(0.811, 2.235)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (77.6, 90.5)	78.1 (73.2, 83.0)
6 months	84.0 (77.6, 90.5)	74.7 (69.1, 80.3)
9 months	84.0 (77.6, 90.5)	71.9 (65.3, 78.5)
12 months	84.0 (77.6, 90.5)	71.9 (65.3, 78.5)
18 months	NE (NE, NE)	47.9 (9.3, 86.5)
Median Follow-up Time (months)	2.69	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	7 (5.2)	47 (16.5)
Number of Subjects Censored, n (%)	128 (94.8)	238 (83.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.697 (0.409)
95% CI		(1.209, 6.015)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (90.3, 98.4)	84.4 (80.1, 88.8)
6 months	94.4 (90.3, 98.4)	82.7 (78.0, 87.4)
9 months	94.4 (90.3, 98.4)	81.1 (75.6, 86.6)
12 months	94.4 (90.3, 98.4)	81.1 (75.6, 86.6)
18 months	NE (NE, NE)	54.1 (10.7, 97.5)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	3 (2.2)	5 (1.8)
Number of Subjects Censored, n (%)	132 (97.8)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.760 (0.732)
95% CI		(0.181, 3.192)
Log-rank p-value		0.677

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	98.2 (96.7, 99.8)
6 months	97.6 (94.9, 100.0)	98.2 (96.7, 99.8)
9 months	97.6 (94.9, 100.0)	98.2 (96.7, 99.8)
12 months	97.6 (94.9, 100.0)	98.2 (96.7, 99.8)
18 months	NE (NE, NE)	98.2 (96.7, 99.8)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	17 (12.6)	65 (22.8)
Number of Subjects Censored, n (%)	118 (87.4)	220 (77.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	5.72 (3.71, 6.93)
Median (95% CI)	NE (NE, NE)	17.48 (17.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.296 (0.281)
95% CI		(0.747, 2.249)
Log-rank p-value		0.304

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (82.2, 93.7)	82.5 (78.0, 87.1)
6 months	80.5 (68.9, 92.1)	72.9 (66.2, 79.6)
9 months	80.5 (68.9, 92.1)	66.6 (58.5, 74.7)
12 months	80.5 (68.9, 92.1)	66.6 (58.5, 74.7)
18 months	NE (NE, NE)	50.0 (21.0, 78.9)
Median Follow-up Time (months)	2.79	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	13 (4.6)
Number of Subjects Censored, n (%)	130 (96.3)	272 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.584 (0.572)
95% CI		(0.190, 1.790)
Log-rank p-value		0.415

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	97.4 (95.6, 99.3)
6 months	85.3 (70.5, 100.0)	94.7 (91.1, 98.3)
9 months	85.3 (70.5, 100.0)	91.0 (85.5, 96.4)
12 months	85.3 (70.5, 100.0)	91.0 (85.5, 96.4)
18 months	NE (NE, NE)	91.0 (85.5, 96.4)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	5 (3.7)	8 (2.8)
Number of Subjects Censored, n (%)	130 (96.3)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.411 (0.611)
95% CI		(0.124, 1.362)
Log-rank p-value		0.113

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (92.3, 99.4)	98.8 (97.5, 100.0)
6 months	95.9 (92.3, 99.4)	96.0 (92.9, 99.1)
9 months	95.9 (92.3, 99.4)	94.7 (90.8, 98.6)
12 months	95.9 (92.3, 99.4)	94.7 (90.8, 98.6)
18 months	NE (NE, NE)	94.7 (90.8, 98.6)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	4 (1.4)
Number of Subjects Censored, n (%)	134 (99.3)	281 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.338 (1.124)
95% CI		(0.148, 12.113)
Log-rank p-value		0.801

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.8, 100.0)	98.5 (97.0, 100.0)
6 months	99.2 (97.8, 100.0)	98.5 (97.0, 100.0)
9 months	99.2 (97.8, 100.0)	98.5 (97.0, 100.0)
12 months	99.2 (97.8, 100.0)	98.5 (97.0, 100.0)
18 months	NE (NE, NE)	98.5 (97.0, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	27 (20.0)	37 (13.0)
Number of Subjects Censored, n (%)	108 (80.0)	248 (87.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.84, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.518 (0.260)
95% CI		(0.311, 0.862)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.1 (70.7, 85.5)	88.2 (84.3, 92.0)
6 months	78.1 (70.7, 85.5)	86.0 (81.4, 90.5)
9 months	78.1 (70.7, 85.5)	83.7 (78.3, 89.1)
12 months	78.1 (70.7, 85.5)	83.7 (78.3, 89.1)
18 months	NE (NE, NE)	83.7 (78.3, 89.1)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	23 (17.0)	21 (7.4)
Number of Subjects Censored, n (%)	112 (83.0)	264 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.282 (0.319)
95% CI		(0.151, 0.527)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (74.2, 88.3)	94.8 (92.1, 97.4)
6 months	81.3 (74.2, 88.3)	91.7 (87.6, 95.7)
9 months	81.3 (74.2, 88.3)	89.5 (84.6, 94.4)
12 months	81.3 (74.2, 88.3)	89.5 (84.6, 94.4)
18 months	NE (NE, NE)	59.7 (11.8, 100.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	18 (6.3)
Number of Subjects Censored, n (%)	133 (98.5)	267 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.118 (0.748)
95% CI		(0.951, 17.823)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	93.4 (90.4, 96.4)
6 months	98.5 (96.4, 100.0)	93.4 (90.4, 96.4)
9 months	98.5 (96.4, 100.0)	93.4 (90.4, 96.4)
12 months	98.5 (96.4, 100.0)	93.4 (90.4, 96.4)
18 months	NE (NE, NE)	93.4 (90.4, 96.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	64 (22.5)
Number of Subjects Censored, n (%)	134 (99.3)	221 (77.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.65, 9.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		23.950 (1.010)
95% CI		(3.310, 173.312)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	82.4 (77.8, 87.0)
6 months	99.2 (97.7, 100.0)	69.8 (62.5, 77.1)
9 months	99.2 (97.7, 100.0)	68.6 (61.0, 76.1)
12 months	99.2 (97.7, 100.0)	65.0 (55.0, 74.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	59 (20.7)
Number of Subjects Censored, n (%)	134 (99.3)	226 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (3.81, 9.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		21.226 (1.011)
95% CI		(2.927, 153.944)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	84.3 (79.9, 88.7)
6 months	99.2 (97.7, 100.0)	72.5 (65.4, 79.6)
9 months	99.2 (97.7, 100.0)	69.3 (61.1, 77.4)
12 months	99.2 (97.7, 100.0)	65.6 (55.2, 76.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	11 (8.1)	35 (12.3)
Number of Subjects Censored, n (%)	124 (91.9)	250 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.165 (0.353)
95% CI		(0.584, 2.326)
Log-rank p-value		0.771

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (87.6, 96.9)	90.2 (86.6, 93.8)
6 months	89.7 (83.1, 96.3)	83.4 (77.9, 88.9)
9 months	89.7 (83.1, 96.3)	83.4 (77.9, 88.9)
12 months	89.7 (83.1, 96.3)	83.4 (77.9, 88.9)
18 months	NE (NE, NE)	83.4 (77.9, 88.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	8 (5.9)	15 (5.3)
Number of Subjects Censored, n (%)	127 (94.1)	270 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.673 (0.444)
95% CI		(0.282, 1.607)
Log-rank p-value		0.324

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (89.5, 97.9)	95.7 (93.3, 98.2)
6 months	93.7 (89.5, 97.9)	93.0 (89.4, 96.6)
9 months	93.7 (89.5, 97.9)	93.0 (89.4, 96.6)
12 months	93.7 (89.5, 97.9)	93.0 (89.4, 96.6)
18 months	NE (NE, NE)	93.0 (89.4, 96.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	2 (1.5)	6 (2.1)
Number of Subjects Censored, n (%)	133 (98.5)	279 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.164 (0.846)
95% CI		(0.222, 6.109)
Log-rank p-value		0.989

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	98.0 (96.3, 99.8)
6 months	96.5 (91.0, 100.0)	97.1 (94.7, 99.6)
9 months	96.5 (91.0, 100.0)	97.1 (94.7, 99.6)
12 months	96.5 (91.0, 100.0)	97.1 (94.7, 99.6)
18 months	NE (NE, NE)	97.1 (94.7, 99.6)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	5 (1.8)
Number of Subjects Censored, n (%)	134 (99.3)	280 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (1.121)
95% CI		(0.159, 12.868)
Log-rank p-value		0.767

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.8 (97.6, 100.0)
6 months	99.2 (97.7, 100.0)	97.3 (94.8, 99.8)
9 months	99.2 (97.7, 100.0)	97.3 (94.8, 99.8)
12 months	99.2 (97.7, 100.0)	97.3 (94.8, 99.8)
18 months	NE (NE, NE)	97.3 (94.8, 99.8)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	13 (9.6)	30 (10.5)
Number of Subjects Censored, n (%)	122 (90.4)	255 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.829 (0.340)
95% CI		(0.425, 1.614)
Log-rank p-value		0.579

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (86.0, 95.8)	90.6 (87.1, 94.2)
6 months	88.3 (81.4, 95.2)	87.7 (83.2, 92.2)
9 months	88.3 (81.4, 95.2)	86.0 (80.6, 91.5)
12 months	88.3 (81.4, 95.2)	86.0 (80.6, 91.5)
18 months	NE (NE, NE)	86.0 (80.6, 91.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	0	9 (3.2)
Number of Subjects Censored, n (%)	135 (100.0)	276 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.7, 99.0)
6 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.8)
9 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.8)
12 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.8)
18 months	NE (NE, NE)	95.9 (93.1, 98.8)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	1 (0.7)	11 (3.9)
Number of Subjects Censored, n (%)	134 (99.3)	274 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.294 (1.059)
95% CI		(0.414, 26.225)
Log-rank p-value		0.244

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>3

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.8, 100.0)	97.1 (95.0, 99.1)
6 months	99.2 (97.8, 100.0)	95.4 (92.4, 98.4)
9 months	99.2 (97.8, 100.0)	93.7 (89.2, 98.2)
12 months	99.2 (97.8, 100.0)	93.7 (89.2, 98.2)
18 months	NE (NE, NE)	93.7 (89.2, 98.2)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	16 (13.6)	29 (11.9)
Number of Subjects Censored, n (%)	102 (86.4)	215 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	11.04 (7.79, NE)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.546 (0.330)
95% CI		(0.286, 1.042)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (80.5, 93.4)	93.3 (90.1, 96.5)
6 months	79.9 (68.5, 91.3)	87.5 (82.6, 92.4)
9 months	NE (NE, NE)	83.1 (75.6, 90.7)
12 months	NE (NE, NE)	68.2 (47.4, 89.0)
18 months	NE (NE, NE)	54.5 (25.4, 83.7)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	13 (11.0)	14 (5.7)
Number of Subjects Censored, n (%)	105 (89.0)	230 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.349 (0.402)
95% CI		(0.159, 0.767)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.5, 94.8)	96.5 (94.1, 98.9)
6 months	85.9 (78.0, 93.8)	92.7 (88.8, 96.7)
9 months	NE (NE, NE)	92.7 (88.8, 96.7)
12 months	NE (NE, NE)	92.7 (88.8, 96.7)
18 months	NE (NE, NE)	74.2 (41.5, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	22 (19.6)	19 (9.0)
Number of Subjects Censored, n (%)	90 (80.4)	193 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.27, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.332 (0.329)
95% CI		(0.174, 0.632)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.1 (71.0, 87.2)	93.0 (89.5, 96.6)
6 months	74.4 (62.8, 86.1)	87.4 (81.5, 93.4)
9 months	74.4 (62.8, 86.1)	87.4 (81.5, 93.4)
12 months	74.4 (62.8, 86.1)	87.4 (81.5, 93.4)
18 months	NE (NE, NE)	87.4 (81.5, 93.4)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	15 (13.4)	12 (5.7)
Number of Subjects Censored, n (%)	97 (86.6)	200 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.300 (0.405)
95% CI		(0.136, 0.664)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.5, 92.7)	95.5 (92.7, 98.4)
6 months	80.8 (69.6, 92.1)	92.0 (87.1, 96.9)
9 months	80.8 (69.6, 92.1)	92.0 (87.1, 96.9)
12 months	80.8 (69.6, 92.1)	92.0 (87.1, 96.9)
18 months	NE (NE, NE)	92.0 (87.1, 96.9)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	26 (18.6)	29 (12.0)
Number of Subjects Censored, n (%)	114 (81.4)	212 (88.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (2.60, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.429 (0.283)
95% CI		(0.246, 0.747)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (75.5, 88.8)	91.5 (87.9, 95.0)
6 months	69.7 (54.9, 84.6)	86.1 (80.9, 91.3)
9 months	69.7 (54.9, 84.6)	83.7 (76.8, 90.6)
12 months	69.7 (54.9, 84.6)	79.3 (68.7, 89.9)
18 months	NE (NE, NE)	79.3 (68.7, 89.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	19 (13.6)	14 (5.8)
Number of Subjects Censored, n (%)	121 (86.4)	227 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.309 (0.363)
95% CI		(0.152, 0.630)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (80.4, 92.5)	95.7 (93.1, 98.3)
6 months	79.8 (69.1, 90.4)	92.8 (89.0, 96.6)
9 months	79.8 (69.1, 90.4)	92.8 (89.0, 96.6)
12 months	79.8 (69.1, 90.4)	92.8 (89.0, 96.6)
18 months	NE (NE, NE)	92.8 (89.0, 96.6)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	12 (13.3)	19 (8.8)
Number of Subjects Censored, n (%)	78 (86.7)	196 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.76, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.437 (0.388)
95% CI		(0.204, 0.935)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.7 (76.5, 92.8)	95.1 (92.2, 98.1)
6 months	84.7 (76.5, 92.8)	89.4 (84.1, 94.7)
9 months	NE (NE, NE)	87.2 (80.5, 93.9)
12 months	NE (NE, NE)	79.3 (63.3, 95.3)
18 months	NE (NE, NE)	66.1 (38.9, 93.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	12 (5.6)
Number of Subjects Censored, n (%)	81 (90.0)	203 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.382 (0.459)
95% CI		(0.155, 0.940)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (80.8, 95.6)	96.4 (93.8, 99.0)
6 months	88.2 (80.8, 95.6)	92.3 (87.6, 97.1)
9 months	NE (NE, NE)	92.3 (87.6, 97.1)
12 months	NE (NE, NE)	92.3 (87.6, 97.1)
18 months	NE (NE, NE)	76.9 (49.1, 100.0)
Median Follow-up Time (months)	2.83	3.78

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	7 (17.1)	7 (8.8)
Number of Subjects Censored, n (%)	34 (82.9)	73 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (1.31, NE)	NE (NE, NE)
Median (95% CI)	NE (4.14, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Min, Max	0.4, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.307 (0.560)
95% CI		(0.103, 0.921)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (73.2, 96.0)	93.4 (87.7, 99.0)
6 months	70.5 (43.5, 97.5)	89.1 (81.3, 97.0)
9 months	NE (NE, NE)	89.1 (81.3, 97.0)
12 months	NE (NE, NE)	89.1 (81.3, 97.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	3 (3.8)
Number of Subjects Censored, n (%)	37 (90.2)	77 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.230 (0.782)
95% CI		(0.050, 1.065)
Log-rank p-value		0.095

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (79.2, 99.3)	98.7 (96.3, 100.0)
6 months	89.2 (79.2, 99.3)	94.5 (88.2, 100.0)
9 months	NE (NE, NE)	94.5 (88.2, 100.0)
12 months	NE (NE, NE)	94.5 (88.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	29 (17.4)	37 (11.3)
Number of Subjects Censored, n (%)	138 (82.6)	290 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.429 (0.260)
95% CI		(0.258, 0.715)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.3 (76.2, 88.5)	93.0 (90.2, 95.8)
6 months	78.1 (69.8, 86.4)	87.2 (82.8, 91.7)
9 months	78.1 (69.8, 86.4)	84.3 (78.4, 90.1)
12 months	78.1 (69.8, 86.4)	77.3 (66.4, 88.1)
18 months	NE (NE, NE)	71.3 (56.3, 86.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	22 (13.2)	20 (6.1)
Number of Subjects Censored, n (%)	145 (86.8)	307 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.329 (0.318)
95% CI		(0.176, 0.614)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (81.1, 92.2)	95.4 (93.1, 97.8)
6 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
9 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
12 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
18 months	NE (NE, NE)	85.3 (71.6, 99.1)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	4 (8.2)
Number of Subjects Censored, n (%)	20 (90.9)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.287 (1.055)
95% CI		(0.036, 2.264)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	93.9 (87.2, 100.0)
6 months	85.7 (67.4, 100.0)	88.7 (76.9, 100.0)
9 months	NE (NE, NE)	88.7 (76.9, 100.0)
12 months	NE (NE, NE)	88.7 (76.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	3 (6.1)
Number of Subjects Censored, n (%)	20 (90.9)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.243 (1.102)
95% CI		(0.028, 2.106)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	95.9 (90.4, 100.0)
6 months	85.7 (67.4, 100.0)	90.6 (79.2, 100.0)
9 months	NE (NE, NE)	90.6 (79.2, 100.0)
12 months	NE (NE, NE)	90.6 (79.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	10 (9.8)	15 (7.8)
Number of Subjects Censored, n (%)	92 (90.2)	178 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.395 (0.450)
95% CI		(0.164, 0.954)
Log-rank p-value		0.081

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (85.4, 97.1)	97.4 (95.1, 99.6)
6 months	83.5 (71.5, 95.5)	91.1 (85.9, 96.2)
9 months	NE (NE, NE)	86.8 (79.3, 94.4)
12 months	NE (NE, NE)	82.5 (71.5, 93.4)
18 months	NE (NE, NE)	82.5 (71.5, 93.4)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	7 (6.9)	7 (3.6)
Number of Subjects Censored, n (%)	95 (93.1)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.300 (0.561)
95% CI		(0.100, 0.902)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (88.1, 98.5)	98.9 (97.5, 100.0)
6 months	90.4 (82.9, 98.0)	94.6 (90.4, 98.7)
9 months	NE (NE, NE)	94.6 (90.4, 98.7)
12 months	NE (NE, NE)	94.6 (90.4, 98.7)
18 months	NE (NE, NE)	94.6 (90.4, 98.7)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	28 (21.9)	33 (12.5)
Number of Subjects Censored, n (%)	100 (78.1)	230 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (1.94, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.420 (0.264)
95% CI		(0.250, 0.704)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.5 (68.5, 84.4)	89.9 (86.2, 93.7)
6 months	72.4 (61.7, 83.2)	85.2 (80.0, 90.3)
9 months	72.4 (61.7, 83.2)	85.2 (80.0, 90.3)
12 months	72.4 (61.7, 83.2)	78.1 (64.0, 92.2)
18 months	NE (NE, NE)	66.9 (43.3, 90.5)
Median Follow-up Time (months)	2.56	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	21 (16.4)	19 (7.2)
Number of Subjects Censored, n (%)	107 (83.6)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.40, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.320 (0.323)
95% CI		(0.170, 0.604)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (74.5, 89.2)	93.8 (90.7, 96.8)
6 months	77.8 (67.3, 88.3)	91.0 (86.8, 95.3)
9 months	77.8 (67.3, 88.3)	91.0 (86.8, 95.3)
12 months	77.8 (67.3, 88.3)	91.0 (86.8, 95.3)
18 months	NE (NE, NE)	78.0 (54.2, 100.0)
Median Follow-up Time (months)	2.58	3.25

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	3 (23.1)	5 (13.5)
Number of Subjects Censored, n (%)	10 (76.9)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.30 (1.94, NE)	NE (1.74, NE)
Median (95% CI)	4.14 (1.94, NE)	NE (4.57, NE)
75% percentile (95% CI)	4.14 (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Min, Max	1.3*, 4.1	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.349 (0.790)
95% CI		(0.074, 1.643)
Log-rank p-value		0.204

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.4 (38.0, 100.0)	89.1 (79.0, 99.2)
6 months	0.0 (NE, NE)	78.0 (55.7, 100.0)
9 months	0.0 (NE, NE)	78.0 (55.7, 100.0)
12 months	0.0 (NE, NE)	78.0 (55.7, 100.0)
18 months	0.0 (NE, NE)	78.0 (55.7, 100.0)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.57, NE)
Median (95% CI)	NE (NE, NE)	NE (4.57, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.234

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	80.3 (57.9, 100.0)
9 months	NE (NE, NE)	80.3 (57.9, 100.0)
12 months	NE (NE, NE)	80.3 (57.9, 100.0)
18 months	NE (NE, NE)	80.3 (57.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	35 (16.1)	43 (10.3)
Number of Subjects Censored, n (%)	182 (83.9)	376 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.409 (0.240)
95% CI		(0.256, 0.654)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (78.2, 88.7)	93.6 (91.1, 96.0)
6 months	79.7 (72.6, 86.9)	88.2 (84.4, 92.0)
9 months	79.7 (72.6, 86.9)	85.8 (80.9, 90.7)
12 months	79.7 (72.6, 86.9)	79.6 (70.1, 89.2)
18 months	NE (NE, NE)	73.9 (60.0, 87.9)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	28 (12.9)	22 (5.3)
Number of Subjects Censored, n (%)	189 (87.1)	397 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.263 (0.298)
95% CI		(0.146, 0.472)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (81.6, 91.4)	96.4 (94.6, 98.3)
6 months	82.8 (75.8, 89.8)	93.2 (90.1, 96.2)
9 months	82.8 (75.8, 89.8)	93.2 (90.1, 96.2)
12 months	82.8 (75.8, 89.8)	93.2 (90.1, 96.2)
18 months	NE (NE, NE)	86.5 (73.6, 99.4)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	29 (21.0)	30 (10.9)
Number of Subjects Censored, n (%)	109 (79.0)	246 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.27, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Min, Max	0.4, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.335 (0.279)
95% CI		(0.194, 0.578)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (71.2, 85.8)	92.7 (89.6, 95.9)
6 months	71.0 (59.0, 83.1)	87.3 (82.5, 92.1)
9 months	NE (NE, NE)	85.2 (78.9, 91.4)
12 months	NE (NE, NE)	76.6 (59.9, 93.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	20 (14.5)	16 (5.8)
Number of Subjects Censored, n (%)	118 (85.5)	260 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.244 (0.356)
95% CI		(0.121, 0.491)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (78.4, 91.5)	96.1 (93.7, 98.5)
6 months	77.3 (65.3, 89.2)	92.5 (88.6, 96.4)
9 months	NE (NE, NE)	92.5 (88.6, 96.4)
12 months	NE (NE, NE)	92.5 (88.6, 96.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	16 (11.3)
Number of Subjects Censored, n (%)	62 (89.9)	125 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (7.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.793 (0.488)
95% CI		(0.305, 2.062)
Log-rank p-value		0.626

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (83.9, 97.8)	92.9 (88.6, 97.1)
6 months	83.3 (67.7, 98.9)	87.9 (81.7, 94.2)
9 months	83.3 (67.7, 98.9)	85.1 (76.9, 93.3)
12 months	83.3 (67.7, 98.9)	79.8 (67.1, 92.5)
18 months	NE (NE, NE)	79.8 (67.1, 92.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	6 (8.7)	8 (5.7)
Number of Subjects Censored, n (%)	63 (91.3)	133 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.601 (0.563)
95% CI		(0.199, 1.811)
Log-rank p-value		0.422

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (83.9, 97.8)	95.6 (92.1, 99.0)
6 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
9 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
12 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
18 months	NE (NE, NE)	93.2 (88.5, 97.9)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	2 (5.1)
Number of Subjects Censored, n (%)	21 (91.3)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.08, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.570 (1.082)
95% CI		(0.068, 4.746)
Log-rank p-value		0.681

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (76.8, 100.0)	97.4 (92.3, 100.0)
6 months	90.0 (76.8, 100.0)	89.9 (75.0, 100.0)
9 months	NE (NE, NE)	89.9 (75.0, 100.0)
12 months	NE (NE, NE)	89.9 (75.0, 100.0)
18 months	NE (NE, NE)	89.9 (75.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	2 (5.1)
Number of Subjects Censored, n (%)	21 (91.3)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.08, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.570 (1.082)
95% CI		(0.068, 4.746)
Log-rank p-value		0.681

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (76.8, 100.0)	97.4 (92.3, 100.0)
6 months	90.0 (76.8, 100.0)	89.9 (75.0, 100.0)
9 months	NE (NE, NE)	89.9 (75.0, 100.0)
12 months	NE (NE, NE)	89.9 (75.0, 100.0)
18 months	NE (NE, NE)	89.9 (75.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	15 (17.6)	18 (10.7)
Number of Subjects Censored, n (%)	70 (82.4)	151 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (2.76, NE)	NE (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Min, Max	0.2*, 6.8*	0.2, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.372 (0.373)
95% CI		(0.179, 0.771)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (75.6, 92.4)	93.3 (89.5, 97.1)
6 months	70.4 (54.2, 86.6)	88.0 (82.2, 93.8)
9 months	NE (NE, NE)	82.2 (72.6, 91.7)
12 months	NE (NE, NE)	82.2 (72.6, 91.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	11 (12.9)	9 (5.3)
Number of Subjects Censored, n (%)	74 (87.1)	160 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.259 (0.473)
95% CI		(0.103, 0.655)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (79.7, 95.2)	96.1 (93.1, 99.2)
6 months	79.5 (66.6, 92.3)	92.6 (87.7, 97.5)
9 months	NE (NE, NE)	92.6 (87.7, 97.5)
12 months	NE (NE, NE)	92.6 (87.7, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	23 (15.9)	30 (10.5)
Number of Subjects Censored, n (%)	122 (84.1)	257 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.476 (0.288)
95% CI		(0.271, 0.836)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.4, 89.3)	93.1 (90.1, 96.1)
6 months	82.8 (76.4, 89.3)	87.4 (82.5, 92.3)
9 months	82.8 (76.4, 89.3)	87.4 (82.5, 92.3)
12 months	82.8 (76.4, 89.3)	78.1 (65.0, 91.3)
18 months	NE (NE, NE)	68.4 (47.1, 89.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	17 (11.7)	17 (5.9)
Number of Subjects Censored, n (%)	128 (88.3)	270 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.375 (0.352)
95% CI		(0.188, 0.748)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (81.4, 92.9)	96.0 (93.7, 98.3)
6 months	87.1 (81.4, 92.9)	92.5 (88.6, 96.3)
9 months	87.1 (81.4, 92.9)	92.5 (88.6, 96.3)
12 months	87.1 (81.4, 92.9)	92.5 (88.6, 96.3)
18 months	NE (NE, NE)	80.9 (59.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	35 (17.8)	40 (10.1)
Number of Subjects Censored, n (%)	162 (82.2)	357 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (3.19, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.377 (0.242)
95% CI		(0.234, 0.606)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (76.1, 87.7)	93.4 (91.0, 95.9)
6 months	74.8 (65.3, 84.3)	88.2 (84.3, 92.1)
9 months	NE (NE, NE)	85.5 (80.1, 90.8)
12 months	NE (NE, NE)	78.2 (67.3, 89.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	26 (13.2)	20 (5.0)
Number of Subjects Censored, n (%)	171 (86.8)	377 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.285 (0.303)
95% CI		(0.157, 0.517)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (80.8, 91.3)	96.2 (94.3, 98.2)
6 months	81.8 (74.2, 89.5)	93.4 (90.4, 96.3)
9 months	NE (NE, NE)	93.4 (90.4, 96.3)
12 months	NE (NE, NE)	93.4 (90.4, 96.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	NE (NE, NE)
Median (95% CI)	NE (0.49, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.82, NE)	NE (NE, NE)
Median (95% CI)	NE (0.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	8 (15.4)
Number of Subjects Censored, n (%)	21 (91.3)	44 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	12.22 (4.37, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Min, Max	1.6, 6.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.689 (0.846)
95% CI		(0.322, 8.861)
Log-rank p-value		0.580

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (78.2, 100.0)	90.2 (82.0, 98.4)
6 months	90.6 (78.2, 100.0)	81.9 (68.6, 95.2)
9 months	NE (NE, NE)	81.9 (68.6, 95.2)
12 months	NE (NE, NE)	81.9 (68.6, 95.2)
18 months	NE (NE, NE)	61.4 (25.3, 97.5)
Median Follow-up Time (months)	2.86	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	6 (11.5)
Number of Subjects Censored, n (%)	22 (95.7)	46 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	12.22 (4.37, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Min, Max	1.6*, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.047 (1.193)
95% CI		(0.294, 31.564)
Log-rank p-value		0.447

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (84.7, 100.0)	94.0 (87.5, 100.0)
6 months	94.7 (84.7, 100.0)	85.4 (72.4, 98.3)
9 months	NE (NE, NE)	85.4 (72.4, 98.3)
12 months	NE (NE, NE)	85.4 (72.4, 98.3)
18 months	NE (NE, NE)	64.0 (26.5, 100.0)
Median Follow-up Time (months)	2.86	3.76

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	5 (11.1)	8 (10.5)
Number of Subjects Censored, n (%)	40 (88.9)	68 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.40, NE)	NE (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (9.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Min, Max	0.4, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.621)
95% CI		(0.251, 2.863)
Log-rank p-value		0.720

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.9 (77.8, 97.9)	92.0 (85.9, 98.2)
6 months	NE (NE, NE)	92.0 (85.9, 98.2)
9 months	NE (NE, NE)	85.9 (73.0, 98.9)
12 months	NE (NE, NE)	77.3 (57.6, 97.1)
18 months	NE (NE, NE)	77.3 (57.6, 97.1)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	5 (6.6)
Number of Subjects Censored, n (%)	42 (93.3)	71 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.266 (0.754)
95% CI		(0.289, 5.543)
Log-rank p-value		0.814

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (84.2, 100.0)	93.4 (87.7, 99.0)
6 months	NE (NE, NE)	93.4 (87.7, 99.0)
9 months	NE (NE, NE)	93.4 (87.7, 99.0)
12 months	NE (NE, NE)	93.4 (87.7, 99.0)
18 months	NE (NE, NE)	93.4 (87.7, 99.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	33 (17.8)	40 (10.5)
Number of Subjects Censored, n (%)	152 (82.2)	340 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (3.19, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.402 (0.244)
95% CI		(0.249, 0.649)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.1, 88.0)	93.4 (90.8, 96.0)
6 months	74.7 (64.9, 84.5)	86.8 (82.5, 91.1)
9 months	74.7 (64.9, 84.5)	85.4 (80.4, 90.4)
12 months	74.7 (64.9, 84.5)	80.7 (70.4, 90.9)
18 months	NE (NE, NE)	72.6 (55.0, 90.2)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	25 (13.5)	21 (5.5)
Number of Subjects Censored, n (%)	160 (86.5)	359 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.280 (0.305)
95% CI		(0.154, 0.509)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (80.4, 91.3)	96.6 (94.7, 98.5)
6 months	81.5 (73.7, 89.4)	92.3 (88.9, 95.8)
9 months	81.5 (73.7, 89.4)	92.3 (88.9, 95.8)
12 months	81.5 (73.7, 89.4)	92.3 (88.9, 95.8)
18 months	NE (NE, NE)	83.1 (65.7, 100.0)
Median Follow-up Time (months)	2.79	4.01

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	10 (15.6)	13 (10.5)
Number of Subjects Censored, n (%)	54 (84.4)	111 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	NE (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Min, Max	0.4, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.447 (0.455)
95% CI		(0.183, 1.089)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (75.0, 93.8)	92.7 (88.1, 97.3)
6 months	NE (NE, NE)	89.6 (83.4, 95.7)
9 months	NE (NE, NE)	85.7 (76.2, 95.2)
12 months	NE (NE, NE)	79.6 (65.0, 94.1)
18 months	NE (NE, NE)	79.6 (65.0, 94.1)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	6 (9.4)	8 (6.5)
Number of Subjects Censored, n (%)	58 (90.6)	116 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.537 (0.562)
95% CI		(0.179, 1.615)
Log-rank p-value		0.253

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (83.4, 98.6)	95.1 (91.3, 98.9)
6 months	NE (NE, NE)	92.0 (86.2, 97.7)
9 months	NE (NE, NE)	92.0 (86.2, 97.7)
12 months	NE (NE, NE)	92.0 (86.2, 97.7)
18 months	NE (NE, NE)	92.0 (86.2, 97.7)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	28 (16.9)	35 (10.5)
Number of Subjects Censored, n (%)	138 (83.1)	297 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	12.22 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.435 (0.262)
95% CI		(0.260, 0.728)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.7, 88.9)	93.3 (90.6, 96.1)
6 months	77.0 (67.3, 86.6)	86.9 (82.3, 91.5)
9 months	77.0 (67.3, 86.6)	85.2 (79.8, 90.7)
12 months	77.0 (67.3, 86.6)	79.6 (67.6, 91.5)
18 months	NE (NE, NE)	70.7 (51.3, 90.2)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	22 (13.3)	18 (5.4)
Number of Subjects Censored, n (%)	144 (86.7)	314 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.291 (0.326)
95% CI		(0.154, 0.552)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (79.9, 91.5)	96.4 (94.2, 98.5)
6 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
9 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
12 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
18 months	NE (NE, NE)	82.3 (63.0, 100.0)
Median Follow-up Time (months)	2.81	4.07

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	36 (16.3)	46 (10.5)
Number of Subjects Censored, n (%)	185 (83.7)	394 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.436 (0.232)
95% CI		(0.277, 0.687)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.6 (78.4, 88.8)	93.2 (90.7, 95.6)
6 months	77.3 (68.7, 85.9)	87.7 (83.8, 91.5)
9 months	77.3 (68.7, 85.9)	85.2 (80.1, 90.2)
12 months	77.3 (68.7, 85.9)	78.8 (68.9, 88.6)
18 months	NE (NE, NE)	72.7 (58.1, 87.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	27 (12.2)	26 (5.9)
Number of Subjects Censored, n (%)	194 (87.8)	414 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.348 (0.282)
95% CI		(0.200, 0.605)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (82.4, 91.9)	95.9 (94.0, 97.8)
6 months	83.5 (76.8, 90.3)	92.2 (89.0, 95.4)
9 months	83.5 (76.8, 90.3)	92.2 (89.0, 95.4)
12 months	83.5 (76.8, 90.3)	92.2 (89.0, 95.4)
18 months	NE (NE, NE)	85.1 (71.4, 98.7)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	2 (12.5)
Number of Subjects Censored, n (%)	7 (77.8)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.30 (1.22, NE)	NE (1.51, NE)
Median (95% CI)	NE (1.22, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Min, Max	1.2, 4.7*	1.5, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.377 (1.584)
95% CI		(0.017, 8.407)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (35.9, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	85.2 (66.0, 100.0)
9 months	NE (NE, NE)	85.2 (66.0, 100.0)
12 months	NE (NE, NE)	85.2 (66.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.22, NE)	NE (NE, NE)
Median (95% CI)	NE (1.22, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	14 (15.9)	21 (11.7)
Number of Subjects Censored, n (%)	74 (84.1)	158 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (3.19, NE)	11.04 (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Min, Max	0.2*, 6.8*	0.2, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.412 (0.371)
95% CI		(0.199, 0.853)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (78.1, 93.7)	93.1 (89.3, 96.9)
6 months	71.3 (54.2, 88.3)	87.3 (81.5, 93.0)
9 months	NE (NE, NE)	81.6 (72.4, 90.9)
12 months	NE (NE, NE)	73.5 (56.2, 90.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	11 (6.1)
Number of Subjects Censored, n (%)	77 (87.5)	168 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.298 (0.446)
95% CI		(0.124, 0.716)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (80.6, 95.5)	95.7 (92.7, 98.8)
6 months	79.6 (66.5, 92.8)	91.6 (86.6, 96.6)
9 months	NE (NE, NE)	91.6 (86.6, 96.6)
12 months	NE (NE, NE)	91.6 (86.6, 96.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	24 (16.9)	27 (9.7)
Number of Subjects Censored, n (%)	118 (83.1)	250 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.405 (0.293)
95% CI		(0.228, 0.718)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (74.8, 88.3)	93.2 (90.2, 96.3)
6 months	81.5 (74.8, 88.3)	87.8 (82.9, 92.8)
9 months	81.5 (74.8, 88.3)	87.8 (82.9, 92.8)
12 months	81.5 (74.8, 88.3)	84.0 (75.3, 92.7)
18 months	NE (NE, NE)	73.5 (52.8, 94.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	17 (12.0)	15 (5.4)
Number of Subjects Censored, n (%)	125 (88.0)	262 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.344 (0.364)
95% CI		(0.168, 0.702)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (80.9, 92.7)	96.2 (93.9, 98.5)
6 months	86.8 (80.9, 92.7)	93.1 (89.3, 97.0)
9 months	86.8 (80.9, 92.7)	93.1 (89.3, 97.0)
12 months	86.8 (80.9, 92.7)	93.1 (89.3, 97.0)
18 months	NE (NE, NE)	81.5 (59.9, 100.0)
Median Follow-up Time (months)	2.81	3.78

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	23 (19.0)	22 (9.3)
Number of Subjects Censored, n (%)	98 (81.0)	215 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (2.40, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.318 (0.315)
95% CI		(0.171, 0.589)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.9 (73.4, 88.3)	93.9 (90.7, 97.0)
6 months	73.5 (60.8, 86.1)	90.2 (85.6, 94.9)
9 months	73.5 (60.8, 86.1)	86.5 (79.7, 93.3)
12 months	73.5 (60.8, 86.1)	75.5 (59.6, 91.4)
18 months	NE (NE, NE)	75.5 (59.6, 91.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	16 (13.2)	12 (5.1)
Number of Subjects Censored, n (%)	105 (86.8)	225 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.307 (0.387)
95% CI		(0.144, 0.654)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (78.7, 92.4)	95.5 (92.8, 98.3)
6 months	83.2 (75.2, 91.3)	93.8 (90.3, 97.4)
9 months	83.2 (75.2, 91.3)	93.8 (90.3, 97.4)
12 months	83.2 (75.2, 91.3)	93.8 (90.3, 97.4)
18 months	NE (NE, NE)	93.8 (90.3, 97.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	6 (15.0)
Number of Subjects Censored, n (%)	17 (94.4)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.79, NE)	NE (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.224 (1.087)
95% CI		(0.264, 18.714)
Log-rank p-value		0.454

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	87.4 (77.0, 97.7)
6 months	94.4 (83.9, 100.0)	83.9 (71.9, 95.9)
9 months	NE (NE, NE)	83.9 (71.9, 95.9)
12 months	NE (NE, NE)	83.9 (71.9, 95.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	4 (10.0)
Number of Subjects Censored, n (%)	18 (100.0)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.231

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.3 (83.9, 100.0)
6 months	100.0 (100.0, 100.0)	88.7 (78.2, 99.3)
9 months	NE (NE, NE)	88.7 (78.2, 99.3)
12 months	NE (NE, NE)	88.7 (78.2, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	14 (15.4)	20 (11.2)
Number of Subjects Censored, n (%)	77 (84.6)	159 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.434 (0.368)
95% CI		(0.211, 0.892)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.3 (76.4, 92.3)	93.6 (90.0, 97.3)
6 months	78.3 (64.8, 91.9)	85.2 (78.5, 91.9)
9 months	NE (NE, NE)	85.2 (78.5, 91.9)
12 months	NE (NE, NE)	85.2 (78.5, 91.9)
18 months	NE (NE, NE)	71.0 (45.0, 97.0)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.2)	10 (5.6)
Number of Subjects Censored, n (%)	79 (86.8)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.232 (0.461)
95% CI		(0.094, 0.574)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (79.8, 94.2)	97.6 (95.3, 99.9)
6 months	80.8 (67.3, 94.3)	91.6 (85.9, 97.4)
9 months	NE (NE, NE)	91.6 (85.9, 97.4)
12 months	NE (NE, NE)	91.6 (85.9, 97.4)
18 months	NE (NE, NE)	76.4 (48.6, 100.0)
Median Follow-up Time (months)	2.79	4.37

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	34 (21.9)	40 (11.9)
Number of Subjects Censored, n (%)	121 (78.1)	295 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.19 (2.27, NE)	11.04 (7.79, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Min, Max	0.4, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.321 (0.252)
95% CI		(0.195, 0.526)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.0 (69.9, 84.2)	92.3 (89.3, 95.2)
6 months	69.7 (57.9, 81.5)	85.8 (80.9, 90.6)
9 months	NE (NE, NE)	82.0 (75.2, 88.9)
12 months	NE (NE, NE)	72.1 (57.6, 86.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	25 (16.1)	23 (6.9)
Number of Subjects Censored, n (%)	130 (83.9)	312 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (0.307)
95% CI		(0.144, 0.478)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.3, 89.4)	95.2 (92.9, 97.6)
6 months	75.3 (63.6, 87.1)	90.7 (86.5, 94.8)
9 months	NE (NE, NE)	90.7 (86.5, 94.8)
12 months	NE (NE, NE)	90.7 (86.5, 94.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	4 (5.3)	8 (6.6)
Number of Subjects Censored, n (%)	71 (94.7)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.876 (0.635)
95% CI		(0.252, 3.042)
Log-rank p-value		0.958

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.7, 100.0)	95.7 (92.0, 99.4)
6 months	90.6 (79.9, 100.0)	92.0 (86.5, 97.4)
9 months	90.6 (79.9, 100.0)	92.0 (86.5, 97.4)
12 months	90.6 (79.9, 100.0)	92.0 (86.5, 97.4)
18 months	NE (NE, NE)	92.0 (86.5, 97.4)
Median Follow-up Time (months)	2.86	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	3 (4.0)	3 (2.5)
Number of Subjects Censored, n (%)	72 (96.0)	118 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.437 (0.837)
95% CI		(0.085, 2.255)
Log-rank p-value		0.368

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.7, 100.0)	98.2 (95.8, 100.0)
6 months	95.6 (90.7, 100.0)	96.8 (93.2, 100.0)
9 months	95.6 (90.7, 100.0)	96.8 (93.2, 100.0)
12 months	95.6 (90.7, 100.0)	96.8 (93.2, 100.0)
18 months	NE (NE, NE)	96.8 (93.2, 100.0)
Median Follow-up Time (months)	2.86	4.67

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	2 (9.5)
Number of Subjects Censored, n (%)	9 (81.8)	19 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.99, NE)
Median (95% CI)	NE (1.28, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Min, Max	0.7, 6.5*	1.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.082 (1.632)
95% CI		(0.003, 2.000)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	90.2 (77.3, 100.0)
6 months	81.8 (59.0, 100.0)	90.2 (77.3, 100.0)
9 months	NE (NE, NE)	90.2 (77.3, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	1 (4.8)
Number of Subjects Censored, n (%)	9 (81.8)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (0.99, NE)
Median (95% CI)	NE (1.28, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	1.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
6 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	36 (16.4)	46 (10.6)
Number of Subjects Censored, n (%)	183 (83.6)	389 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.433 (0.232)
95% CI		(0.275, 0.683)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (78.1, 88.6)	93.3 (90.9, 95.7)
6 months	77.0 (68.4, 85.7)	87.4 (83.6, 91.3)
9 months	77.0 (68.4, 85.7)	85.1 (80.2, 90.1)
12 months	77.0 (68.4, 85.7)	79.3 (70.1, 88.5)
18 months	NE (NE, NE)	74.0 (60.8, 87.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3P
Summary of Time to Onset of TEAE by SOC/PT by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	26 (11.9)	25 (5.7)
Number of Subjects Censored, n (%)	193 (88.1)	410 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.341 (0.289)
95% CI		(0.193, 0.600)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (82.8, 92.3)	96.1 (94.2, 98.0)
6 months	83.9 (77.1, 90.7)	92.3 (89.1, 95.5)
9 months	83.9 (77.1, 90.7)	92.3 (89.1, 95.5)
12 months	83.9 (77.1, 90.7)	92.3 (89.1, 95.5)
18 months	NE (NE, NE)	86.2 (74.1, 98.2)
Median Follow-up Time (months)	2.83	3.94

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	2 (3.3)
Number of Subjects Censored, n (%)	40 (88.9)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.76, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Min, Max	1.1, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.260 (0.946)
95% CI		(0.041, 1.661)
Log-rank p-value		0.154

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (77.4, 97.9)	98.1 (94.6, 100.0)
6 months	87.6 (77.4, 97.9)	95.9 (90.3, 100.0)
9 months	87.6 (77.4, 97.9)	95.9 (90.3, 100.0)
12 months	87.6 (77.4, 97.9)	95.9 (90.3, 100.0)
18 months	NE (NE, NE)	95.9 (90.3, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (8.9)	1 (1.7)
Number of Subjects Censored, n (%)	41 (91.1)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.214 (1.139)
95% CI		(0.023, 1.991)
Log-rank p-value		0.154

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
6 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
9 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
12 months	90.1 (80.9, 99.4)	98.1 (94.6, 100.0)
18 months	NE (NE, NE)	98.1 (94.6, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	33 (17.9)	46 (11.6)
Number of Subjects Censored, n (%)	151 (82.1)	350 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (3.19, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.425 (0.240)
95% CI		(0.266, 0.680)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (76.2, 88.0)	92.4 (89.8, 95.1)
6 months	73.9 (63.3, 84.5)	86.3 (82.0, 90.5)
9 months	NE (NE, NE)	83.6 (78.0, 89.1)
12 months	NE (NE, NE)	76.8 (66.2, 87.3)
18 months	NE (NE, NE)	70.4 (54.9, 85.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3Q
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	24 (13.0)	25 (6.3)
Number of Subjects Censored, n (%)	160 (87.0)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.297)
95% CI		(0.189, 0.606)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (81.0, 91.8)	95.7 (93.7, 97.8)
6 months	81.8 (73.7, 89.9)	91.5 (88.0, 95.0)
9 months	NE (NE, NE)	91.5 (88.0, 95.0)
12 months	NE (NE, NE)	91.5 (88.0, 95.0)
18 months	NE (NE, NE)	83.9 (69.2, 98.6)
Median Follow-up Time (months)	2.81	3.75

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	2 (3.3)
Number of Subjects Censored, n (%)	38 (90.5)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Min, Max	1.1, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.281 (0.995)
95% CI		(0.040, 1.979)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (80.1, 99.3)	98.1 (94.6, 100.0)
6 months	89.7 (80.1, 99.3)	95.9 (90.3, 100.0)
9 months	89.7 (80.1, 99.3)	95.9 (90.3, 100.0)
12 months	89.7 (80.1, 99.3)	95.9 (90.3, 100.0)
18 months	NE (NE, NE)	95.9 (90.3, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	3 (7.1)	1 (1.7)
Number of Subjects Censored, n (%)	39 (92.9)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.234 (1.179)
95% CI		(0.023, 2.366)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
6 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
9 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
12 months	92.5 (84.3, 100.0)	98.1 (94.6, 100.0)
18 months	NE (NE, NE)	98.1 (94.6, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	34 (18.1)	46 (11.6)
Number of Subjects Censored, n (%)	154 (81.9)	350 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (2.76, NE)	12.22 (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.422 (0.238)
95% CI		(0.264, 0.672)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.7 (75.8, 87.6)	92.4 (89.8, 95.1)
6 months	73.9 (63.6, 84.1)	86.3 (82.0, 90.5)
9 months	NE (NE, NE)	83.6 (78.0, 89.1)
12 months	NE (NE, NE)	76.8 (66.2, 87.3)
18 months	NE (NE, NE)	70.4 (54.9, 85.8)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3R
Summary of Time to Onset of TEAE by SOC/PT by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	25 (13.3)	25 (6.3)
Number of Subjects Censored, n (%)	163 (86.7)	371 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.332 (0.294)
95% CI		(0.187, 0.591)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (80.5, 91.3)	95.7 (93.7, 97.8)
6 months	81.5 (73.5, 89.4)	91.5 (88.0, 95.0)
9 months	NE (NE, NE)	91.5 (88.0, 95.0)
12 months	NE (NE, NE)	91.5 (88.0, 95.0)
18 months	NE (NE, NE)	83.9 (69.2, 98.6)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	3 (21.4)	7 (35.0)
Number of Subjects Censored, n (%)	11 (78.6)	13 (65.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	2.66 (0.62, 9.82)
Median (95% CI)	NE (1.94, NE)	9.82 (2.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Min, Max	0.4, 4.1*	0.6, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.566 (0.821)
95% CI		(0.113, 2.830)
Log-rank p-value		0.468

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (52.2, 100.0)	73.8 (53.9, 93.7)
6 months	NE (NE, NE)	63.3 (37.7, 88.9)
9 months	NE (NE, NE)	63.3 (37.7, 88.9)
12 months	NE (NE, NE)	31.6 (0.0, 77.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	4 (20.0)
Number of Subjects Censored, n (%)	12 (85.7)	16 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	5.03 (1.51, NE)
Median (95% CI)	NE (1.94, NE)	NE (5.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 4.1*	0.6*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.462 (1.006)
95% CI		(0.064, 3.314)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.5 (60.0, 100.0)	82.1 (63.6, 100.0)
6 months	NE (NE, NE)	70.4 (43.8, 96.9)
9 months	NE (NE, NE)	70.4 (43.8, 96.9)
12 months	NE (NE, NE)	70.4 (43.8, 96.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	15 (19.7)	24 (17.1)
Number of Subjects Censored, n (%)	61 (80.3)	116 (82.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	7.75 (4.37, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.664 (0.349)
95% CI		(0.335, 1.317)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.9 (66.4, 87.3)	89.6 (84.4, 94.8)
6 months	76.9 (66.4, 87.3)	78.8 (69.6, 87.9)
9 months	NE (NE, NE)	70.0 (56.0, 84.0)
12 months	NE (NE, NE)	70.0 (56.0, 84.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	9 (11.8)	12 (8.6)
Number of Subjects Censored, n (%)	67 (88.2)	128 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.60, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.534 (0.472)
95% CI		(0.212, 1.345)
Log-rank p-value		0.267

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.5 (75.0, 94.0)	94.8 (91.0, 98.5)
6 months	84.5 (75.0, 94.0)	88.3 (81.0, 95.6)
9 months	NE (NE, NE)	88.3 (81.0, 95.6)
12 months	NE (NE, NE)	88.3 (81.0, 95.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	19 (14.1)	16 (5.6)
Number of Subjects Censored, n (%)	116 (85.9)	269 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (0.358)
95% CI		(0.130, 0.528)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (81.8, 93.3)	96.4 (94.2, 98.6)
6 months	76.7 (63.6, 89.7)	93.3 (90.0, 96.7)
9 months	76.7 (63.6, 89.7)	93.3 (90.0, 96.7)
12 months	76.7 (63.6, 89.7)	86.7 (73.7, 99.7)
18 months	NE (NE, NE)	86.7 (73.7, 99.7)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.3.3S
Summary of Time to Onset of TEAE by SOC/PT by Body Mass Index
Safety Population
Serious TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	16 (11.9)	10 (3.5)
Number of Subjects Censored, n (%)	119 (88.1)	275 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.221 (0.419)
95% CI		(0.097, 0.502)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (83.8, 94.6)	97.4 (95.6, 99.3)
6 months	83.0 (73.2, 92.9)	95.6 (92.9, 98.4)
9 months	83.0 (73.2, 92.9)	95.6 (92.9, 98.4)
12 months	83.0 (73.2, 92.9)	95.6 (92.9, 98.4)
18 months	NE (NE, NE)	95.6 (92.9, 98.4)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	20 (16.9)	45 (18.4)
Number of Subjects Censored, n (%)	98 (83.1)	199 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	11.04 (3.91, 16.07)
Median (95% CI)	NE (NE, NE)	16.07 (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.769 (0.277)
95% CI		(0.447, 1.324)
Log-rank p-value		0.359

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.8 (76.8, 90.7)	86.9 (82.4, 91.3)
6 months	76.9 (65.5, 88.3)	77.9 (71.6, 84.2)
9 months	NE (NE, NE)	77.9 (71.6, 84.2)
12 months	NE (NE, NE)	68.1 (49.5, 86.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	13 (11.0)	14 (5.7)
Number of Subjects Censored, n (%)	105 (89.0)	230 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.349 (0.402)
95% CI		(0.159, 0.766)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.5, 94.8)	96.5 (94.1, 98.9)
6 months	85.9 (78.0, 93.8)	92.7 (88.8, 96.7)
9 months	NE (NE, NE)	92.7 (88.8, 96.7)
12 months	NE (NE, NE)	92.7 (88.8, 96.7)
18 months	NE (NE, NE)	74.2 (41.5, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	14 (5.7)
Number of Subjects Censored, n (%)	113 (95.8)	230 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	16.07 (11.04, NE)
Median (95% CI)	NE (NE, NE)	16.07 (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.07, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.938 (0.540)
95% CI		(0.326, 2.700)
Log-rank p-value		0.912

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.4, 99.4)	95.4 (92.6, 98.2)
6 months	95.4 (91.4, 99.4)	93.5 (89.6, 97.4)
9 months	NE (NE, NE)	93.5 (89.6, 97.4)
12 months	NE (NE, NE)	81.8 (60.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	37 (15.2)
Number of Subjects Censored, n (%)	118 (100.0)	207 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.5 (79.9, 89.1)
6 months	100.0 (100.0, 100.0)	84.5 (79.9, 89.1)
9 months	NE (NE, NE)	84.5 (79.9, 89.1)
12 months	NE (NE, NE)	84.5 (79.9, 89.1)
18 months	NE (NE, NE)	84.5 (79.9, 89.1)
Median Follow-up Time (months)	2.83	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	35 (14.3)
Number of Subjects Censored, n (%)	118 (100.0)	209 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.4 (80.9, 89.9)
6 months	100.0 (100.0, 100.0)	85.4 (80.9, 89.9)
9 months	NE (NE, NE)	85.4 (80.9, 89.9)
12 months	NE (NE, NE)	85.4 (80.9, 89.9)
18 months	NE (NE, NE)	85.4 (80.9, 89.9)
Median Follow-up Time (months)	2.83	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	17 (7.0)
Number of Subjects Censored, n (%)	117 (99.2)	227 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.2*, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.511 (1.037)
95% CI		(0.984, 57.342)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	94.0 (90.9, 97.0)
6 months	99.1 (97.5, 100.0)	92.8 (89.0, 96.6)
9 months	NE (NE, NE)	90.6 (84.9, 96.2)
12 months	NE (NE, NE)	90.6 (84.9, 96.2)
18 months	NE (NE, NE)	45.3 (0.0, 100.0)
Median Follow-up Time (months)	2.83	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	15 (6.1)
Number of Subjects Censored, n (%)	118 (100.0)	229 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (91.4, 97.4)
6 months	100.0 (100.0, 100.0)	93.2 (89.5, 96.9)
9 months	NE (NE, NE)	91.0 (85.4, 96.6)
12 months	NE (NE, NE)	91.0 (85.4, 96.6)
18 months	NE (NE, NE)	91.0 (85.4, 96.6)
Median Follow-up Time (months)	2.83	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	24 (21.4)	46 (21.7)
Number of Subjects Censored, n (%)	88 (78.6)	166 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (1.94, NE)	5.65 (3.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.870 (0.258)
95% CI		(0.524, 1.442)
Log-rank p-value		0.548

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.2 (68.9, 85.5)	82.0 (76.8, 87.3)
6 months	72.9 (61.6, 84.3)	73.4 (66.2, 80.7)
9 months	72.9 (61.6, 84.3)	73.4 (66.2, 80.7)
12 months	72.9 (61.6, 84.3)	73.4 (66.2, 80.7)
18 months	NE (NE, NE)	73.4 (66.2, 80.7)
Median Follow-up Time (months)	2.79	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	15 (13.4)	13 (6.1)
Number of Subjects Censored, n (%)	97 (86.6)	199 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.310 (0.398)
95% CI		(0.142, 0.678)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.5, 92.7)	95.5 (92.7, 98.4)
6 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
9 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
12 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
18 months	NE (NE, NE)	91.1 (85.9, 96.2)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	4 (3.6)	21 (9.9)
Number of Subjects Censored, n (%)	108 (96.4)	191 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.634 (0.549)
95% CI		(0.899, 7.719)
Log-rank p-value		0.073

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (92.2, 99.9)	91.2 (87.2, 95.1)
6 months	96.0 (92.2, 99.9)	88.4 (83.5, 93.4)
9 months	96.0 (92.2, 99.9)	88.4 (83.5, 93.4)
12 months	96.0 (92.2, 99.9)	88.4 (83.5, 93.4)
18 months	NE (NE, NE)	88.4 (83.5, 93.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	4 (3.6)	30 (14.2)
Number of Subjects Censored, n (%)	108 (96.4)	182 (85.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	NE (10.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.497 (0.536)
95% CI		(1.222, 10.007)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.1, 100.0)	86.9 (82.2, 91.5)
6 months	91.5 (80.2, 100.0)	84.1 (78.2, 90.0)
9 months	91.5 (80.2, 100.0)	84.1 (78.2, 90.0)
12 months	91.5 (80.2, 100.0)	77.6 (64.3, 90.9)
18 months	NE (NE, NE)	77.6 (64.3, 90.9)
Median Follow-up Time (months)	2.79	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	27 (12.7)
Number of Subjects Censored, n (%)	110 (98.2)	185 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.503 (0.736)
95% CI		(1.538, 27.492)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.5, 100.0)	87.8 (83.3, 92.3)
6 months	98.1 (95.5, 100.0)	86.5 (81.4, 91.6)
9 months	98.1 (95.5, 100.0)	86.5 (81.4, 91.6)
12 months	98.1 (95.5, 100.0)	80.3 (67.7, 92.9)
18 months	NE (NE, NE)	80.3 (67.7, 92.9)
Median Follow-up Time (months)	2.79	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	14 (6.6)
Number of Subjects Censored, n (%)	112 (100.0)	198 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.7)
6 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
9 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
12 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
18 months	NE (NE, NE)	88.3 (81.7, 94.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	14 (6.6)
Number of Subjects Censored, n (%)	112 (100.0)	198 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.7)
6 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
9 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
12 months	100.0 (100.0, 100.0)	88.3 (81.7, 94.8)
18 months	NE (NE, NE)	88.3 (81.7, 94.8)
Median Follow-up Time (months)	2.79	3.75

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	29 (20.7)	46 (19.1)
Number of Subjects Censored, n (%)	111 (79.3)	195 (80.9)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.27, NE)	16.07 (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (16.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.07, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.671 (0.245)
95% CI		(0.415, 1.085)
Log-rank p-value		0.112

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (73.3, 87.1)	85.8 (81.3, 90.3)
6 months	68.7 (54.7, 82.7)	76.6 (70.1, 83.1)
9 months	68.7 (54.7, 82.7)	76.6 (70.1, 83.1)
12 months	68.7 (54.7, 82.7)	76.6 (70.1, 83.1)
18 months	NE (NE, NE)	57.5 (24.6, 90.3)
Median Follow-up Time (months)	2.81	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	19 (13.6)	15 (6.2)
Number of Subjects Censored, n (%)	121 (86.4)	226 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.323 (0.358)
95% CI		(0.160, 0.651)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (80.4, 92.5)	95.7 (93.1, 98.3)
6 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
9 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
12 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
18 months	NE (NE, NE)	92.0 (87.9, 96.1)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	6 (4.3)	17 (7.1)
Number of Subjects Censored, n (%)	134 (95.7)	224 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	16.07 (16.07, NE)
Median (95% CI)	NE (NE, NE)	NE (16.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.07, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.291 (0.485)
95% CI		(0.499, 3.343)
Log-rank p-value		0.585

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (91.6, 99.0)	94.3 (91.3, 97.3)
6 months	95.3 (91.6, 99.0)	91.7 (87.3, 96.0)
9 months	95.3 (91.6, 99.0)	91.7 (87.3, 96.0)
12 months	95.3 (91.6, 99.0)	91.7 (87.3, 96.0)
18 months	NE (NE, NE)	68.7 (29.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	27 (11.2)
Number of Subjects Censored, n (%)	138 (98.6)	214 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	NE (10.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.354 (0.735)
95% CI		(1.741, 31.066)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	88.9 (84.9, 93.0)
6 months	94.8 (86.0, 100.0)	88.9 (84.9, 93.0)
9 months	94.8 (86.0, 100.0)	88.9 (84.9, 93.0)
12 months	94.8 (86.0, 100.0)	82.6 (70.0, 95.2)
18 months	NE (NE, NE)	82.6 (70.0, 95.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	25 (10.4)
Number of Subjects Censored, n (%)	139 (99.3)	216 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		13.646 (1.022)
95% CI		(1.843, 101.054)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	89.9 (86.0, 93.7)
6 months	99.3 (97.8, 100.0)	89.9 (86.0, 93.7)
9 months	99.3 (97.8, 100.0)	89.9 (86.0, 93.7)
12 months	99.3 (97.8, 100.0)	83.4 (70.8, 96.1)
18 months	NE (NE, NE)	83.4 (70.8, 96.1)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	15 (6.2)
Number of Subjects Censored, n (%)	140 (100.0)	226 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
Median (95% CI)	NE (NE, NE)	NE (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.5 (92.8, 98.2)
6 months	100.0 (100.0, 100.0)	92.1 (87.4, 96.7)
9 months	100.0 (100.0, 100.0)	89.6 (82.9, 96.2)
12 months	100.0 (100.0, 100.0)	89.6 (82.9, 96.2)
18 months	NE (NE, NE)	59.7 (11.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	13 (5.4)
Number of Subjects Censored, n (%)	140 (100.0)	228 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (93.4, 98.6)
6 months	100.0 (100.0, 100.0)	92.5 (87.8, 97.1)
9 months	100.0 (100.0, 100.0)	90.0 (83.4, 96.6)
12 months	100.0 (100.0, 100.0)	90.0 (83.4, 96.6)
18 months	NE (NE, NE)	90.0 (83.4, 96.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	15 (16.7)	45 (20.9)
Number of Subjects Censored, n (%)	75 (83.3)	170 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	11.04 (3.32, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.045 (0.303)
95% CI		(0.577, 1.891)
Log-rank p-value		0.970

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (72.6, 90.0)	83.3 (78.1, 88.5)
6 months	81.3 (72.6, 90.0)	75.2 (68.2, 82.1)
9 months	NE (NE, NE)	75.2 (68.2, 82.1)
12 months	NE (NE, NE)	68.3 (54.1, 82.6)
18 months	NE (NE, NE)	57.0 (33.4, 80.5)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	12 (5.6)
Number of Subjects Censored, n (%)	81 (90.0)	203 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.382 (0.459)
95% CI		(0.155, 0.940)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (80.8, 95.6)	96.4 (93.8, 99.0)
6 months	88.2 (80.8, 95.6)	92.3 (87.6, 97.1)
9 months	NE (NE, NE)	92.3 (87.6, 97.1)
12 months	NE (NE, NE)	92.3 (87.6, 97.1)
18 months	NE (NE, NE)	76.9 (49.1, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	18 (8.4)
Number of Subjects Censored, n (%)	87 (96.7)	197 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.242 (0.628)
95% CI		(0.655, 7.678)
Log-rank p-value		0.205

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.2, 100.0)	92.5 (88.8, 96.2)
6 months	96.3 (92.2, 100.0)	90.6 (86.0, 95.1)
9 months	NE (NE, NE)	90.6 (86.0, 95.1)
12 months	NE (NE, NE)	82.3 (66.4, 98.2)
18 months	NE (NE, NE)	82.3 (66.4, 98.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	40 (18.6)
Number of Subjects Censored, n (%)	88 (97.8)	175 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.412 (0.726)
95% CI		(2.267, 39.077)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	81.8 (76.5, 87.0)
6 months	97.7 (94.6, 100.0)	79.4 (73.4, 85.4)
9 months	NE (NE, NE)	79.4 (73.4, 85.4)
12 months	NE (NE, NE)	79.4 (73.4, 85.4)
18 months	NE (NE, NE)	79.4 (73.4, 85.4)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	37 (17.2)
Number of Subjects Censored, n (%)	89 (98.9)	178 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		17.494 (1.015)
95% CI		(2.395, 127.812)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	82.7 (77.5, 87.9)
6 months	98.9 (96.6, 100.0)	81.6 (76.1, 87.1)
9 months	NE (NE, NE)	81.6 (76.1, 87.1)
12 months	NE (NE, NE)	81.6 (76.1, 87.1)
18 months	NE (NE, NE)	81.6 (76.1, 87.1)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	16 (7.4)
Number of Subjects Censored, n (%)	89 (98.9)	199 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.952 (1.035)
95% CI		(0.783, 45.272)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	94.1 (90.8, 97.3)
6 months	98.9 (96.7, 100.0)	89.5 (84.0, 94.9)
9 months	NE (NE, NE)	89.5 (84.0, 94.9)
12 months	NE (NE, NE)	89.5 (84.0, 94.9)
18 months	NE (NE, NE)	89.5 (84.0, 94.9)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	16 (7.4)
Number of Subjects Censored, n (%)	90 (100.0)	199 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (90.8, 97.3)
6 months	100.0 (100.0, 100.0)	89.5 (84.0, 94.9)
9 months	NE (NE, NE)	89.5 (84.0, 94.9)
12 months	NE (NE, NE)	89.5 (84.0, 94.9)
18 months	NE (NE, NE)	89.5 (84.0, 94.9)
Median Follow-up Time (months)	2.83	3.61

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	6 (14.6)	13 (16.3)
Number of Subjects Censored, n (%)	35 (85.4)	67 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (1.94, NE)	NE (3.32, NE)
Median (95% CI)	NE (4.14, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Min, Max	1.0, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.825 (0.500)
95% CI		(0.310, 2.197)
Log-rank p-value		0.871

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (76.4, 97.7)	86.3 (78.3, 94.3)
6 months	74.6 (50.3, 99.0)	79.5 (69.0, 89.9)
9 months	NE (NE, NE)	79.5 (69.0, 89.9)
12 months	NE (NE, NE)	79.5 (69.0, 89.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	3 (3.8)
Number of Subjects Censored, n (%)	37 (90.2)	77 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.230 (0.782)
95% CI		(0.050, 1.065)
Log-rank p-value		0.095

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (79.2, 99.3)	98.7 (96.3, 100.0)
6 months	89.2 (79.2, 99.3)	94.5 (88.2, 100.0)
9 months	NE (NE, NE)	94.5 (88.2, 100.0)
12 months	NE (NE, NE)	94.5 (88.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	11 (13.8)
Number of Subjects Censored, n (%)	40 (97.6)	69 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.545 (1.049)
95% CI		(0.710, 43.329)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	85.6 (77.7, 93.5)
6 months	97.6 (92.8, 100.0)	85.6 (77.7, 93.5)
9 months	NE (NE, NE)	85.6 (77.7, 93.5)
12 months	NE (NE, NE)	85.6 (77.7, 93.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	10 (12.5)
Number of Subjects Censored, n (%)	41 (100.0)	70 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.9 (79.3, 94.5)
6 months	100.0 (100.0, 100.0)	86.9 (79.3, 94.5)
9 months	NE (NE, NE)	86.9 (79.3, 94.5)
12 months	NE (NE, NE)	86.9 (79.3, 94.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	7 (8.8)
Number of Subjects Censored, n (%)	41 (100.0)	73 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (85.5, 98.1)
6 months	100.0 (100.0, 100.0)	87.7 (77.6, 97.7)
9 months	NE (NE, NE)	87.7 (77.6, 97.7)
12 months	NE (NE, NE)	87.7 (77.6, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	7 (8.8)
Number of Subjects Censored, n (%)	41 (100.0)	73 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (85.5, 98.1)
6 months	100.0 (100.0, 100.0)	87.7 (77.6, 97.7)
9 months	NE (NE, NE)	87.7 (77.6, 97.7)
12 months	NE (NE, NE)	87.7 (77.6, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	36 (21.6)	71 (21.7)
Number of Subjects Censored, n (%)	131 (78.4)	256 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.23, NE)	5.65 (3.61, 16.07)
Median (95% CI)	NE (NE, NE)	NE (16.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.775 (0.209)
95% CI		(0.515, 1.167)
Log-rank p-value		0.237

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.2 (71.7, 84.7)	83.5 (79.3, 87.6)
6 months	74.1 (65.7, 82.5)	74.5 (68.8, 80.1)
9 months	74.1 (65.7, 82.5)	74.5 (68.8, 80.1)
12 months	74.1 (65.7, 82.5)	70.8 (61.9, 79.7)
18 months	NE (NE, NE)	52.3 (27.1, 77.5)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	22 (13.2)	20 (6.1)
Number of Subjects Censored, n (%)	145 (86.8)	307 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.329 (0.318)
95% CI		(0.176, 0.613)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (81.1, 92.2)	95.4 (93.1, 97.8)
6 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
9 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
12 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
18 months	NE (NE, NE)	85.3 (71.6, 99.1)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	9 (5.4)	35 (10.7)
Number of Subjects Censored, n (%)	158 (94.6)	292 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	16.07 (11.04, NE)
Median (95% CI)	NE (NE, NE)	NE (16.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.637 (0.378)
95% CI		(0.781, 3.435)
Log-rank p-value		0.171

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (90.2, 97.8)	90.9 (87.7, 94.1)
6 months	94.0 (90.2, 97.8)	87.7 (83.5, 92.0)
9 months	94.0 (90.2, 97.8)	87.7 (83.5, 92.0)
12 months	94.0 (90.2, 97.8)	83.4 (74.1, 92.6)
18 months	NE (NE, NE)	66.7 (36.5, 96.8)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	46 (14.1)
Number of Subjects Censored, n (%)	165 (98.8)	281 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		11.915 (0.723)
95% CI		(2.888, 49.155)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	86.3 (82.5, 90.0)
6 months	96.4 (90.7, 100.0)	84.7 (80.3, 89.0)
9 months	96.4 (90.7, 100.0)	84.7 (80.3, 89.0)
12 months	96.4 (90.7, 100.0)	84.7 (80.3, 89.0)
18 months	NE (NE, NE)	84.7 (80.3, 89.0)
Median Follow-up Time (months)	2.83	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	43 (13.1)
Number of Subjects Censored, n (%)	166 (99.4)	284 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		22.878 (1.012)
95% CI		(3.148, 166.260)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	86.9 (83.2, 90.6)
6 months	99.4 (98.1, 100.0)	86.2 (82.2, 90.1)
9 months	99.4 (98.1, 100.0)	86.2 (82.2, 90.1)
12 months	99.4 (98.1, 100.0)	86.2 (82.2, 90.1)
18 months	NE (NE, NE)	86.2 (82.2, 90.1)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	17 (5.2)
Number of Subjects Censored, n (%)	166 (99.4)	310 (94.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
Median (95% CI)	NE (NE, NE)	NE (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.597 (1.039)
95% CI		(0.730, 42.902)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	96.7 (94.7, 98.7)
6 months	99.4 (98.2, 100.0)	93.0 (89.3, 96.8)
9 months	99.4 (98.2, 100.0)	91.5 (86.7, 96.2)
12 months	99.4 (98.2, 100.0)	91.5 (86.7, 96.2)
18 months	NE (NE, NE)	68.6 (29.6, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	0	15 (4.6)
Number of Subjects Censored, n (%)	167 (100.0)	312 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.1, 99.0)
6 months	100.0 (100.0, 100.0)	93.3 (89.6, 97.0)
9 months	100.0 (100.0, 100.0)	91.8 (87.1, 96.5)
12 months	100.0 (100.0, 100.0)	91.8 (87.1, 96.5)
18 months	NE (NE, NE)	91.8 (87.1, 96.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	7 (14.3)
Number of Subjects Censored, n (%)	20 (90.9)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	NE (4.27, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.705 (0.864)
95% CI		(0.130, 3.831)
Log-rank p-value		0.504

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	89.6 (81.0, 98.2)
6 months	85.7 (67.4, 100.0)	80.8 (66.7, 94.9)
9 months	NE (NE, NE)	80.8 (66.7, 94.9)
12 months	NE (NE, NE)	80.8 (66.7, 94.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	4 (8.2)
Number of Subjects Censored, n (%)	20 (90.9)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.293 (1.007)
95% CI		(0.041, 2.106)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	95.9 (90.4, 100.0)
6 months	85.7 (67.4, 100.0)	87.0 (74.0, 100.0)
9 months	NE (NE, NE)	87.0 (74.0, 100.0)
12 months	NE (NE, NE)	87.0 (74.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	10 (20.4)
Number of Subjects Censored, n (%)	21 (95.5)	39 (79.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	10.35 (0.62, NE)
Median (95% CI)	NE (NE, NE)	10.35 (10.35, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (10.35, NE)
Min, Max	0.6, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.705 (1.062)
95% CI		(0.462, 29.716)
Log-rank p-value		0.191

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	81.2 (70.0, 92.3)
6 months	95.5 (86.8, 100.0)	81.2 (70.0, 92.3)
9 months	NE (NE, NE)	81.2 (70.0, 92.3)
12 months	NE (NE, NE)	40.6 (0.0, 97.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	9 (18.4)
Number of Subjects Censored, n (%)	21 (95.5)	40 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	10.35 (0.62, NE)
Median (95% CI)	NE (NE, NE)	10.35 (10.35, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (10.35, NE)
Min, Max	0.6, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.490 (1.070)
95% CI		(0.429, 28.392)
Log-rank p-value		0.224

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	83.4 (72.9, 93.9)
6 months	95.5 (86.8, 100.0)	83.4 (72.9, 93.9)
9 months	NE (NE, NE)	83.4 (72.9, 93.9)
12 months	NE (NE, NE)	41.7 (0.0, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	7 (14.3)
Number of Subjects Censored, n (%)	22 (100.0)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.30, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.4 (77.9, 96.8)
6 months	100.0 (100.0, 100.0)	80.6 (65.3, 96.0)
9 months	NE (NE, NE)	80.6 (65.3, 96.0)
12 months	NE (NE, NE)	80.6 (65.3, 96.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	7 (14.3)
Number of Subjects Censored, n (%)	22 (100.0)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.30, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.4 (77.9, 96.8)
6 months	100.0 (100.0, 100.0)	80.6 (65.3, 96.0)
9 months	NE (NE, NE)	80.6 (65.3, 96.0)
12 months	NE (NE, NE)	80.6 (65.3, 96.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	11 (10.8)	29 (15.0)
Number of Subjects Censored, n (%)	91 (89.2)	164 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	16.07 (5.95, NE)
Median (95% CI)	NE (NE, NE)	16.07 (16.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.07, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Min, Max	0.4*, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.006 (0.366)
95% CI		(0.491, 2.062)
Log-rank p-value		0.803

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.5.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3 in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (84.2, 96.4)	91.0 (86.9, 95.1)
6 months	82.6 (70.6, 94.5)	81.6 (75.0, 88.1)
9 months	NE (NE, NE)	81.6 (75.0, 88.1)
12 months	NE (NE, NE)	81.6 (75.0, 88.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.