Modul 4A Anhang 4-G

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Trametinib (Spexotras®)

Novartis Pharma GmbH

Modul 4 A – Anhang 4-G

*Kombination mit Dabrafenib zur Behandlung von pädiatrischen Patienten ab einem Alter von 1 Jahr mit einem **LGG** mit einer BRAF-V600E-Mutation, die eine systemische Therapie benötigen*

Ergänzende Analysen zu der Studie CDRB436G2201 (Datenschnitt: 28.04.2023)

Stand: 25.04.2024

Inhaltsverzeichnis

Seite

Ergänzende Analysen zur Studie CDRB436G2201 – Gesamtpopulation

1. PROMIS PGH-7+2

1.1. Änderung der T-Scores gegenüber Studienbeginn mittels MMRM-Analyse zu den verschiedenen Erhebungszeitpunkten

1.1.1. Gesamtpopulation

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis
Full Analysis Set - L

Scale: Global Health Scores

	Treatment Groups						Comparison		
	Dabrafenib+Trametinib (N=73)			Carboplatin+Vincristine (N=37)					
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	50	0.2 (1.02)	[-1.78, 2.26]	18	-3.2 (1.67)	[-6.52, 0.14]	3.43[a]	[-0.47, 7.33]	0.084
Week 8 Day 1	53	1.2 (0.97)	[-0.69, 3.17]	18	-4.6 (1.63)	[-7.84, -1.36]	5.84[a]	[2.07, 9.60]	0.003
Week 16 Day 1	48	1.7 (1.08)	[-0.44, 3.89]	10	-6.1 (2.11)	[-10.35, -1.93]	7.86[a]	[3.13, 12.59]	0.001
Week 24 Day 1	46	3.1 (1.17)	[0.80, 5.45]	10	-7.3 (2.34)	[-11.96, -2.66]	10.44[a]	[5.24, 15.64]	<0.001
Week 32 Day 1	47	2.9 (1.06)	[0.77, 4.99]	11	-5.5 (2.03)	[-9.57, -1.46]	8.40[a]	[3.82, 12.97]	<0.001
Week 48 Day 1	43	2.2 (1.12)	[-0.08, 4.40]	10	-5.4 (2.19)	[-9.71, -1.00]	7.52[a]	[2.63, 12.42]	0.003
End Of Treatment	50	2.6 (1.29)	[-0.01, 5.12]	14	-3.9 (2.34)	[-8.59, 0.71]	6.49[a]	[1.18, 11.80]	0.017
Overall treatment effect	60	2.0 (0.88)	[0.23, 3.75]	23	-5.2 (1.55)	[-8.24, -2.06]	7.14[b]	[3.58, 10.70]	<0.001

Analogous to CSR table 14.2-7.3L.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis
Full Analysis Set - L

Scale: Pain Scores

	Treatment Groups						Comparison		
	Dabrafenib+Trametinib (N=73)			Carboplatin+Vincristine (N=37)					
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	51	-1.5 (0.97)	[-3.45, 0.41]	18	-0.8 (1.63)	[-4.07, 2.42]	-0.69[a]	[-4.47, 3.09]	0.717
Week 8 Day 1	54	-2.0 (0.89)	[-3.81, -0.25]	18	-1.7 (1.56)	[-4.77, 1.43]	-0.36[a]	[-3.93, 3.22]	0.844
Week 16 Day 1	48	-1.7 (0.92)	[-3.56, 0.11]	10	-1.0 (1.98)	[-5.01, 2.92]	-0.68[a]	[-5.05, 3.69]	0.758
Week 24 Day 1	46	-1.5 (1.02)	[-3.51, 0.57]	10	-0.6 (2.06)	[-4.72, 3.49]	-0.86[a]	[-5.44, 3.72]	0.710
Week 32 Day 1	47	-3.0 (0.93)	[-4.85, -1.11]	11	-2.9 (1.90)	[-6.68, 0.91]	-0.09[a]	[-4.33, 4.14]	0.965
Week 48 Day 1	43	-2.2 (0.90)	[-3.99, -0.39]	10	-0.7 (1.82)	[-4.38, 2.89]	-1.45[a]	[-5.51, 2.61]	0.478
End Of Treatment	50	-0.4 (0.94)	[-2.27, 1.48]	14	1.4 (1.76)	[-2.09, 4.92]	-1.81[a]	[-5.78, 2.16]	0.366
Overall treatment effect	60	-1.8 (0.62)	[-2.99, -0.53]	23	-0.9 (1.13)	[-3.15, 1.33]	-0.85[b]	[-3.40, 1.71]	0.512

Analogous to CSR table 14.2-7.3L.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis
Full Analysis Set - L

Scale: Fatigue Scores

	Treatment Groups								
	Dabrafenib+Trametinib (N=73)			Carboplatin+Vincristine (N=37)			Comparison		
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	51	0.4 (0.91)	[-1.46, 2.17]	18	2.8 (1.51)	[-0.16, 5.85]	-2.49[a]	[-6.00, 1.02]	0.162
Week 8 Day 1	54	-0.4 (0.83)	[-2.04, 1.27]	18	4.5 (1.40)	[1.71, 7.28]	-4.88[a]	[-8.12, -1.64]	0.004
Week 16 Day 1	48	-1.6 (0.86)	[-3.29, 0.13]	10	5.1 (1.73)	[1.61, 8.50]	-6.63[a]	[-10.48, -2.78]	<0.001
Week 24 Day 1	46	-1.6 (1.02)	[-3.68, 0.42]	10	1.9 (2.11)	[-2.27, 6.16]	-3.57[a]	[-8.26, 1.12]	0.133
Week 32 Day 1	47	-0.4 (0.87)	[-2.18, 1.28]	11	4.3 (1.74)	[0.83, 7.77]	-4.75[a]	[-8.63, -0.86]	0.017
Week 48 Day 1	43	-0.8 (1.02)	[-2.82, 1.27]	10	0.6 (2.07)	[-3.53, 4.76]	-1.39[a]	[-6.02, 3.23]	0.549
End Of Treatment	50	-1.4 (0.91)	[-3.17, 0.46]	14	3.2 (1.70)	[-0.18, 6.59]	-4.56[a]	[-8.40, -0.72]	0.021
Overall treatment effect	60	-0.8 (0.63)	[-2.08, 0.42]	23	3.2 (1.11)	[1.01, 5.40]	-4.04[b]	[-6.57, -1.51]	0.002

Analogous to CSR table 14.2-7.3L.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

1.1.2. Patienten ab 5 Jahren

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

	Treatment Groups								
	Dabrafenib+Trametinib (N=58)			Carboplatin+Vincristine (N=27)			Comparison		
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	41	-0.7 (1.17)	[-3.06, 1.64]	15	-4.1 (1.96)	[-8.04, -0.22]	3.42[a]	[-1.14, 7.99]	0.139
Week 8 Day 1	41	0.8 (1.15)	[-1.54, 3.06]	13	-5.6 (1.99)	[-9.56, -1.60]	6.34[a]	[1.74, 10.94]	0.008
End Of Treatment	41	2.3 (1.54)	[-0.82, 5.36]	12	-4.4 (2.79)	[-9.97, 1.18]	6.66[a]	[0.29, 13.03]	0.041
Overall treatment effect	47	1.6 (1.04)	[-0.47, 3.70]	17	-6.3 (1.90)	[-10.05, -2.47]	7.88[b]	[3.55, 12.20]	<0.001

Analogous to CSR table 14.2-7.3L, but for patients aged >= 5 years.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

	Treatment Groups						Comparison		
	Dabrafenib+Trametinib (N=58)			Carboplatin+Vincristine (N=27)					
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	41	-1.8 (1.16)	[-4.07, 0.56]	15	-0.4 (1.91)	[-4.21, 3.44]	-1.37[a]	[-5.84, 3.11]	0.543
Week 8 Day 1	42	-2.7 (1.04)	[-4.75, -0.60]	13	-2.0 (1.88)	[-5.75, 1.80]	-0.70[a]	[-5.01, 3.61]	0.746
End Of Treatment	41	-0.5 (1.04)	[-2.62, 1.56]	12	0.2 (1.91)	[-3.61, 4.06]	-0.76[a]	[-5.12, 3.61]	0.729
Overall treatment effect	47	-2.5 (0.70)	[-3.88, -1.08]	17	-2.0 (1.34)	[-4.64, 0.71]	-0.52[b]	[-3.54, 2.51]	0.734

Analogous to CSR table 14.2-7.3L, but for patients aged >= 5 years.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

PROMIS Parent Proxy Global Health 7+2 – Repeated measures analysis for patients aged >= 5 years
Full Analysis Set - L

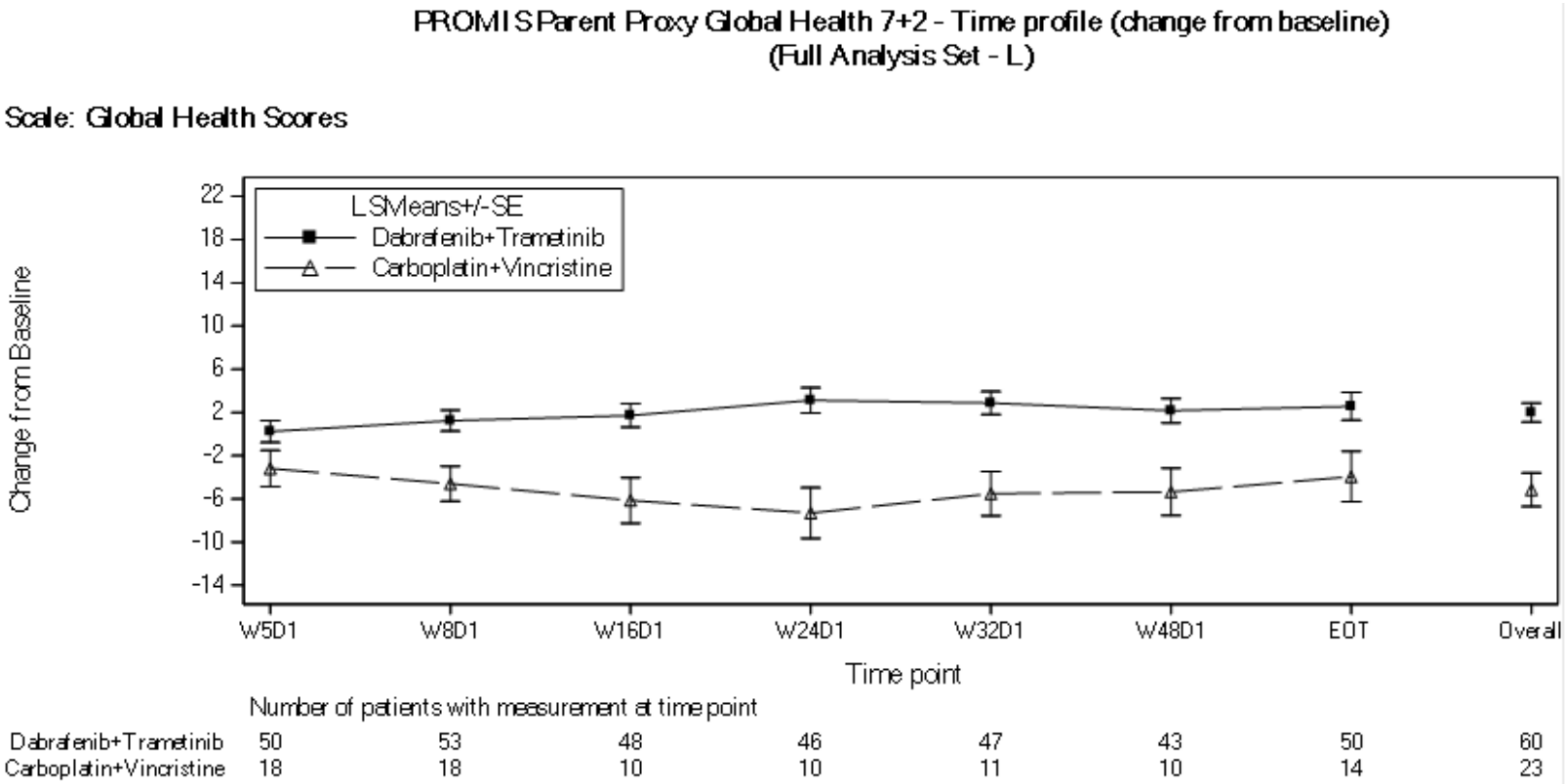
Scale: Fatigue Scores

	Treatment Groups								
	Dabrafenib+Trametinib (N=58)			Carboplatin+Vincristine (N=27)			Comparison		
Time point	**N***	**LS Means (SE)**	**[95% CI]**	**N***	**LS Means (SE)**	**[95% CI]**	**Difference/ Parameter**	**[95% CI]**	**p-value**
Week 5 Day 1	41	0.9 (1.00)	[-1.07, 2.92]	15	3.9 (1.65)	[0.57, 7.16]	-2.94[a]	[-6.79, 0.91]	0.132
Week 8 Day 1	42	-0.2 (1.02)	[-2.28, 1.79]	13	4.3 (1.77)	[0.73, 7.81]	-4.51[a]	[-8.60, -0.43]	0.031
End Of Treatment	41	-1.6 (1.09)	[-3.78, 0.60]	12	2.7 (2.00)	[-1.32, 6.72]	-4.29[a]	[-8.87, 0.28]	0.065
Overall treatment effect	47	-1.0 (0.77)	[-2.58, 0.50]	17	2.9 (1.40)	[0.14, 5.74]	-3.98[b]	[-7.17, -0.78]	0.015

Analogous to CSR table 14.2-7.3L, but for patients aged >= 5 years.
N*: Number of patients included in the analysis.
MMRM on change from baseline in adjusted for treatment, baseline value, visit and interaction between treatment and visit.
a: LS-Means: difference of Least Squares Means between D+T and C+V group.
b: Parameter displayed for treatment group comparison: ”Treatment” effect from the MMRM model.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Patients with baseline scores and at least one non-missing post-baseline assessment are included in the analysis.
MMRM: Mixed Model for Repeated Measures, LS Mean: Least Square Mean, SE: Standard Error, CI: Confidence Interval.

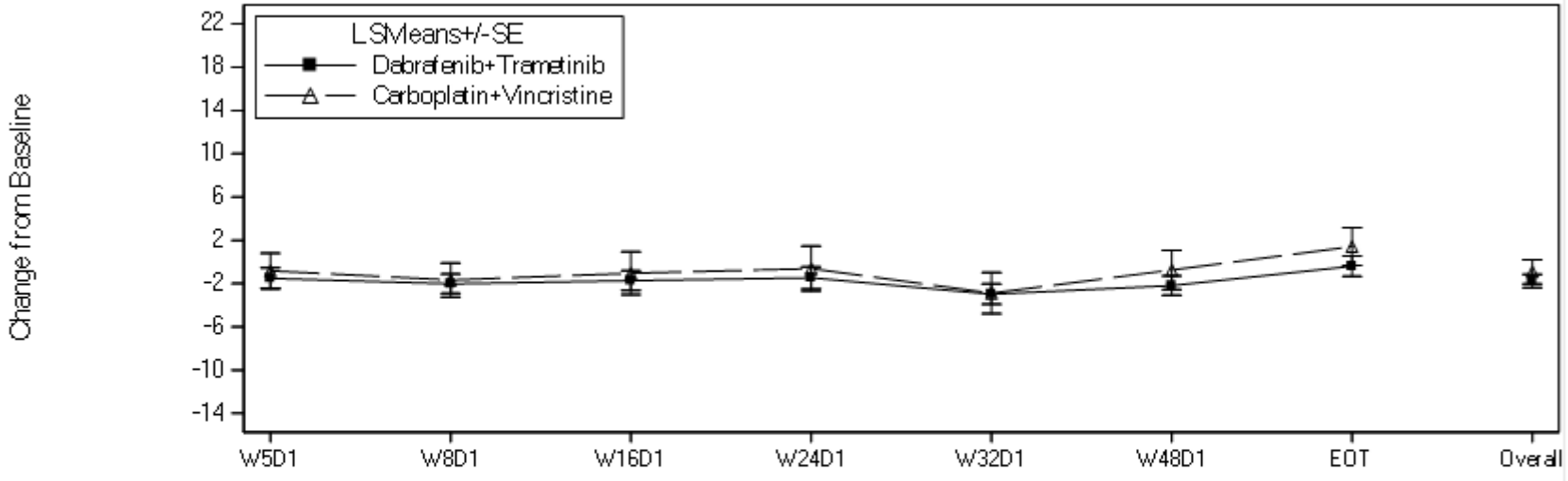
1.2. Graphische Darstellung der Veränderung der T-Scores gegenüber Studienbeginn mittels MMRM-Analyse zu den verschiedenen Erhebungszeitpunkten

1.2.1. Gesamtpopulation



PROMIS Parent Proxy Global Health 7+2 - Time profile (change from baseline)
(Full Analysis Set - L)

Scale: Pain Scores

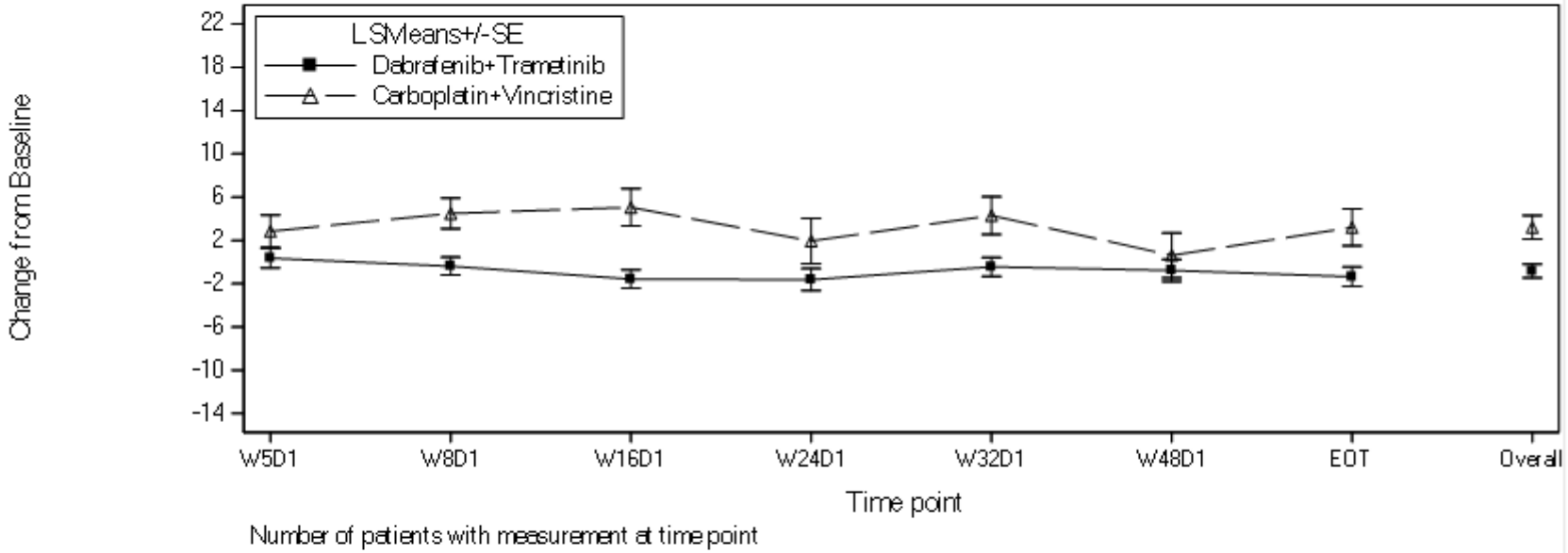


Number of patients with measurement at time point								
Dabrafenib+Trametinib	51	54	48	46	47	43	50	60
Carboplatin+Vincristine	18	18	10	10	11	10	14	23

Mixed effects model includes terms for treatment, visit and baseline score as main effects and an interaction term for visit and treatment.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Baseline is defined as the last assessment on or prior to first treatment date.
LS Mean: Least Square Mean, SE: Standard Error, EOT: End Of Treatment.

PROMIS Parent Proxy Global Health 7+2 - Time profile (change from baseline)
(Full Analysis Set - L)

Scale: Fatigue Scores



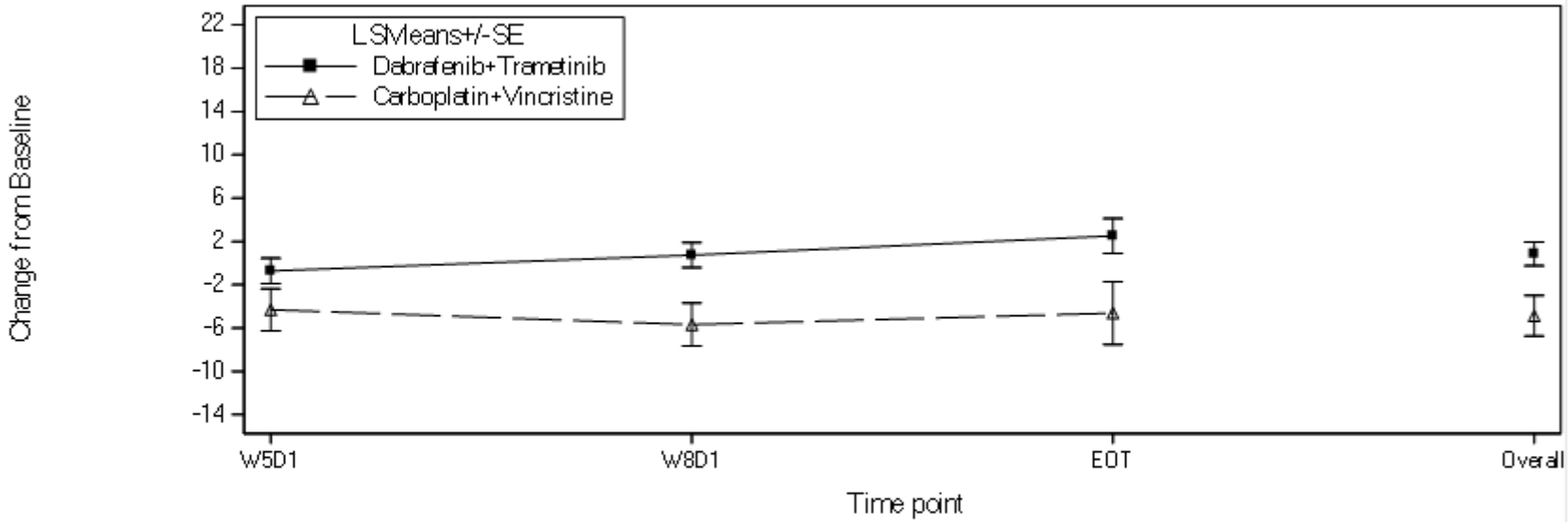
Number of patients with measurement at time point								
Dabrafenib+Trametinib	51	54	48	46	47	43	50	60
Carboplatin+Vincristine	18	18	10	10	11	10	14	23

Mixed effects model includes terms for treatment, visit and baseline score as main effects and an interaction term for visit and treatment.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Baseline is defined as the last assessment on or prior to first treatment date.
LS Mean: Least Square Mean, SE: Standard Error, EOT: End Of Treatment.

1.2.2. Patienten ab 5 Jahren

PROMIS Parent Proxy Global Health 7+2 - Time profile (change from baseline) for patients aged >= 5 years
(Full Analysis Set - L)

Scale: Global Health Scores

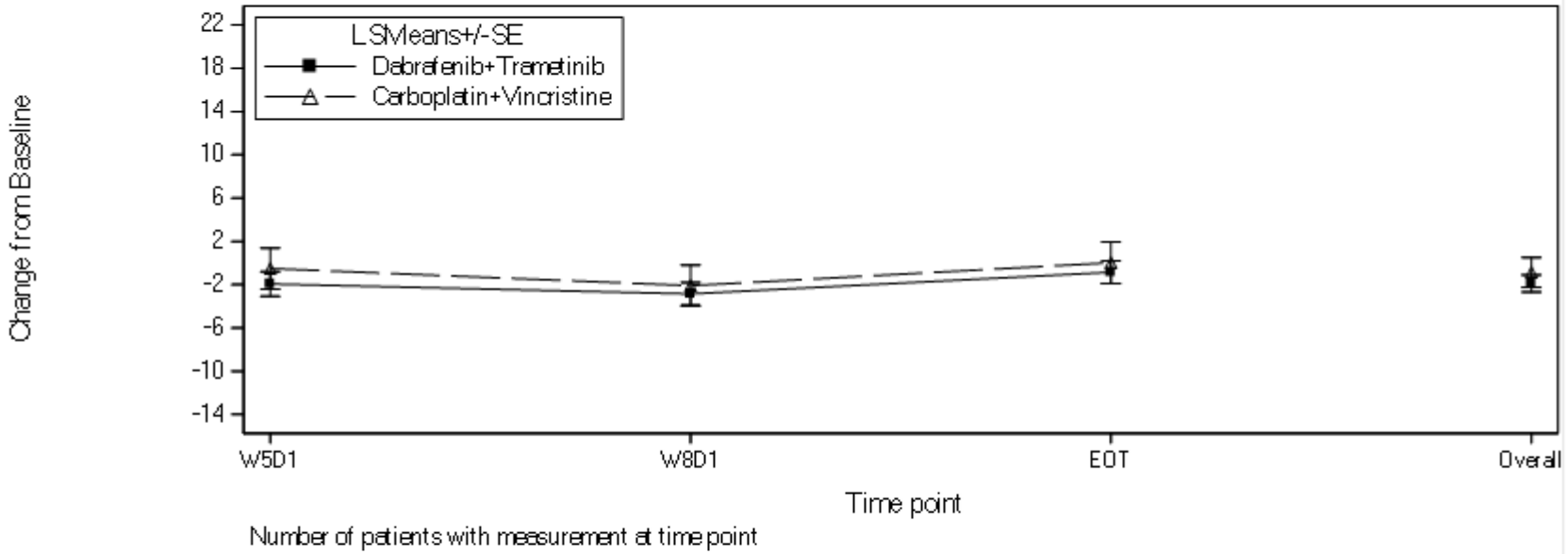


Number of patients with measurement at time point				
Dabrafenib+Trametinib	41	41	41	47
Carboplatin+Vincristine	15	13	12	17

Mixed effects model includes terms for treatment, visit and baseline score as main effects and an interaction term for visit and treatment.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Baseline is defined as the last assessment on or prior to first treatment date.
LS Mean: Least Square Mean, SE: Standard Error, EOT: End Of Treatment.

PROMIS Parent Proxy Global Health 7+2 - Time profile (change from baseline) for patients aged >= 5 years (Full Analysis Set - L)

Scale: Pain Scores

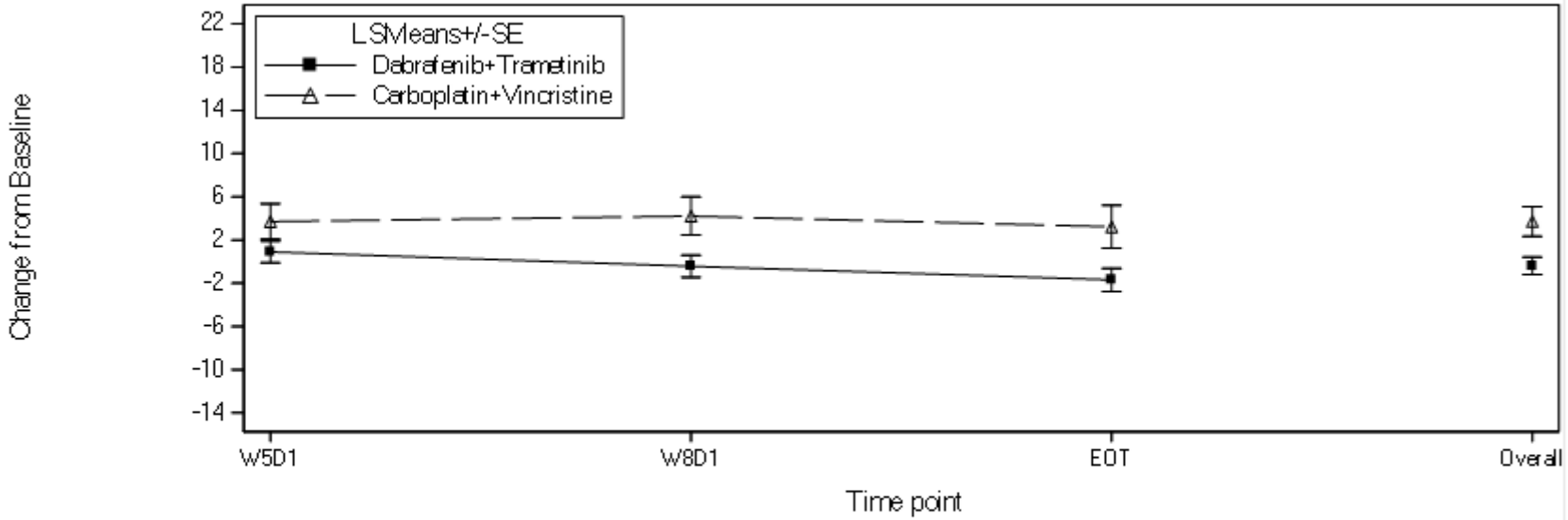


	Number of patients with measurement at time point			
Dabrafenib+Trametinib	41	42	41	47
Carboplatin+Vincristine	15	13	12	17

Mixed effects model includes terms for treatment, visit and baseline score as main effects and an interaction term for visit and treatment.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Baseline is defined as the last assessment on or prior to first treatment date.
LS Mean: Least Square Mean, SE: Standard Error, EOT: End Of Treatment.

PROMIS Parent Proxy Global Health 7+2 - Time profile (change from baseline) for patients aged >= 5 years
(Full Analysis Set - L)

Scale: Fatigue Scores



	Number of patients with measurement at time point			
Dabrafenib+Trametinib	41	42	41	47
Carboplatin+Vincristine	15	13	12	17

Mixed effects model includes terms for treatment, visit and baseline score as main effects and an interaction term for visit and treatment.
The analysis only includes assessment time-points where there are at least 10 evaluable subjects on each of the treatment groups.
Baseline is defined as the last assessment on or prior to first treatment date.
LS Mean: Least Square Mean, SE: Standard Error, EOT: End Of Treatment.

1.3. Deskriptive Darstellung der T-Scores sowie der Änderung gegenüber Studienbeginn zu den verschiedenen Erhebungszeitpunkten

1.3.1. Gesamtpopulation

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	61		23	
	Mean (SD)	42.67 (10.068)		42.89 (10.502)	
	Median	41.70		41.70	
	Q1-Q3	37.90 - 49.30		34.60 - 54.50	
	Min-Max	19.4 - 63.2		27.7 - 63.2	
Week 5 Day 1	n	50	50	18	18
	Mean (SD)	42.14 (9.439)	-0.39 (7.960)	39.06 (10.109)	-4.15 (9.529)
	Median	39.70	0.00	36.20	-1.00
	Q1-Q3	36.20 - 49.30	-3.80 - 5.20	32.90 - 45.40	-10.10 - 0.00
	Min-Max	24.4 - 66.1	-21.5 - 22.5	22.7 - 60.2	-24.4 - 10.3
Week 8 Day 1	n	53	53	18	18
	Mean (SD)	43.83 (9.461)	1.61 (8.008)	38.36 (7.759)	-4.77 (10.293)
	Median	41.70	1.70	37.05	-3.40
	Q1-Q3	37.90 - 49.30	-3.80 - 5.70	32.90 - 43.60	-8.50 - 0.00

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	24.4 - 66.1	-16.4 - 20.3	26.1 - 54.5	-28.6 - 10.9
Week 16 Day 1	n	48	48	10	10
	Mean (SD)	44.68 (9.159)	1.87 (8.555)	41.11 (10.798)	-2.99 (9.422)
	Median	44.50	0.85	40.70	-3.80
	Q1-Q3	37.90 - 49.30	-3.30 - 7.50	32.90 - 45.40	-5.00 - 3.50
	Min-Max	24.4 - 66.1	-14.7 - 30.8	24.4 - 63.2	-24.4 - 8.7
Week 24 Day 1	n	46	46	10	10
	Mean (SD)	45.27 (9.168)	3.35 (11.470)	36.57 (6.241)	-5.37 (7.559)
	Median	43.60	0.00	36.25	-2.65
	Q1-Q3	37.90 - 51.80	-1.70 - 6.80	34.60 - 39.70	-5.70 - -1.60
	Min-Max	32.9 - 66.1	-22.3 - 45.1	26.1 - 47.3	-22.7 - 1.7
Week 32 Day 1	n	47	47	11	11
	Mean (SD)	45.46 (8.887)	2.29 (9.291)	40.96 (7.159)	-2.94 (6.539)

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	45.40	2.00	41.70	-3.70
	Q1-Q3	37.90 - 49.30	-2.00 - 5.70	36.20 - 45.40	-5.70 - 1.70
	Min-Max	31.2 - 66.1	-20.5 - 45.1	31.2 - 54.5	-13.7 - 6.8
Week 40 Day 1	n	40	40	7	7
	Mean (SD)	45.37 (9.687)	3.02 (10.195)	38.84 (4.960)	-6.26 (11.903)
	Median	43.60	3.00	37.90	-3.70
	Q1-Q3	38.80 - 49.30	-2.00 - 7.55	36.20 - 41.70	-18.30 - 1.70
	Min-Max	27.7 - 66.1	-17.8 - 45.1	31.2 - 47.3	-26.1 - 8.5
Week 48 Day 1	n	43	43	10	10
	Mean (SD)	44.83 (9.421)	2.51 (10.028)	41.56 (6.953)	-3.11 (8.228)
	Median	43.60	1.90	42.65	-1.85
	Q1-Q3	37.90 - 49.30	-3.80 - 5.90	34.60 - 47.30	-2.70 - 0.00
	Min-Max	27.7 - 66.1	-14.7 - 39.2	32.9 - 51.8	-24.4 - 5.2

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 56 Day 1	n	46	46	7	7
	Mean (SD)	44.54 (8.876)	2.29 (7.741)	38.66 (8.851)	-4.91 (8.903)
	Median	43.60	1.90	36.20	-2.70
	Q1-Q3	37.90 - 47.30	-2.00 - 6.80	32.90 - 47.30	-3.70 - -1.60
	Min-Max	31.2 - 66.1	-15.9 - 26.3	26.1 - 51.8	-24.4 - 3.3
Week 72 Day 1	n	40	40	0	0
	Mean (SD)	44.21 (8.967)	2.64 (7.060)		
	Median	44.50	1.85		
	Q1-Q3	37.05 - 49.30	-2.00 - 6.35		
	Min-Max	29.4 - 66.1	-11.4 - 21.1		
Week 88 Day 1	n	38	38	0	0
	Mean (SD)	44.91 (8.847)	2.35 (6.239)		
	Median	43.60	2.90		
	Q1-Q3	37.90 - 49.30	-2.00 - 5.90		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	31.2 - 66.1	-12.9 - 16.6		
Week 104 Day 1	n	39	39	0	0
	Mean (SD)	45.60 (8.231)	2.86 (7.761)		
	Median	45.40	1.80		
	Q1-Q3	39.70 - 49.30	-2.90 - 8.50		
	Min-Max	31.2 - 66.1	-10.9 - 19.6		
Week 120 Day 1	n	33	33	0	0
	Mean (SD)	44.41 (7.317)	2.55 (6.805)		
	Median	45.40	1.70		
	Q1-Q3	37.90 - 47.30	-1.70 - 7.60		
	Min-Max	32.9 - 60.2	-14.8 - 16.1		
Week 136 Day 1	n	24	24	0	0
	Mean (SD)	44.45 (8.074)	1.00 (9.146)		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	43.55	0.85		
	Q1-Q3	37.05 - 49.30	-6.40 - 7.60		
	Min-Max	32.9 - 66.1	-11.4 - 20.7		
Week 152 Day 1	n	17	17	0	0
	Mean (SD)	47.88 (10.534)	5.79 (11.549)		
	Median	47.30	5.00		
	Q1-Q3	39.70 - 54.50	0.00 - 12.70		
	Min-Max	31.2 - 66.1	-11.9 - 28.2		
Week 168 Day 1	n	13	13	0	0
	Mean (SD)	46.48 (9.888)	5.22 (12.687)		
	Median	49.30	8.80		
	Q1-Q3	39.70 - 51.80	-7.10 - 13.60		
	Min-Max	29.4 - 66.1	-12.3 - 28.2		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
End Of Treatment	n	50	50	14	14
	Mean (SD)	44.98 (10.274)	2.90 (11.382)	39.69 (10.536)	-5.21 (13.276)
	Median	45.40	0.80	37.90	-2.75
	Q1-Q3	37.90 - 51.80	-3.80 - 7.50	31.20 - 47.30	-10.00 - 0.00
	Min-Max	27.7 - 66.1	-17.6 - 30.8	26.1 - 63.2	-32.0 - 19.6
Post Treatment Follow-Up 1	n	1	1	4	4
	Mean (SD)	45.40 (NE)	-3.90 (NE)	45.53 (6.288)	-3.95 (6.984)
	Median	45.40	-3.90	48.30	-5.75
	Q1-Q3	45.40 - 45.40	-3.90 - -3.90	41.75 - 49.30	-9.00 - 1.10
	Min-Max	45.4 - 45.4	-3.9 - -3.9	36.2 - 49.3	-10.0 - 5.7
Post Treatment Follow-Up 2	n	1	1	1	1

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	27.70 (NE)	-1.70 (NE)	39.70 (NE)	-3.90 (NE)
	Median	27.70	-1.70	39.70	-3.90
	Q1-Q3	27.70 - 27.70	-1.70 - -1.70	39.70 - 39.70	-3.90 - -3.90
	Min-Max	27.7 - 27.7	-1.7 - -1.7	39.7 - 39.7	-3.9 - -3.9
Post Treatment Follow-Up 3	n	1	1	1	1
	Mean (SD)	43.60 (NE)	14.20 (NE)	34.60 (NE)	1.70 (NE)
	Median	43.60	14.20	34.60	1.70
	Q1-Q3	43.60 - 43.60	14.20 - 14.20	34.60 - 34.60	1.70 - 1.70
	Min-Max	43.6 - 43.6	14.2 - 14.2	34.6 - 34.6	1.7 - 1.7
Post Treatment Follow-Up 4	n	1	1	2	2
	Mean (SD)	31.20 (NE)	1.80 (NE)	43.60 (8.061)	-0.90 (1.273)
	Median	31.20	1.80	43.60	-0.90

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	31.20 - 31.20	1.80 - 1.80	37.90 - 49.30	-1.80 - 0.00
	Min-Max	31.2 - 31.2	1.8 - 1.8	37.9 - 49.3	-1.8 - 0.0
Post Treatment Follow-Up 5	n	1	1	1	1
	Mean (SD)	29.40 (NE)	0.00 (NE)	37.90 (NE)	5.00 (NE)
	Median	29.40	0.00	37.90	5.00
	Q1-Q3	29.40 - 29.40	0.00 - 0.00	37.90 - 37.90	5.00 - 5.00
	Min-Max	29.4 - 29.4	0.0 - 0.0	37.9 - 37.9	5.0 - 5.0
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			36.45 (7.425)	0.15 (2.616)
	Median			36.45	0.15
	Q1-Q3			31.20 - 41.70	-1.70 - 2.00
	Min-Max			31.2 - 41.7	-1.7 - 2.0

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 8	n	0	0	1	1
	Mean (SD)			37.90 (NE)	5.00 (NE)
	Median			37.90	5.00
	Q1-Q3			37.90 - 37.90	5.00 - 5.00
	Min-Max			37.9 - 37.9	5.0 - 5.0

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	61		23	
	Mean (SD)	52.14 (7.658)		52.64 (7.054)	
	Median	53.05		53.05	
	Q1-Q3	43.25 - 58.51		43.25 - 58.51	
	Min-Max	43.3 - 68.8		43.3 - 63.5	
Week 5 Day 1	n	51	51	18	18
	Mean (SD)	50.11 (7.275)	-1.70 (9.536)	50.97 (6.263)	-0.64 (8.044)
	Median	53.05	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 53.05	0.00 - 0.00
	Min-Max	43.3 - 68.8	-25.5 - 20.2	43.3 - 63.5	-15.3 - 9.8
Week 8 Day 1	n	54	54	18	18
	Mean (SD)	49.93 (7.727)	-1.58 (7.477)	51.00 (6.037)	-2.61 (9.397)
	Median	43.25	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-5.30 - 0.00	43.25 - 53.05	-9.80 - 0.00

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	43.3 - 68.8	-15.3 - 20.2	43.3 - 58.5	-20.2 - 15.3
Week 16 Day 1	n	48	48	10	10
	Mean (SD)	49.72 (7.300)	-1.68 (6.821)	51.75 (6.330)	-2.57 (10.454)
	Median	48.15	0.00	53.05	-2.73
	Q1-Q3	43.25 - 53.05	-5.46 - 0.00	43.25 - 58.51	-9.80 - 5.46
	Min-Max	43.3 - 68.8	-15.7 - 15.3	43.3 - 58.5	-20.2 - 9.8
Week 24 Day 1	n	46	46	10	10
	Mean (SD)	50.65 (7.450)	-1.87 (8.595)	51.81 (7.937)	-0.98 (11.671)
	Median	53.05	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 58.51	-9.80 - 9.80
	Min-Max	43.3 - 68.8	-20.2 - 20.2	43.3 - 63.5	-20.2 - 15.3
Week 32 Day 1	n	47	47	11	11
	Mean (SD)	48.77 (6.647)	-2.82 (9.350)	49.59 (6.387)	-3.27 (5.749)

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	43.25	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 53.05	-5.46 - 0.00
	Min-Max	43.3 - 63.5	-25.5 - 15.3	43.3 - 58.5	-15.3 - 5.5
Week 40 Day 1	n	40	40	7	7
	Mean (SD)	49.87 (6.389)	-0.89 (8.365)	52.52 (7.402)	2.11 (12.241)
	Median	53.05	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-7.63 - 2.73	43.25 - 58.51	-9.80 - 9.80
	Min-Max	43.3 - 58.5	-15.3 - 15.3	43.3 - 63.5	-15.3 - 20.2
Week 48 Day 1	n	43	43	10	10
	Mean (SD)	49.89 (6.581)	-0.70 (7.395)	51.20 (5.903)	-1.64 (8.947)
	Median	53.05	0.00	53.05	-2.73
	Q1-Q3	43.25 - 58.51	-4.97 - 0.00	43.25 - 53.05	-5.46 - 0.00
	Min-Max	43.3 - 58.5	-15.3 - 15.3	43.3 - 58.5	-15.3 - 15.3

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 56 Day 1	n	46	46	7	7
	Mean (SD)	48.14 (6.496)	-2.73 (7.606)	53.99 (5.466)	0.62 (8.389)
	Median	43.25	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	53.05 - 58.51	0.00 - 9.80
	Min-Max	43.3 - 63.5	-20.2 - 20.2	43.3 - 58.5	-15.3 - 9.8
Week 72 Day 1	n	40	40	0	0
	Mean (SD)	49.46 (6.498)	-1.81 (8.164)		
	Median	53.05	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 63.5	-15.3 - 15.3		
Week 88 Day 1	n	38	38	0	0
	Mean (SD)	47.82 (6.083)	-2.93 (7.523)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	43.3 - 63.5	-15.3 - 15.3		
Week 104 Day 1	n	39	39	0	0
	Mean (SD)	48.74 (6.605)	-2.07 (7.390)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-5.46 - 0.00		
	Min-Max	43.3 - 68.8	-20.2 - 15.7		
Week 120 Day 1	n	33	33	0	0
	Mean (SD)	48.56 (7.583)	-3.01 (7.722)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 68.8	-15.3 - 15.7		
Week 136 Day 1	n	24	24	0	0
	Mean (SD)	46.16 (5.305)	-4.18 (6.730)		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	43.25	0.00		
	Q1-Q3	43.25 - 48.15	-9.80 - 0.00		
	Min-Max	43.3 - 58.5	-15.3 - 9.8		
Week 152 Day 1	n	17	17	0	0
	Mean (SD)	47.42 (6.765)	-6.18 (9.598)		
	Median	43.25	-9.80		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 58.5	-25.5 - 15.3		
Week 168 Day 1	n	13	13	0	0
	Mean (SD)	48.61 (6.298)	-6.62 (5.580)		
	Median	43.25	-5.46		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 58.5	-15.3 - 0.0		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
End Of Treatment	n	50	50	14	14
	Mean (SD)	51.46 (6.830)	-1.16 (9.192)	52.87 (6.113)	1.71 (10.164)
	Median	53.05	0.00	53.05	2.48
	Q1-Q3	43.25 - 58.51	-5.46 - 0.00	53.05 - 58.51	-5.46 - 9.80
	Min-Max	43.3 - 63.5	-20.2 - 15.3	43.3 - 63.5	-15.3 - 15.3
Post Treatment Follow-Up 1	n	1	1	4	4
	Mean (SD)	53.05 (NE)	-5.46 (NE)	50.60 (4.900)	-0.28 (12.308)
	Median	53.05	-5.46	53.05	2.17
	Q1-Q3	53.05 - 53.05	-5.46 - -5.46	48.15 - 53.05	-10.36 - 9.80
	Min-Max	53.1 - 53.1	-5.5 - -5.5	43.3 - 53.1	-15.3 - 9.8
Post Treatment Follow-Up 2	n	1	1	1	1

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	58.51 (NE)	15.26 (NE)	43.25 (NE)	0.00 (NE)
	Median	58.51	15.26	43.25	0.00
	Q1-Q3	58.51 - 58.51	15.26 - 15.26	43.25 - 43.25	0.00 - 0.00
	Min-Max	58.5 - 58.5	15.3 - 15.3	43.3 - 43.3	0.0 - 0.0
Post Treatment Follow-Up 3	n	1	1	1	1
	Mean (SD)	53.05 (NE)	9.80 (NE)	43.25 (NE)	0.00 (NE)
	Median	53.05	9.80	43.25	0.00
	Q1-Q3	53.05 - 53.05	9.80 - 9.80	43.25 - 43.25	0.00 - 0.00
	Min-Max	53.1 - 53.1	9.8 - 9.8	43.3 - 43.3	0.0 - 0.0
Post Treatment Follow-Up 4	n	1	1	2	2
	Mean (SD)	58.51 (NE)	15.26 (NE)	43.25 (0.000)	-7.63 (10.790)
	Median	58.51	15.26	43.25	-7.63

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	58.51 - 58.51	15.26 - 15.26	43.25 - 43.25	-15.26 - 0.00
	Min-Max	58.5 - 58.5	15.3 - 15.3	43.3 - 43.3	-15.3 - 0.0
Post Treatment Follow-Up 5	n	1	1	1	1
	Mean (SD)	58.51 (NE)	15.26 (NE)	43.25 (NE)	0.00 (NE)
	Median	58.51	15.26	43.25	0.00
	Q1-Q3	58.51 - 58.51	15.26 - 15.26	43.25 - 43.25	0.00 - 0.00
	Min-Max	58.5 - 58.5	15.3 - 15.3	43.3 - 43.3	0.0 - 0.0
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			50.88 (10.790)	-7.63 (10.790)
	Median			50.88	-7.63
	Q1-Q3			43.25 - 58.51	-15.26 - 0.00
	Min-Max			43.3 - 58.5	-15.3 - 0.0

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 8	n	0	0	1	1
	Mean (SD)			43.25 (NE)	0.00 (NE)
	Median			43.25	0.00
	Q1-Q3			43.25 - 43.25	0.00 - 0.00
	Min-Max			43.3 - 43.3	0.0 - 0.0

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	61		23	
	Mean (SD)	53.30 (6.731)		54.37 (7.981)	
	Median	56.07		56.07	
	Q1-Q3	48.94 - 56.07		48.94 - 62.62	
	Min-Max	40.2 - 68.1		40.2 - 68.1	
Week 5 Day 1	n	51	51	18	18
	Mean (SD)	53.96 (7.588)	0.62 (7.409)	56.88 (6.430)	2.93 (9.025)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-5.50 - 7.13	56.07 - 62.62	0.00 - 7.13
	Min-Max	40.2 - 68.1	-22.5 - 13.7	40.2 - 68.1	-15.9 - 22.5
Week 8 Day 1	n	54	54	18	18
	Mean (SD)	52.68 (6.967)	-0.33 (7.217)	58.10 (4.823)	4.15 (9.204)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	0.00 - 0.00	56.07 - 62.62	0.00 - 7.13

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	40.2 - 68.1	-22.5 - 19.2	48.9 - 68.1	-6.5 - 28.0
Week 16 Day 1	n	48	48	10	10
	Mean (SD)	51.22 (6.983)	-2.11 (7.445)	57.81 (6.193)	2.25 (8.445)
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	56.07 - 62.62	0.00 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 19.2	48.9 - 68.1	-7.1 - 22.5
Week 24 Day 1	n	46	46	10	10
	Mean (SD)	51.04 (8.005)	-1.96 (7.228)	55.02 (7.248)	-1.92 (9.936)
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	48.94 - 62.62	-6.55 - 0.00
	Min-Max	40.2 - 68.1	-22.5 - 8.8	40.2 - 62.6	-22.5 - 15.9
Week 32 Day 1	n	47	47	11	11
	Mean (SD)	52.49 (7.219)	-0.19 (7.071)	57.66 (5.899)	2.04 (6.424)

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	0.00 - 6.55	56.07 - 62.62	0.00 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 15.9	48.9 - 68.1	-7.1 - 15.9
Week 40 Day 1	n	40	40	7	7
	Mean (SD)	52.27 (7.450)	-0.29 (7.397)	58.49 (7.072)	4.00 (6.915)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	0.00 - 3.27	56.07 - 68.12	0.00 - 12.05
	Min-Max	40.2 - 68.1	-22.5 - 13.7	48.9 - 68.1	0.0 - 15.9
Week 48 Day 1	n	43	43	10	10
	Mean (SD)	51.65 (7.362)	-0.10 (7.826)	53.48 (8.004)	-1.43 (7.242)
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-6.55 - 7.13	48.94 - 56.07	0.00 - 0.00
	Min-Max	40.2 - 68.1	-22.5 - 15.9	40.2 - 62.6	-15.9 - 7.1

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 56 Day 1	n	46	46	7	7
	Mean (SD)	50.51 (7.150)	-1.80 (8.090)	57.63 (7.254)	0.94 (2.476)
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	48.94 - 62.62	0.00 - 0.00
	Min-Max	40.2 - 68.1	-22.5 - 13.7	48.9 - 68.1	0.0 - 6.5
Week 72 Day 1	n	40	40	0	0
	Mean (SD)	49.93 (6.910)	-2.58 (7.229)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 8.8		
Week 88 Day 1	n	38	38	0	0
	Mean (SD)	50.52 (7.358)	-2.54 (8.325)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	40.2 - 68.1	-15.9 - 15.9		
Week 104 Day 1	n	39	39	0	0
	Mean (SD)	51.11 (6.899)	-1.49 (8.005)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 15.9		
Week 120 Day 1	n	33	33	0	0
	Mean (SD)	50.40 (7.317)	-3.72 (8.915)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 56.07	-8.79 - 0.00		
	Min-Max	40.2 - 68.1	-22.5 - 15.9		
Week 136 Day 1	n	24	24	0	0
	Mean (SD)	50.97 (8.667)	-2.25 (9.120)		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	48.94	0.00		
	Q1-Q3	40.15 - 56.07	-8.79 - 3.27		
	Min-Max	40.2 - 68.1	-15.9 - 15.9		
Week 152 Day 1	n	17	17	0	0
	Mean (SD)	47.71 (8.037)	-6.56 (10.939)		
	Median	48.94	-7.13		
	Q1-Q3	40.15 - 56.07	-15.92 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 15.9		
Week 168 Day 1	n	13	13	0	0
	Mean (SD)	48.21 (8.188)	-6.72 (9.956)		
	Median	48.94	-7.13		
	Q1-Q3	40.15 - 48.94	-15.92 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 13.7		

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
End Of Treatment	n	50	50	14	14
	Mean (SD)	52.35 (7.565)	-1.53 (7.395)	56.88 (5.246)	3.49 (9.386)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	56.07 - 62.62	-5.50 - 7.13
	Min-Max	40.2 - 68.1	-19.2 - 15.9	48.9 - 62.6	-7.1 - 22.5
Post Treatment Follow-Up 1	n	1	1	4	4
	Mean (SD)	48.94 (NE)	8.79 (NE)	52.36 (6.840)	-3.57 (11.904)
	Median	48.94	8.79	48.94	-7.13
	Q1-Q3	48.94 - 48.94	8.79 - 8.79	48.94 - 55.78	-10.41 - 3.27
	Min-Max	48.9 - 48.9	8.8 - 8.8	48.9 - 62.6	-13.7 - 13.7
Post Treatment Follow-Up 2	n	1	1	1	1

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	62.62 (NE)	13.68 (NE)	62.62 (NE)	6.55 (NE)
	Median	62.62	13.68	62.62	6.55
	Q1-Q3	62.62 - 62.62	13.68 - 13.68	62.62 - 62.62	6.55 - 6.55
	Min-Max	62.6 - 62.6	13.7 - 13.7	62.6 - 62.6	6.5 - 6.5
Post Treatment Follow-Up 3	n	1	1	1	1
	Mean (SD)	48.94 (NE)	0.00 (NE)	48.94 (NE)	0.00 (NE)
	Median	48.94	0.00	48.94	0.00
	Q1-Q3	48.94 - 48.94	0.00 - 0.00	48.94 - 48.94	0.00 - 0.00
	Min-Max	48.9 - 48.9	0.0 - 0.0	48.9 - 48.9	0.0 - 0.0
Post Treatment Follow-Up 4	n	1	1	2	2
	Mean (SD)	56.07 (NE)	7.13 (NE)	48.94 (0.000)	0.00 (0.000)
	Median	56.07	7.13	48.94	0.00

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	56.07 - 56.07	7.13 - 7.13	48.94 - 48.94	0.00 - 0.00
	Min-Max	56.1 - 56.1	7.1 - 7.1	48.9 - 48.9	0.0 - 0.0
Post Treatment Follow-Up 5	n	1	1	1	1
	Mean (SD)	62.62 (NE)	13.68 (NE)	48.94 (NE)	0.00 (NE)
	Median	62.62	13.68	48.94	0.00
	Q1-Q3	62.62 - 62.62	13.68 - 13.68	48.94 - 48.94	0.00 - 0.00
	Min-Max	62.6 - 62.6	13.7 - 13.7	48.9 - 48.9	0.0 - 0.0
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			55.78 (9.673)	0.00 (0.000)
	Median			55.78	0.00
	Q1-Q3			48.94 - 62.62	0.00 - 0.00
	Min-Max			48.9 - 62.6	0.0 - 0.0

Baseline is defined as the last assessment on or prior to first treatment date.

PROMIS Parent Proxy Global Health – T-Scores by time point
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=37	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 8	n	0	0	1	1
	Mean (SD)			48.94 (NE)	0.00 (NE)
	Median			48.94	0.00
	Q1-Q3			48.94 - 48.94	0.00 - 0.00
	Min-Max			48.9 - 48.9	0.0 - 0.0

Baseline is defined as the last assessment on or prior to first treatment date.

1.3.2. Patienten ab 5 Jahren

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	48		17	
	Mean (SD)	42.97 (9.966)		43.89 (10.876)	
	Median	41.70		41.70	
	Q1-Q3	37.90 - 49.30		36.20 - 54.50	
	Min-Max	21.0 - 63.2		29.4 - 63.2	
Week 5 Day 1	n	41	41	15	15
	Mean (SD)	41.42 (9.557)	-1.22 (8.344)	39.81 (10.553)	-5.09 (9.964)
	Median	39.70	-1.70	36.20	-2.00
	Q1-Q3	36.20 - 47.30	-5.50 - 3.30	32.90 - 47.30	-11.90 - 0.00
	Min-Max	24.4 - 66.1	-21.5 - 22.5	22.7 - 60.2	-24.4 - 10.3
Week 8 Day 1	n	41	41	13	13

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	43.74 (9.666)	0.94 (8.213)	37.63 (7.189)	-5.72 (11.951)
	Median	41.70	0.00	36.20	-3.50
	Q1-Q3	37.90 - 49.30	-3.90 - 5.70	32.90 - 41.70	-12.80 - 0.00
	Min-Max	24.4 - 66.1	-16.4 - 18.7	27.7 - 54.5	-28.6 - 10.9
Week 16 Day 1	n	39	39	7	7
	Mean (SD)	44.52 (9.470)	2.07 (9.202)	39.29 (8.559)	-4.27 (10.379)
	Median	43.60	1.80	39.70	-3.90
	Q1-Q3	37.90 - 49.30	-3.50 - 8.70	32.90 - 45.40	-9.10 - 3.50
	Min-Max	24.4 - 66.1	-14.7 - 30.8	24.4 - 49.3	-24.4 - 5.7
Week 24 Day 1	n	35	35	7	7
	Mean (SD)	45.28 (9.133)	2.79 (11.061)	35.66 (6.948)	-6.37 (8.946)

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	43.60	0.00	34.60	-3.30
	Q1-Q3	37.90 - 54.50	-2.00 - 8.00	29.40 - 39.70	-14.80 - 0.00
	Min-Max	32.9 - 66.1	-22.3 - 45.1	26.1 - 47.3	-22.7 - 1.7
Week 32 Day 1	n	38	38	7	7
	Mean (SD)	45.61 (9.185)	2.46 (10.290)	40.76 (6.107)	-2.56 (8.221)
	Median	45.40	2.75	41.70	-1.70
	Q1-Q3	37.90 - 49.30	-3.40 - 7.50	36.20 - 45.40	-12.80 - 5.70
	Min-Max	31.2 - 66.1	-20.5 - 45.1	31.2 - 49.3	-13.7 - 6.8
Week 40 Day 1	n	32	32	5	5
	Mean (SD)	45.16 (9.967)	2.56 (11.221)	38.10 (5.830)	-7.24 (14.432)
	Median	43.60	2.00	37.90	-2.00

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	37.90 - 49.30	-3.80 - 7.40	36.20 - 37.90	-18.30 - 1.70
	Min-Max	27.7 - 66.1	-17.8 - 45.1	31.2 - 47.3	-26.1 - 8.5
Week 48 Day 1	n	32	32	7	7
	Mean (SD)	45.36 (9.746)	2.22 (10.680)	39.79 (7.118)	-3.53 (10.040)
	Median	43.60	0.95	36.20	0.00
	Q1-Q3	37.90 - 50.55	-4.15 - 6.70	32.90 - 47.30	-7.20 - 3.70
	Min-Max	27.7 - 66.1	-14.7 - 39.2	32.9 - 47.3	-24.4 - 5.2
Week 56 Day 1	n	35	35	5	5
	Mean (SD)	44.41 (9.289)	2.12 (8.483)	35.42 (7.675)	-5.60 (10.804)
	Median	45.40	1.80	34.60	-2.00
	Q1-Q3	36.20 - 47.30	-3.50 - 6.80	32.90 - 36.20	-3.30 - -1.60

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	31.2 - 66.1	-15.9 - 26.3	26.1 - 47.3	-24.4 - 3.3
Week 72 Day 1	n	30	30	0	0
	Mean (SD)	44.41 (9.776)	2.95 (7.647)		
	Median	44.50	1.85		
	Q1-Q3	36.20 - 49.30	-2.00 - 7.50		
	Min-Max	29.4 - 66.1	-11.4 - 21.1		
Week 88 Day 1	n	32	32	0	0
	Mean (SD)	45.37 (8.960)	2.91 (6.430)		
	Median	43.60	3.75		
	Q1-Q3	38.80 - 49.30	-1.00 - 6.35		
	Min-Max	31.2 - 66.1	-12.9 - 16.6		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 104 Day 1	n	31	31	0	0
	Mean (SD)	46.53 (8.700)	3.55 (8.070)		
	Median	47.30	3.70		
	Q1-Q3	39.70 - 54.50	-3.30 - 9.40		
	Min-Max	31.2 - 66.1	-10.9 - 19.6		
Week 120 Day 1	n	27	27	0	0
	Mean (SD)	44.43 (7.311)	2.32 (7.340)		
	Median	45.40	0.00		
	Q1-Q3	37.90 - 49.30	-2.00 - 8.40		
	Min-Max	32.9 - 60.2	-14.8 - 16.1		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 136 Day 1	n	19	19	0	0
	Mean (SD)	43.73 (6.890)	-0.27 (8.983)		
	Median	45.40	-1.80		
	Q1-Q3	36.20 - 49.30	-8.40 - 7.60		
	Min-Max	32.9 - 54.5	-11.4 - 20.7		
Week 152 Day 1	n	13	13	0	0
	Mean (SD)	48.45 (9.820)	6.53 (11.646)		
	Median	47.30	5.20		
	Q1-Q3	41.70 - 54.50	0.00 - 12.70		
	Min-Max	31.2 - 66.1	-10.5 - 28.2		
Week 168 Day 1	n	11	11	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	45.93 (10.149)	4.45 (13.746)		
	Median	49.30	6.40		
	Q1-Q3	39.70 - 51.80	-8.40 - 15.60		
	Min-Max	29.4 - 66.1	-12.3 - 28.2		
End Of Treatment	n	41	41	12	12
	Mean (SD)	44.89 (10.962)	2.59 (11.665)	40.49 (10.598)	-5.52 (14.335)
	Median	43.60	0.00	37.90	-2.75
	Q1-Q3	37.90 - 51.80	-3.80 - 7.50	32.05 - 47.30	-10.00 - 0.00
	Min-Max	27.7 - 66.1	-17.6 - 30.8	27.7 - 63.2	-32.0 - 19.6
Post Treatment Follow-Up 1	n	0	0	4	4

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)			45.53 (6.288)	-3.95 (6.984)
	Median			48.30	-5.75
	Q1-Q3			41.75 - 49.30	-9.00 - 1.10
	Min-Max			36.2 - 49.3	-10.0 - 5.7
Post Treatment Follow-Up 2	n	1	1	0	0
	Mean (SD)	27.70 (NE)	-1.70 (NE)		
	Median	27.70	-1.70		
	Q1-Q3	27.70 - 27.70	-1.70 - -1.70		
	Min-Max	27.7 - 27.7	-1.7 - -1.7		
Post Treatment	n	1	1	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Follow-Up 3					
	Mean (SD)	43.60 (NE)	14.20 (NE)		
	Median	43.60	14.20		
	Q1-Q3	43.60 - 43.60	14.20 - 14.20		
	Min-Max	43.6 - 43.6	14.2 - 14.2		
Post Treatment	n	1	1	2	2
Follow-Up 4					
	Mean (SD)	31.20 (NE)	1.80 (NE)	43.60 (8.061)	-0.90 (1.273)
	Median	31.20	1.80	43.60	-0.90
	Q1-Q3	31.20 - 31.20	1.80 - 1.80	37.90 - 49.30	-1.80 - 0.00
	Min-Max	31.2 - 31.2	1.8 - 1.8	37.9 - 49.3	-1.8 - 0.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Global Health Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 5	n	1	1	0	0
	Mean (SD)	29.40 (NE)	0.00 (NE)		
	Median	29.40	0.00		
	Q1-Q3	29.40 - 29.40	0.00 - 0.00		
	Min-Max	29.4 - 29.4	0.0 - 0.0		
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			36.45 (7.425)	0.15 (2.616)
	Median			36.45	0.15
	Q1-Q3			31.20 - 41.70	-1.70 - 2.00
	Min-Max			31.2 - 41.7	-1.7 - 2.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	48		17	
	Mean (SD)	51.73 (7.842)		53.90 (6.930)	
	Median	53.05		53.05	
	Q1-Q3	43.25 - 58.51		53.05 - 58.51	
	Min-Max	43.3 - 68.8		43.3 - 63.5	
Week 5 Day 1	n	41	41	15	15
	Mean (SD)	49.98 (7.717)	-1.86 (10.469)	51.86 (6.161)	-1.42 (8.371)
	Median	43.25	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 53.05	-4.97 - 0.00
	Min-Max	43.3 - 68.8	-25.5 - 20.2	43.3 - 63.5	-15.3 - 9.8
Week 8 Day 1	n	42	42	13	13

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	49.10 (7.885)	-1.91 (8.110)	50.87 (5.644)	-4.04 (8.739)
	Median	43.25	0.00	53.05	-5.46
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 53.05	-9.80 - 0.00
	Min-Max	43.3 - 68.8	-15.3 - 20.2	43.3 - 58.5	-20.2 - 9.8
Week 16 Day 1	n	39	39	7	7
	Mean (SD)	49.17 (7.607)	-1.80 (7.305)	48.85 (5.238)	-5.23 (11.535)
	Median	43.25	0.00	53.05	-5.46
	Q1-Q3	43.25 - 53.05	-5.46 - 0.00	43.25 - 53.05	-15.26 - 9.80
	Min-Max	43.3 - 68.8	-15.7 - 15.3	43.3 - 53.1	-20.2 - 9.8
Week 24 Day 1	n	35	35	7	7
	Mean (SD)	49.82 (7.220)	-2.62 (8.831)	50.41 (7.059)	-3.67 (12.927)

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	53.05	0.00	53.05	-5.46
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 58.51	-15.26 - 9.80
	Min-Max	43.3 - 68.8	-20.2 - 20.2	43.3 - 58.5	-20.2 - 15.3
Week 32 Day 1	n	38	38	7	7
	Mean (SD)	48.24 (6.713)	-3.21 (9.931)	48.23 (6.472)	-5.14 (5.825)
	Median	43.25	0.00	43.25	-5.46
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	43.25 - 53.05	-9.80 - 0.00
	Min-Max	43.3 - 63.5	-25.5 - 15.3	43.3 - 58.5	-15.3 - 0.0
Week 40 Day 1	n	32	32	5	5
	Mean (SD)	49.52 (6.661)	-1.09 (9.012)	52.31 (9.054)	0.99 (14.398)
	Median	48.15	0.00	53.05	0.00

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	43.25 - 55.78	-9.80 - 5.46	43.25 - 58.51	-9.80 - 9.80
	Min-Max	43.3 - 58.5	-15.3 - 15.3	43.3 - 63.5	-15.3 - 20.2
Week 48 Day 1	n	32	32	7	7
	Mean (SD)	47.95 (6.393)	-2.05 (7.644)	51.81 (6.337)	-1.56 (10.804)
	Median	43.25	0.00	53.05	-5.46
	Q1-Q3	43.25 - 53.05	-7.63 - 0.00	43.25 - 58.51	-9.80 - 9.80
	Min-Max	43.3 - 58.5	-15.3 - 15.3	43.3 - 58.5	-15.3 - 15.3
Week 56 Day 1	n	35	35	5	5
	Mean (SD)	47.13 (6.488)	-3.29 (7.788)	53.27 (6.233)	0.87 (10.261)
	Median	43.25	0.00	53.05	0.00
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00	53.05 - 58.51	0.00 - 9.80

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	43.3 - 63.5	-15.3 - 20.2	43.3 - 58.5	-15.3 - 9.8
Week 72 Day 1	n	30	30	0	0
	Mean (SD)	48.72 (6.356)	-1.91 (8.373)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 63.5	-15.3 - 15.3		
Week 88 Day 1	n	32	32	0	0
	Mean (SD)	47.74 (5.716)	-3.32 (7.921)		
	Median	43.25	-2.48		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 58.5	-15.3 - 15.3		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 104 Day 1	n	31	31	0	0
	Mean (SD)	48.22 (6.614)	-2.78 (8.110)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 68.8	-20.2 - 15.7		
Week 120 Day 1	n	27	27	0	0
	Mean (SD)	48.29 (8.088)	-3.12 (8.115)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 68.8	-15.3 - 15.7		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 136 Day 1	n	19	19	0	0
	Mean (SD)	46.12 (5.060)	-3.73 (6.418)		
	Median	43.25	0.00		
	Q1-Q3	43.25 - 53.05	-9.80 - 0.00		
	Min-Max	43.3 - 58.5	-15.3 - 9.8		
Week 152 Day 1	n	13	13	0	0
	Mean (SD)	47.95 (7.331)	-6.15 (10.836)		
	Median	43.25	-9.80		
	Q1-Q3	43.25 - 58.51	-15.26 - 0.00		
	Min-Max	43.3 - 58.5	-25.5 - 15.3		
Week 168 Day 1	n	11	11	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	47.81 (6.553)	-7.83 (5.197)		
	Median	43.25	-9.80		
	Q1-Q3	43.25 - 53.05	-10.27 - -4.97		
	Min-Max	43.3 - 58.5	-15.3 - 0.0		
End Of Treatment	n	41	41	12	12
	Mean (SD)	51.20 (6.967)	-1.02 (9.235)	52.38 (6.404)	-0.09 (9.793)
	Median	53.05	0.00	53.05	-2.48
	Q1-Q3	43.25 - 58.51	-5.46 - 0.00	48.15 - 55.78	-7.63 - 9.80
	Min-Max	43.3 - 63.5	-15.3 - 15.3	43.3 - 63.5	-15.3 - 15.3
Post Treatment Follow-Up 1	n	0	0	4	4

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)			50.60 (4.900)	-0.28 (12.308)
	Median			53.05	2.17
	Q1-Q3			48.15 - 53.05	-10.36 - 9.80
	Min-Max			43.3 - 53.1	-15.3 - 9.8
Post Treatment	n	1	1	0	0
Follow-Up 2					
	Mean (SD)	58.51 (NE)	15.26 (NE)		
	Median	58.51	15.26		
	Q1-Q3	58.51 - 58.51	15.26 - 15.26		
	Min-Max	58.5 - 58.5	15.3 - 15.3		
Post Treatment	n	1	1	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Follow-Up 3					
	Mean (SD)	53.05 (NE)	9.80 (NE)		
	Median	53.05	9.80		
	Q1-Q3	53.05 - 53.05	9.80 - 9.80		
	Min-Max	53.1 - 53.1	9.8 - 9.8		
Post Treatment	n	1	1	2	2
Follow-Up 4					
	Mean (SD)	58.51 (NE)	15.26 (NE)	43.25 (0.000)	-7.63 (10.790)
	Median	58.51	15.26	43.25	-7.63
	Q1-Q3	58.51 - 58.51	15.26 - 15.26	43.25 - 43.25	-15.26 - 0.00
	Min-Max	58.5 - 58.5	15.3 - 15.3	43.3 - 43.3	-15.3 - 0.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Pain Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 5	n	1	1	0	0
	Mean (SD)	58.51 (NE)	15.26 (NE)		
	Median	58.51	15.26		
	Q1-Q3	58.51 - 58.51	15.26 - 15.26		
	Min-Max	58.5 - 58.5	15.3 - 15.3		
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			50.88 (10.790)	-7.63 (10.790)
	Median			50.88	-7.63
	Q1-Q3			43.25 - 58.51	-15.26 - 0.00
	Min-Max			43.3 - 58.5	-15.3 - 0.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Baseline	n	48		17	
	Mean (SD)	53.81 (6.747)		54.64 (8.795)	
	Median	56.07		56.07	
	Q1-Q3	48.94 - 56.07		48.94 - 62.62	
	Min-Max	40.2 - 68.1		40.2 - 68.1	
Week 5 Day 1	n	41	41	15	15
	Mean (SD)	55.14 (7.342)	1.15 (8.047)	58.11 (5.340)	3.62 (8.395)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 62.62	-5.50 - 7.13	56.07 - 62.62	0.00 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 13.7	48.9 - 68.1	-6.5 - 22.5
Week 8 Day 1	n	42	42	13	13

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	53.32 (7.181)	-0.26 (7.992)	58.38 (5.458)	4.65 (9.951)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-5.50 - 6.55	56.07 - 62.62	0.00 - 7.13
	Min-Max	40.2 - 68.1	-22.5 - 19.2	48.9 - 68.1	-6.5 - 28.0
Week 16 Day 1	n	39	39	7	7
	Mean (SD)	51.24 (7.353)	-2.64 (7.978)	57.63 (7.254)	2.19 (10.066)
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	48.94 - 62.62	-6.55 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 19.2	48.9 - 68.1	-7.1 - 22.5
Week 24 Day 1	n	35	35	7	7
	Mean (SD)	51.27 (8.025)	-2.31 (7.755)	54.65 (7.916)	-1.72 (11.928)

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Median	48.94	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 6.55	48.94 - 62.62	-6.55 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 8.8	40.2 - 62.6	-22.5 - 15.9
Week 32 Day 1	n	38	38	7	7
	Mean (SD)	52.46 (7.450)	-0.82 (7.542)	56.84 (6.140)	1.41 (7.785)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-6.55 - 5.50	48.94 - 62.62	-5.50 - 6.55
	Min-Max	40.2 - 68.1	-22.5 - 15.9	48.9 - 62.6	-7.1 - 15.9
Week 40 Day 1	n	32	32	5	5
	Mean (SD)	52.21 (8.157)	-0.64 (7.922)	59.46 (8.421)	5.59 (7.781)
	Median	56.07	0.00	56.07	0.00

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Q1-Q3	48.94 - 56.07	-3.27 - 3.27	56.07 - 68.12	0.00 - 12.05
	Min-Max	40.2 - 68.1	-22.5 - 13.7	48.9 - 68.1	0.0 - 15.9
Week 48 Day 1	n	32	32	7	7
	Mean (SD)	51.09 (7.772)	-1.08 (7.974)	54.65 (7.916)	-0.79 (5.534)
	Median	52.51	0.00	56.07	0.00
	Q1-Q3	44.55 - 56.07	-6.55 - 0.00	48.94 - 62.62	0.00 - 0.00
	Min-Max	40.2 - 68.1	-22.5 - 13.7	40.2 - 62.6	-12.1 - 6.5
Week 56 Day 1	n	35	35	5	5
	Mean (SD)	50.71 (7.399)	-2.35 (8.268)	59.67 (7.364)	1.31 (2.929)
	Median	48.94	0.00	62.62	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	56.07 - 62.62	0.00 - 0.00

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Min-Max	40.2 - 68.1	-22.5 - 13.7	48.9 - 68.1	0.0 - 6.5
Week 72 Day 1	n	30	30	0	0
	Mean (SD)	49.57 (7.546)	-3.24 (7.695)		
	Median	48.94	0.00		
	Q1-Q3	40.15 - 56.07	-7.13 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 8.8		
Week 88 Day 1	n	32	32	0	0
	Mean (SD)	50.00 (7.286)	-3.67 (7.748)		
	Median	48.94	-3.27		
	Q1-Q3	44.55 - 56.07	-7.96 - 0.00		
	Min-Max	40.2 - 68.1	-15.9 - 15.9		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 104 Day 1	n	31	31	0	0
	Mean (SD)	51.04 (7.247)	-2.11 (8.820)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 15.9		
Week 120 Day 1	n	27	27	0	0
	Mean (SD)	49.93 (7.855)	-4.55 (9.487)		
	Median	48.94	-6.55		
	Q1-Q3	40.15 - 56.07	-12.05 - 0.00		
	Min-Max	40.2 - 68.1	-22.5 - 15.9		

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Week 136 Day 1	n	19	19	0	0
	Mean (SD)	50.49 (8.864)	-2.72 (9.637)		
	Median	48.94	0.00		
	Q1-Q3	40.15 - 56.07	-8.79 - 0.00		
	Min-Max	40.2 - 68.1	-15.9 - 15.9		
Week 152 Day 1	n	13	13	0	0
	Mean (SD)	46.90 (8.300)	-7.35 (12.299)		
	Median	40.15	-15.92		
	Q1-Q3	40.15 - 56.07	-15.92 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 15.9		
Week 168 Day 1	n	11	11	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)	47.64 (7.269)	-7.73 (9.989)		
	Median	48.94	-7.13		
	Q1-Q3	40.15 - 48.94	-15.92 - 0.00		
	Min-Max	40.2 - 62.6	-22.5 - 13.7		
End Of Treatment	n	41	41	12	12
	Mean (SD)	52.44 (7.985)	-1.74 (7.744)	57.02 (5.691)	3.47 (10.089)
	Median	56.07	0.00	56.07	0.00
	Q1-Q3	48.94 - 56.07	-7.13 - 0.00	52.51 - 62.62	-6.03 - 11.24
	Min-Max	40.2 - 68.1	-19.2 - 15.9	48.9 - 62.6	-7.1 - 22.5
Post Treatment Follow-Up 1	n	0	0	4	4

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
	Mean (SD)			52.36 (6.840)	-3.57 (11.904)
	Median			48.94	-7.13
	Q1-Q3			48.94 - 55.78	-10.41 - 3.27
	Min-Max			48.9 - 62.6	-13.7 - 13.7
Post Treatment	n	1	1	0	0
Follow-Up 2					
	Mean (SD)	62.62 (NE)	13.68 (NE)		
	Median	62.62	13.68		
	Q1-Q3	62.62 - 62.62	13.68 - 13.68		
	Min-Max	62.6 - 62.6	13.7 - 13.7		
Post Treatment	n	1	1	0	0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Follow-Up 3					
	Mean (SD)	48.94 (NE)	0.00 (NE)		
	Median	48.94	0.00		
	Q1-Q3	48.94 - 48.94	0.00 - 0.00		
	Min-Max	48.9 - 48.9	0.0 - 0.0		
Post Treatment	n	1	1	2	2
Follow-Up 4					
	Mean (SD)	56.07 (NE)	7.13 (NE)	48.94 (0.000)	0.00 (0.000)
	Median	56.07	7.13	48.94	0.00
	Q1-Q3	56.07 - 56.07	7.13 - 7.13	48.94 - 48.94	0.00 - 0.00
	Min-Max	56.1 - 56.1	7.1 - 7.1	48.9 - 48.9	0.0 - 0.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

PROMIS Parent Proxy Global Health 7+2 – T-Scores by time point for patients aged >= 5 years
Full Analysis Set - L

Scale: Fatigue Scores

		Dabrafenib+Trametinib N=58		Carboplatin+Vincristine N=27	
Time point	**Statistics**	**Raw value**	**Change from baseline**	**Raw value**	**Change from baseline**
Post Treatment Follow-Up 5	n	1	1	0	0
	Mean (SD)	62.62 (NE)	13.68 (NE)		
	Median	62.62	13.68		
	Q1-Q3	62.62 - 62.62	13.68 - 13.68		
	Min-Max	62.6 - 62.6	13.7 - 13.7		
Post Treatment Follow-Up 6	n	0	0	2	2
	Mean (SD)			55.78 (9.673)	0.00 (0.000)
	Median			55.78	0.00
	Q1-Q3			48.94 - 62.62	0.00 - 0.00
	Min-Max			48.9 - 62.6	0.0 - 0.0

Analogous to CSR table 14.2-7.2L, but for patients aged >= 5 years.
Baseline is defined as the last assessment on or prior to first treatment date.
SD: Standard Deviation.

2. Verträglichkeit – Spezifische unerwünschte Ereignisse

2.1. Time-to-Event-Analysen zu unerwünschten Ereignissen nach SOC und PT

2.1.1. Unerwünschte Ereignisse nach SOC und PT

Any AE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Blood and lymphatic system disorders	24 / 73 (32.9)	NE (44.0, NE)	25 / 33 (75.8)	1.2 (0.7, 1.9)	0.20 (0.11, 0.36)	<0.001
Anaemia	14 / 73 (19.2)	NE (NE, NE)	20 / 33 (60.6)	1.6 (0.7, NE)	0.16 (0.07, 0.34)	<0.001
Neutropenia	10 / 73 (13.7)	NE (NE, NE)	10 / 33 (30.3)	NE (3.3, NE)	0.31 (0.12, 0.77)	0.008
Thrombocytopenia	1 / 73 (1.4)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.07 (0.01, 0.57)	0.001
Ear and labyrinth disorders	16 / 73 (21.9)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.92 (0.29, 2.91)	0.885
Eye disorders	23 / 73 (31.5)	NE (32.6, NE)	5 / 33 (15.2)	NE (NE, NE)	1.05 (0.38, 2.89)	0.930
Gastrointestinal disorders	59 / 73 (80.8)	2.5 (1.0, 4.7)	27 / 33 (81.8)	0.3 (0.1, 0.8)	0.55 (0.35, 0.88)	0.013
Abdominal pain	15 / 73 (20.5)	NE (NE, NE)	7 / 33 (21.2)	NE (NE, NE)	0.69 (0.28, 1.74)	0.434

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Abdominal pain upper	13 / 73 (17.8)	NE (47.4, NE)	2 / 33 (6.1)	NE (NE, NE)	1.99 (0.44, 9.04)	0.362
Constipation	10 / 73 (13.7)	NE (NE, NE)	12 / 33 (36.4)	NE (1.7, NE)	0.22 (0.09, 0.53)	<0.001
Diarrhoea	27 / 73 (37.0)	46.6 (26.9, NE)	6 / 33 (18.2)	NE (NE, NE)	1.39 (0.56, 3.46)	0.472
Nausea	21 / 73 (28.8)	NE (NE, NE)	17 / 33 (51.5)	4.2 (0.3, NE)	0.31 (0.16, 0.60)	<0.001
Stomatitis	6 / 73 (8.2)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.30 (0.08, 1.12)	0.058
Vomiting	27 / 73 (37.0)	NE (30.0, NE)	17 / 33 (51.5)	4.2 (1.9, NE)	0.47 (0.25, 0.88)	0.016
General disorders and administration site conditions	65 / 73 (89.0)	0.9 (0.5, 2.7)	19 / 33 (57.6)	3.5 (1.0, 10.6)	1.60 (0.95, 2.68)	0.072
Fatigue	25 / 73 (34.2)	NE (NE, NE)	10 / 33 (30.3)	NE (12.5, NE)	1.08 (0.52, 2.27)	0.837
Pyrexia	55 / 73 (75.3)	3.3 (1.5, 9.7)	6 / 33 (18.2)	NE (NE, NE)	4.36 (1.86, 10.18)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Immune system disorders	4 / 73 (5.5)	NE (NE, NE)	6 / 33 (18.2)	NE (8.3, NE)	0.04 (0.00, 0.33)	<0.001
Hypersensitivity	1 / 73 (1.4)	NE (NE, NE)	6 / 33 (18.2)	NE (8.3, NE)	<0.001 (0.00, NE)	<0.001
Infections and infestations	59 / 73 (80.8)	6.9 (4.6, 12.7)	14 / 33 (42.4)	12.6 (3.5, NE)	1.34 (0.74, 2.44)	0.338
COVID-19	26 / 73 (35.6)	NE (32.9, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.171
Nasopharyngitis	9 / 73 (12.3)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	1.29 (0.27, 6.24)	0.754
Paronychia	17 / 73 (23.3)	NE (45.4, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.097
Rhinitis	7 / 73 (9.6)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.39 (0.10, 1.53)	0.163
Upper respiratory tract infection	16 / 73 (21.9)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	1.98 (0.44, 8.96)	0.367
Injury, poisoning and procedural complications	30 / 73 (41.1)	NE (20.5, NE)	12 / 33 (36.4)	NE (3.0, NE)	0.58 (0.28, 1.19)	0.130

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Infusion related reaction	0 / 73 (0.0)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001
Investigations	44 / 73 (60.3)	12.7 (7.7, 25.8)	22 / 33 (66.7)	1.6 (0.7, 3.3)	0.44 (0.25, 0.75)	0.002
Alanine aminotransferase increased	10 / 73 (13.7)	NE (NE, NE)	9 / 33 (27.3)	NE (14.0, NE)	0.30 (0.12, 0.76)	0.007
Aspartate aminotransferase increased	9 / 73 (12.3)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.42 (0.13, 1.35)	0.135
Lymphocyte count decreased	5 / 73 (6.8)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.19 (0.04, 0.79)	0.011
Neutrophil count decreased	11 / 73 (15.1)	NE (NE, NE)	16 / 33 (48.5)	NE (1.6, NE)	0.20 (0.09, 0.44)	<0.001
Platelet count decreased	4 / 73 (5.5)	NE (NE, NE)	10 / 33 (30.3)	NE (7.2, NE)	0.12 (0.04, 0.40)	<0.001
Weight decreased	2 / 73 (2.7)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.20 (0.04, 1.11)	0.041
Weight increased	12 / 73 (16.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.032
White blood cell count decreased	9 / 73 (12.3)	NE (NE, NE)	12 / 33 (36.4)	NE (4.9, NE)	0.18 (0.07, 0.46)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Metabolism and nutrition disorders	17 / 73 (23.3)	NE (NE, NE)	15 / 33 (45.5)	NE (0.5, NE)	0.29 (0.14, 0.60)	<0.001
Decreased appetite	4 / 73 (5.5)	NE (NE, NE)	8 / 33 (24.2)	NE (NE, NE)	0.14 (0.04, 0.54)	<0.001
Hypocalcaemia	2 / 73 (2.7)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.19 (0.03, 1.05)	0.035
Hypokalaemia	3 / 73 (4.1)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.17 (0.03, 0.92)	0.020
Hypomagnesaemia	1 / 73 (1.4)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	0.05 (0.01, 0.46)	<0.001
Musculoskeletal and connective tissue disorders	31 / 73 (42.5)	NE (13.6, NE)	12 / 33 (36.4)	NE (2.2, NE)	0.77 (0.39, 1.52)	0.464
Arthralgia	9 / 73 (12.3)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	3.00 (0.37, 24.11)	0.278
Back pain	7 / 73 (9.6)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.56 (0.16, 2.02)	0.374
Pain in extremity	13 / 73 (17.8)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.95 (0.30, 3.01)	0.937

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Pain in jaw	1 / 73 (1.4)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	15 / 73 (20.5)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.064
Skin papilloma	10 / 73 (13.7)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.202
Nervous system disorders	49 / 73 (67.1)	5.7 (3.3, 19.1)	22 / 33 (66.7)	2.1 (0.9, 12.5)	0.64 (0.38, 1.08)	0.093
Dizziness	8 / 73 (11.0)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	2.73 (0.33, 22.26)	0.330
Headache	40 / 73 (54.8)	18.3 (5.7, NE)	9 / 33 (27.3)	NE (9.7, NE)	1.49 (0.71, 3.13)	0.285
Peripheral motor neuropathy	0 / 73 (0.0)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001
Peripheral sensory neuropathy	0 / 73 (0.0)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Psychiatric disorders	10 / 73 (13.7)	NE (NE, NE)	6 / 33 (18.2)	NE (13.3, NE)	0.35 (0.11, 1.05)	0.050
Anxiety	1 / 73 (1.4)	NE (NE, NE)	5 / 33 (15.2)	NE (13.3, NE)	<0.001 (0.00, NE)	<0.001
Renal and urinary disorders	9 / 73 (12.3)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.76 (0.19, 3.09)	0.705
Respiratory, thoracic and mediastinal disorders	34 / 73 (46.6)	34.1 (10.5, NE)	13 / 33 (39.4)	NE (2.8, NE)	0.81 (0.42, 1.56)	0.522
Cough	11 / 73 (15.1)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.67 (0.20, 2.31)	0.527
Epistaxis	17 / 73 (23.3)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	5.99 (0.79, 45.30)	0.048
Oropharyngeal pain	10 / 73 (13.7)	NE (NE, NE)	7 / 33 (21.2)	NE (NE, NE)	0.41 (0.15, 1.12)	0.074
Rhinorrhoea	2 / 73 (2.7)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.08 (0.01, 0.77)	0.006

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Skin and subcutaneous tissue disorders	64 / 73 (87.7)	1.9 (1.0, 4.0)	17 / 33 (51.5)	9.7 (2.8, NE)	1.83 (1.06, 3.15)	0.028
Acne	10 / 73 (13.7)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.145
Alopecia	2 / 73 (2.7)	NE (NE, NE)	9 / 33 (27.3)	NE (NE, NE)	0.07 (0.02, 0.34)	<0.001
Dermatitis acneiform	10 / 73 (13.7)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.046
Dry skin	20 / 73 (27.4)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	6.61 (0.88, 49.94)	0.034
Eczema	13 / 73 (17.8)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.049
Erythema	12 / 73 (16.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.121
Pruritus	9 / 73 (12.3)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	1.64 (0.35, 7.79)	0.527
Rash	14 / 73 (19.2)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	2.11 (0.61, 7.37)	0.229
Rash maculo-papular	13 / 73 (17.8)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.092

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Any AE by SOC and PT: Time to first event
Safety Set – L

			Treatment groups					
			Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term			n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Vascular disorders			10 / 73 (13.7)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.87 (0.22, 3.41)	0.847

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

2.1.2. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) nach SOC und PT

Grade >= 3 AE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Blood and lymphatic system disorders	7 / 73 (9.6)	NE (NE, NE)	15 / 33 (45.5)	NE (1.9, NE)	0.13 (0.05, 0.33)	<0.001
Anaemia	0 / 73 (0.0)	NE (NE, NE)	8 / 33 (24.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001
Neutropenia	7 / 73 (9.6)	NE (NE, NE)	10 / 33 (30.3)	NE (3.3, NE)	0.21 (0.08, 0.58)	0.001
Thrombocytopenia	0 / 73 (0.0)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001
Gastrointestinal disorders	3 / 73 (4.1)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.16 (0.03, 0.80)	0.012
Diarrhoea	0 / 73 (0.0)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.017
General disorders and administration site conditions	10 / 73 (13.7)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	2.44 (0.29, 20.30)	0.395
Pyrexia	10 / 73 (13.7)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	2.44 (0.29, 20.30)	0.395

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Grade >= 3 AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Infections and infestations	10 / 73 (13.7)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.81 (0.21, 3.15)	0.757
Injury, poisoning and procedural complications	2 / 73 (2.7)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	0.31 (0.04, 2.25)	0.221
Investigations	17 / 73 (23.3)	NE (NE, NE)	18 / 33 (54.5)	3.3 (1.6, NE)	0.21 (0.10, 0.42)	<0.001
Alanine aminotransferase increased	4 / 73 (5.5)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.48 (0.11, 2.18)	0.332
Lymphocyte count decreased	0 / 73 (0.0)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.005
Neutrophil count decreased	4 / 73 (5.5)	NE (NE, NE)	16 / 33 (48.5)	NE (1.7, NE)	0.08 (0.03, 0.24)	<0.001
Platelet count decreased	0 / 73 (0.0)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.002
Weight increased	6 / 73 (8.2)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.156
White blood cell count decreased	0 / 73 (0.0)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	<0.001 (0.00, NE)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

Grade >= 3 AE by SOC and PT: Time to first event
Safety Set – L

System Organ Class Preferred Term	Treatment groups Dabrafenib+Trametinib N=73 n/N* (%)	 Median (95% CI)	 Carboplatin+Vincristine N=33 n/N* (%)	 Median (95% CI)	Comparison HR (95% CI)	 p-value
Metabolism and nutrition disorders	2 / 73 (2.7)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	0.38 (0.05, 2.76)	0.321
Nervous system disorders	10 / 73 (13.7)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.65 (0.22, 1.95)	0.439
Respiratory, thoracic and mediastinal disorders	4 / 73 (5.5)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	1.33 (0.14, 12.76)	0.806
Skin and subcutaneous tissue disorders	3 / 73 (4.1)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	0.35 (0.05, 2.51)	0.274
Vascular disorders	0 / 73 (0.0)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.019

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

2.1.3. Schwerwiegende unerwünschte Ereignisse nach SOC und PT

SAE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Blood and lymphatic system disorders	0 / 73 (0.0)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.011
Gastrointestinal disorders	3 / 73 (4.1)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.39 (0.08, 1.93)	0.229
General disorders and administration site conditions	12 / 73 (16.4)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	0.55 (0.19, 1.56)	0.258
Pyrexia	12 / 73 (16.4)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	0.55 (0.19, 1.56)	0.258
Infections and infestations	11 / 73 (15.1)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	1.30 (0.27, 6.17)	0.743
Injury, poisoning and procedural complications	4 / 73 (5.5)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	1.45 (0.16, 13.18)	0.741

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

SAE by SOC and PT: Time to first event
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
System Organ Class Preferred Term	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Nervous system disorders	8 / 73 (11.0)	NE (NE, NE)	5 / 33 (15.2)	NE (NE, NE)	0.49 (0.15, 1.56)	0.219
Respiratory, thoracic and mediastinal disorders	5 / 73 (6.8)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.184

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.
CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis; PT: Preferred Term; SOC: System Organ Class.

2.2. Time-to-Event-Analysen zu unerwünschten Ereignissen von besonderem Interesse (AESI)

2.2.1. Unerwünschte Ereignisse von besonderem Interesse (AESI)

Time to first AESI
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Bleeding Events	26 / 73 (35.6)	49.3 (45.5, NE)	7 / 33 (21.2)	NE (6.4, NE)	1.02 (0.43, 2.41)	0.971
Cardiac Related Events	2 / 73 (2.7)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.495
Hepatic Disorders	17 / 73 (23.3)	NE (NE, NE)	10 / 33 (30.3)	NE (14.0, NE)	0.45 (0.20, 1.02)	0.051
Hyperglycemia	2 / 73 (2.7)	NE (NE, NE)	3 / 33 (9.1)	NE (NE, NE)	0.22 (0.04, 1.38)	0.079
Hypersensitivity	15 / 73 (20.5)	NE (NE, NE)	9 / 33 (27.3)	NE (7.5, NE)	0.37 (0.15, 0.89)	0.021
Hypertension	1 / 73 (1.4)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	0.34 (0.02, 5.64)	0.434
Neutropenia	20 / 73 (27.4)	NE (40.5, NE)	27 / 33 (81.8)	1.5 (0.9, 1.6)	0.13 (0.07, 0.25)	<0.001
Ocular Events	10 / 73 (13.7)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	1.77 (0.21, 15.01)	0.598
Pancreatitis	3 / 73 (4.1)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.318
Pneumonitis And Interstitial Lung Disease	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.610
Pyrexia	56 / 73 (76.7)	3.3 (1.5, 9.7)	7 / 33 (21.2)	NE (NE, NE)	3.72 (1.68, 8.23)	<0.001
Skin Toxicity	58 / 73 (79.5)	1.9 (1.0, 4.3)	12 / 33 (36.4)	12.6 (9.7, NE)	2.66 (1.42, 4.99)	0.002

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carbaplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
CI: Confidence Interval, HR: Hazard Ratio, n: Number of patients with event, N*: Number of patients included in the analysis.

Time to first AESI
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Uveitis	5 / 73 (6.8)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.498
Venous Thromboembolism	1 / 73 (1.4)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	0.46 (0.03, 7.28)	0.568

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carbaplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
CI: Confidence Interval, HR: Hazard Ratio, n: Number of patients with event, N*: Number of patients included in the analysis.

2.2.2. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) von besonderem Interesse (AESI)

Time to first Grade >= 3 AESI
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Hepatic Disorders	5 / 73 (6.8)	NE (NE, NE)	4 / 33 (12.1)	NE (NE, NE)	0.42 (0.11, 1.60)	0.191
Hypersensitivity	1 / 73 (1.4)	NE (NE, NE)	2 / 33 (6.1)	NE (NE, NE)	<0.001 (0.00, NE)	0.017
Hypertension	0 / 73 (0.0)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	<0.001 (0.00, NE)	0.137
Neutropenia	10 / 73 (13.7)	NE (NE, NE)	25 / 33 (75.8)	1.9 (1.4, 2.1)	0.09 (0.04, 0.19)	<0.001
Pancreatitis	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.610
Pyrexia	10 / 73 (13.7)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	2.44 (0.29, 20.30)	0.395
Skin Toxicity	3 / 73 (4.1)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	0.64 (0.06, 7.19)	0.719
Uveitis	2 / 73 (2.7)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	1.00 (0.00, NE)	NE

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carbaplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
CI: Confidence Interval, HR: Hazard Ratio, n: Number of patients with event, N*: Number of patients included in the analysis.

2.2.3. Schwerwiegende unerwünschte Ereignisse von besonderem Interesse (AESI)

Time to first Serious AESI
Safety Set – L

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Bleeding Events	3 / 73 (4.1)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	1.11 (0.11, 10.77)	0.930
Hypersensitivity	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	1.00 (0.00, NE)	NE
Neutropenia	0 / 73 (0.0)	NE (NE, NE)	1 / 33 (3.0)	NE (NE, NE)	<0.001 (0.00, NE)	0.050
Ocular Events	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	1.00 (0.00, NE)	NE
Pyrexia	12 / 73 (16.4)	NE (NE, NE)	6 / 33 (18.2)	NE (NE, NE)	0.55 (0.19, 1.56)	0.258
Skin Toxicity	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.501
Venous Thromboembolism	1 / 73 (1.4)	NE (NE, NE)	0 / 33 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.501

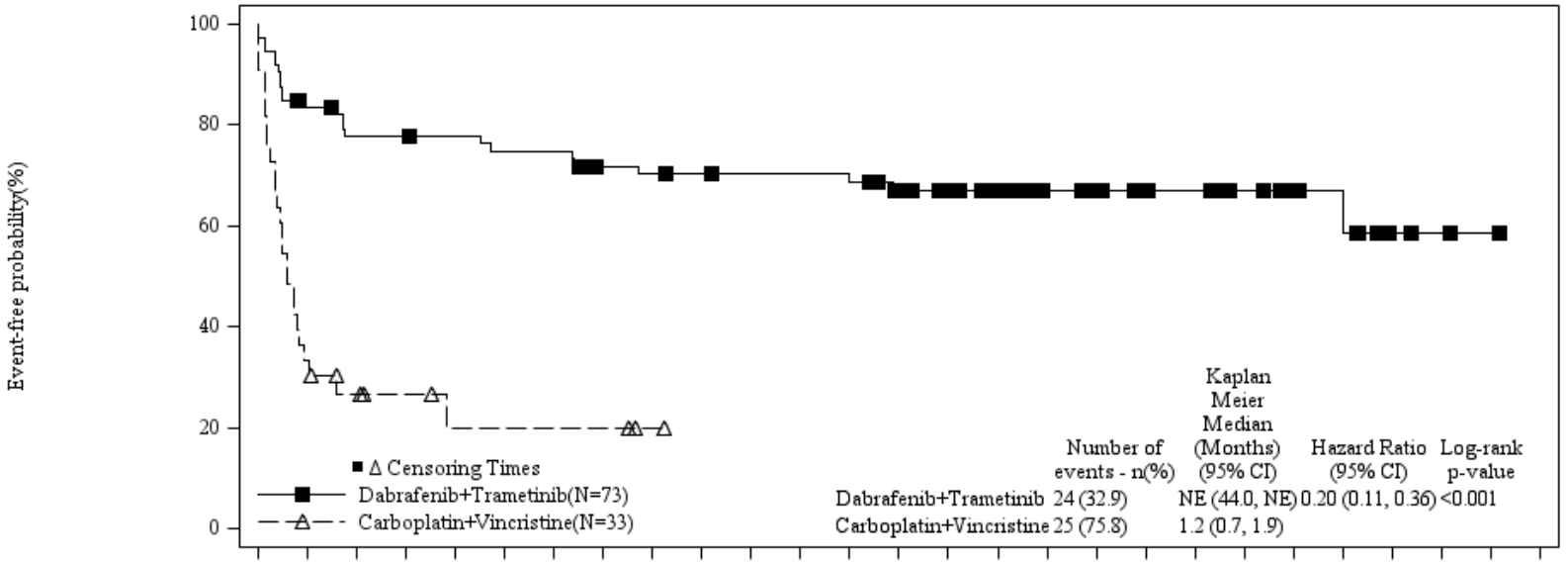
Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carbaplatin + Vincristine) estimated by Cox proportional hazards model and two-sided p-value based on a Log-rank test.
CI: Confidence Interval, HR: Hazard Ratio, n: Number of patients with event, N*: Number of patients included in the analysis.

2.3. Kaplan-Meier-Kurven für die Auswertung spezifischer unerwünschter Ereignisse

2.3.1. Unerwünschte Ereignisse nach SOC

Figure 4-1.2 (Page 1 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Blood and lymphatic system disorders



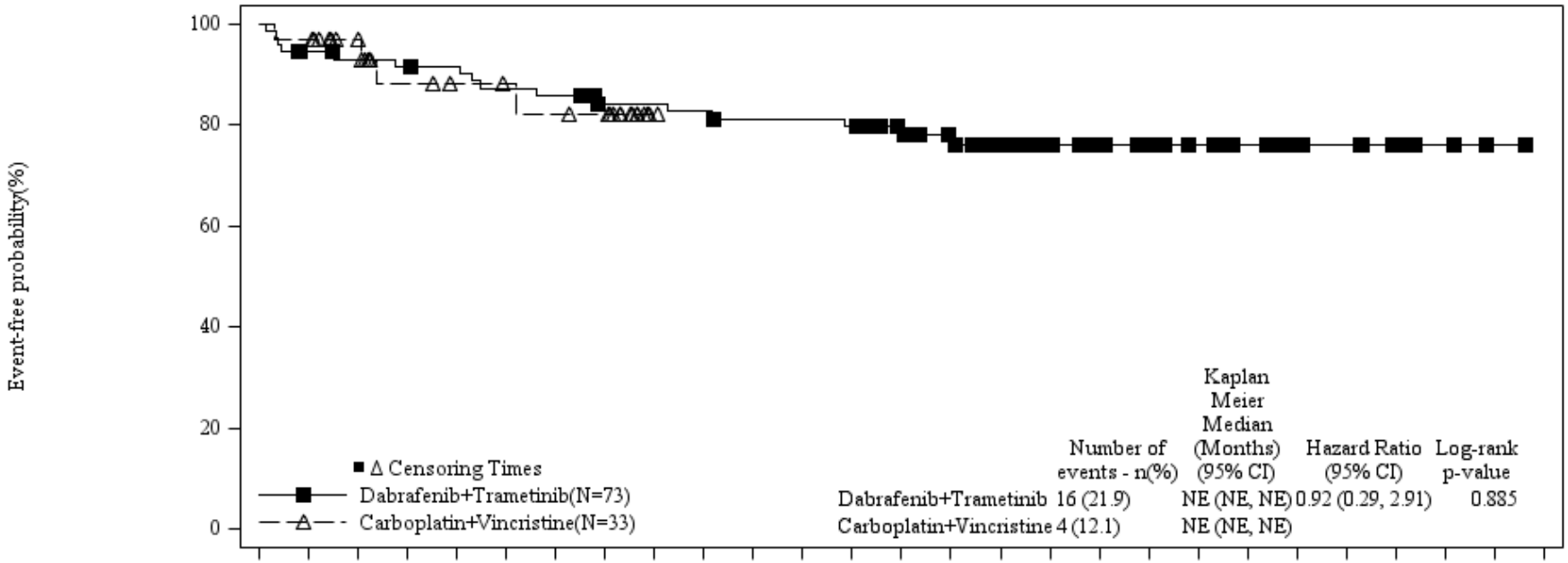
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	59	54	54	53	51	51	46	45	44	43	43	42	38	34	30	24	22	19	18	12	9	7	3	2	1	0
Carboplatin+Vincristine	33	11	7	5	3	3	3	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 2 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Ear and labyrinth disorders



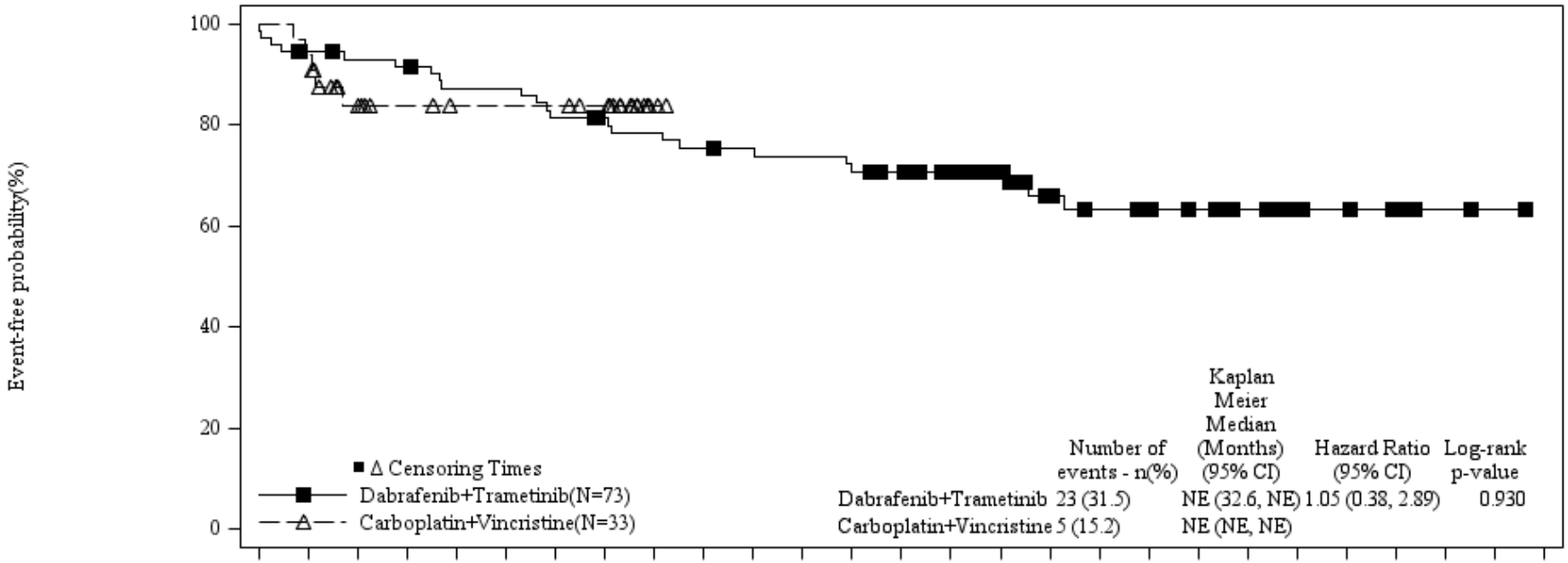
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	65	64	63	60	59	55	55	54	52	52	51	46	39	33	27	23	20	17	13	9	8	5	3	1	0
Carboplatin+Vincristine	33	32	26	18	16	15	14	13	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 3 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Eye disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	23 (31.5)	NE (32.6, NE)	1.05 (0.38, 2.89)	0.930
Carboplatin+Vincristine	5 (15.2)	NE (NE, NE)		

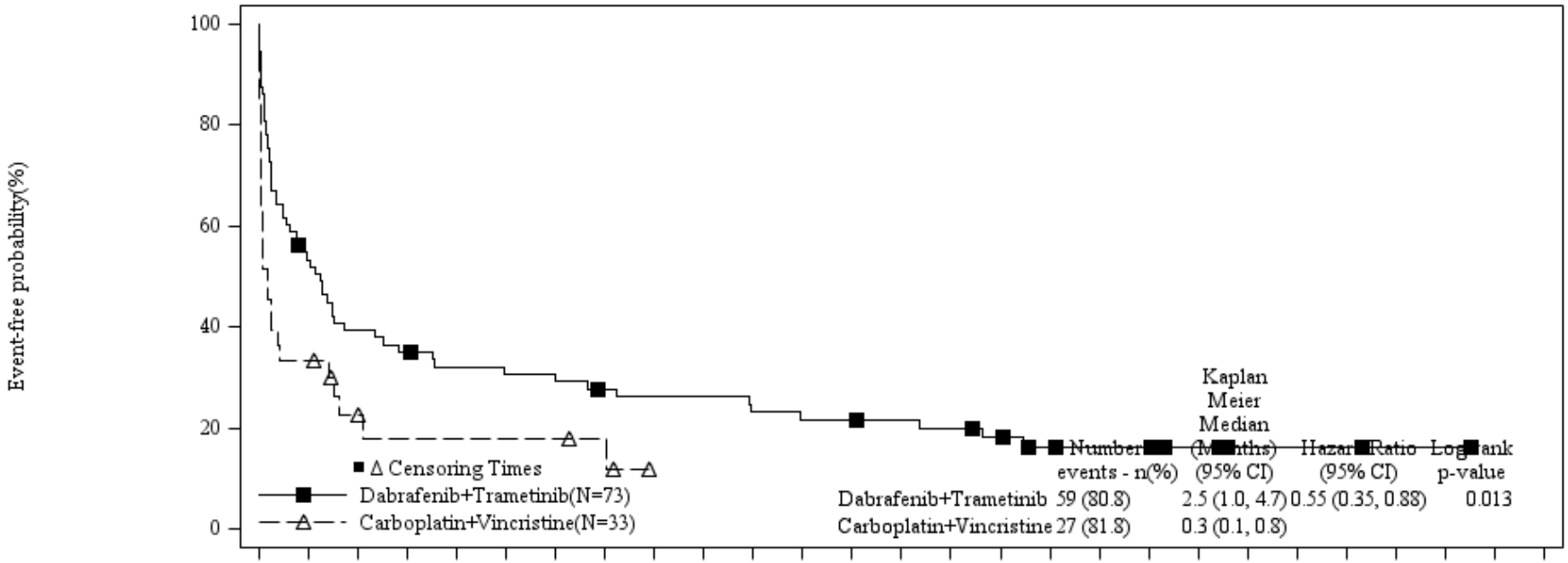
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	65	64	60	60	56	54	52	50	49	48	46	44	37	32	25	22	21	19	12	8	7	5	2	1	0
Carboplatin+Vincristine	33	31	22	18	16	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 4 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Gastrointestinal disorders



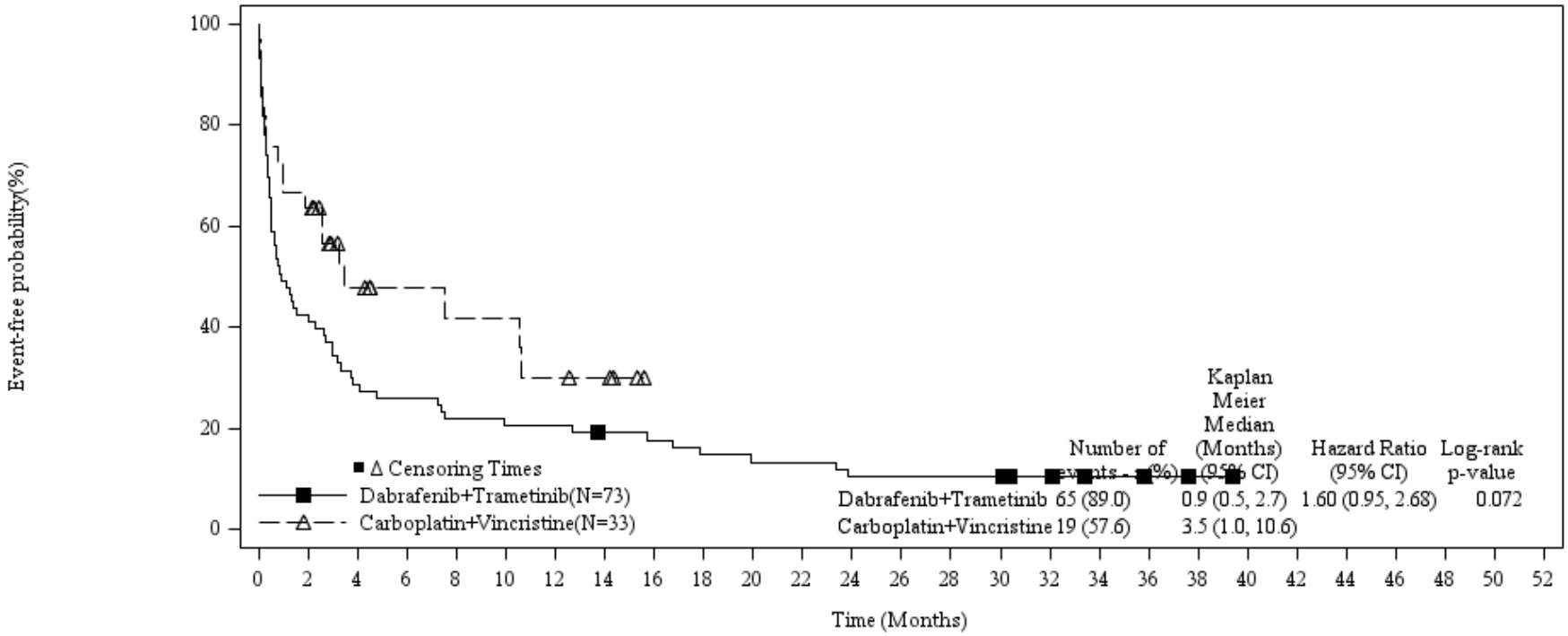
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	38	28	25	22	21	20	18	17	17	15	14	14	13	12	10	7	6	6	4	2	2	2	1	1	0	0
Carboplatin+Vincristine	33	11	6	4	4	4	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 5 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: General disorders and administration site conditions



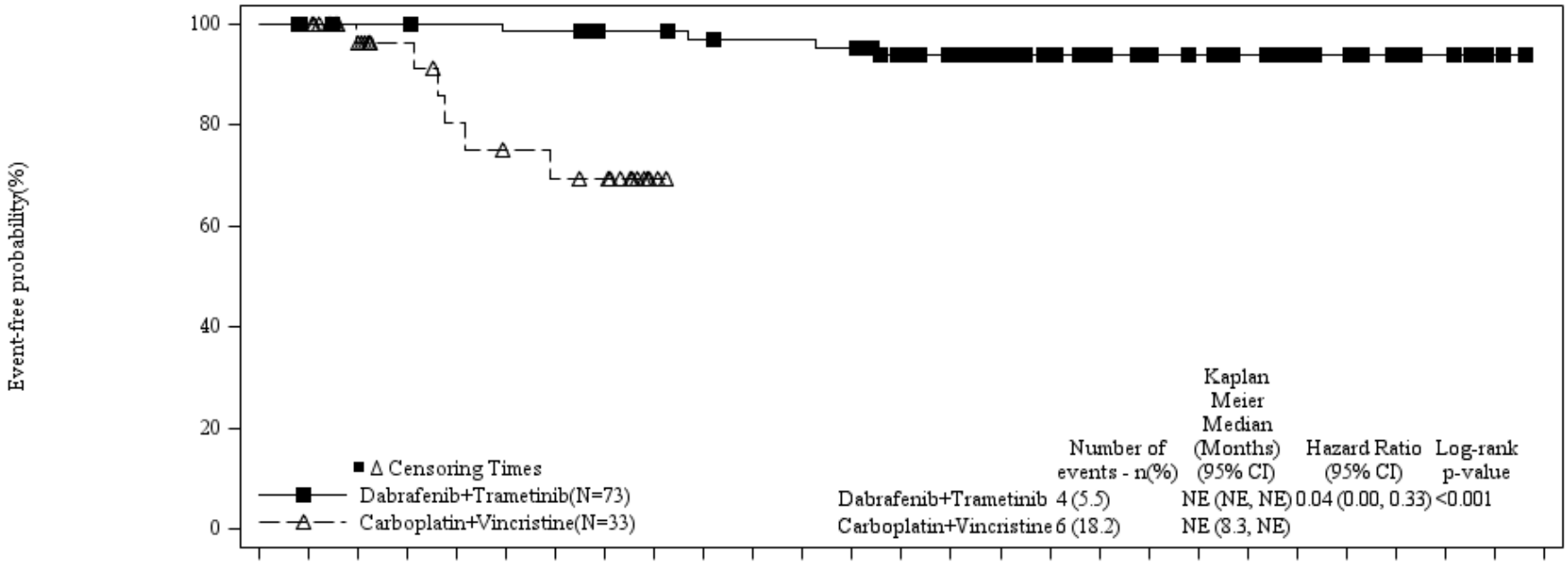
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	31	21	19	16	15	15	13	12	10	9	9	7	7	7	7	5	3	2	1	0	0	0	0	0	0	0
Carboplatin+Vincristine	33	21	11	8	7	7	5	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 6 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Immune system disorders



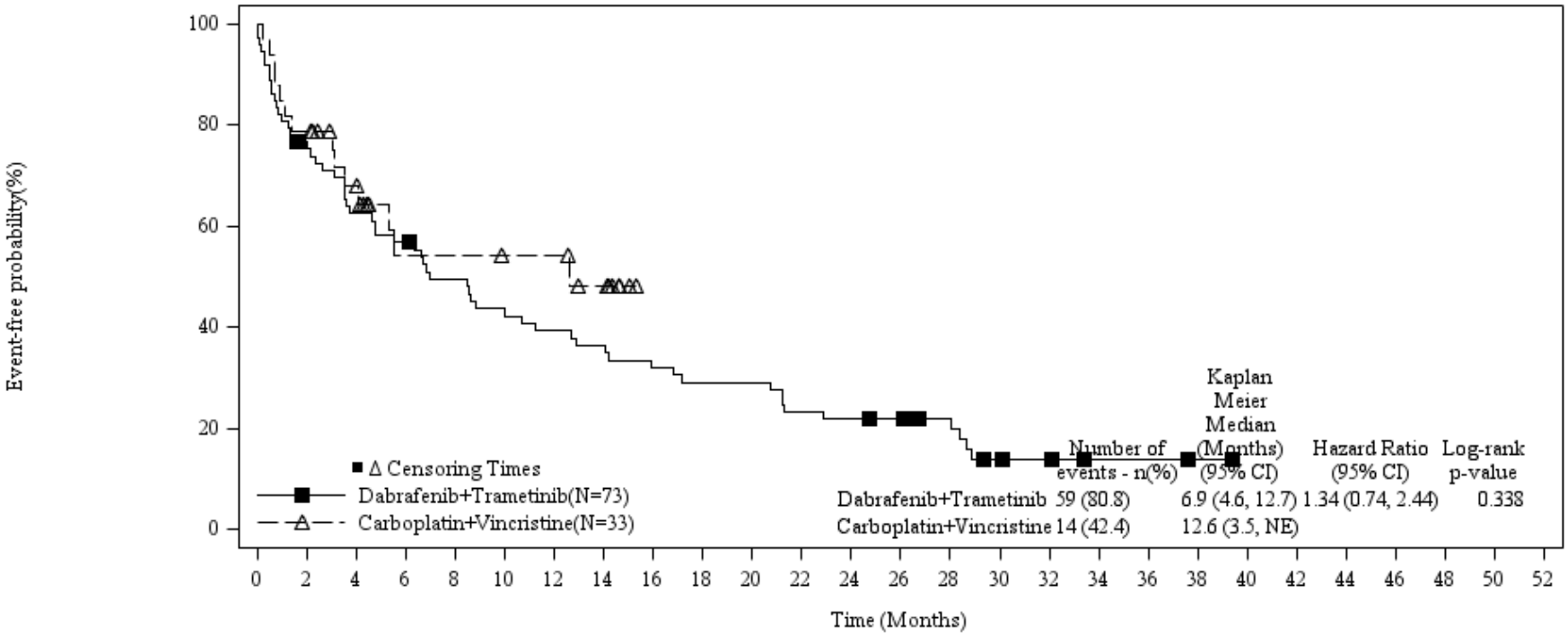
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	68	68	65	65	63	62	62	61	55	49	43	37	31	28	26	18	14	12	8	5	2	0
Carboplatin+Vincristine	33	33	25	19	15	13	12	11	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 7 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Infections and infestations



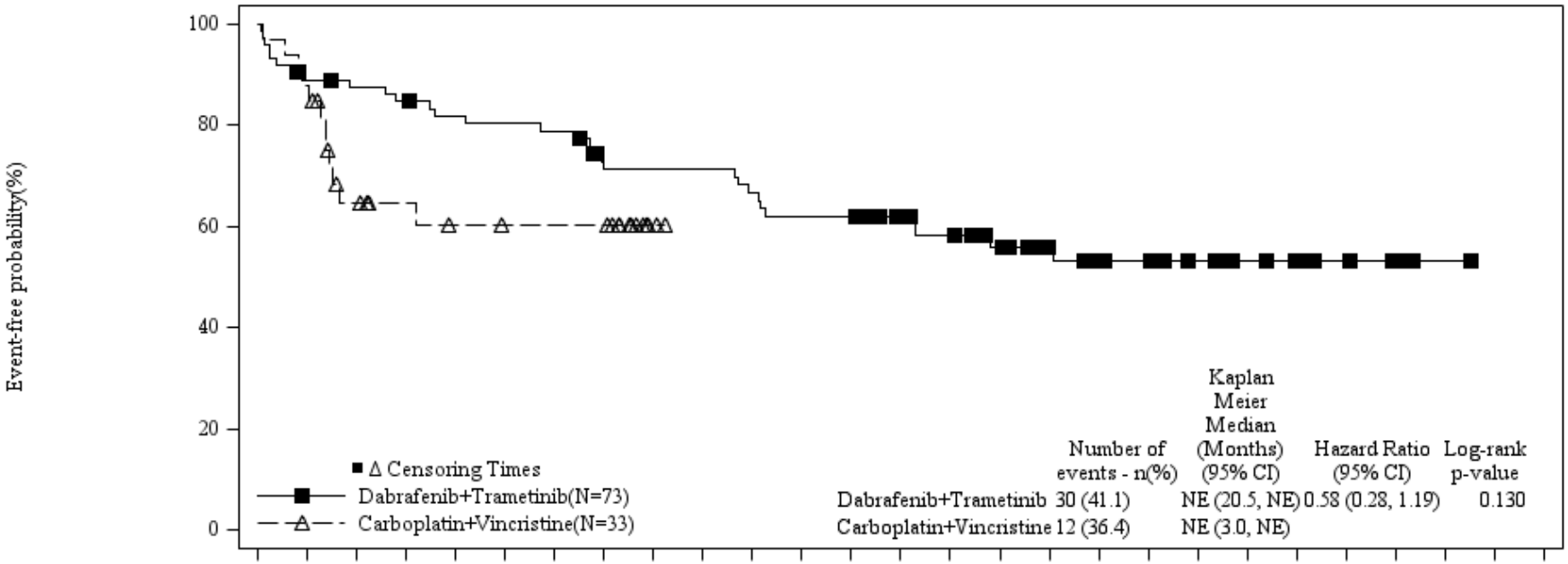
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	54	44	40	34	30	27	25	22	20	20	16	15	14	11	6	5	3	3	2	0	0	0	0	0	0	0
Carboplatin+Vincristine	33	26	19	11	11	10	10	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 8 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Injury poisoning and procedural complications



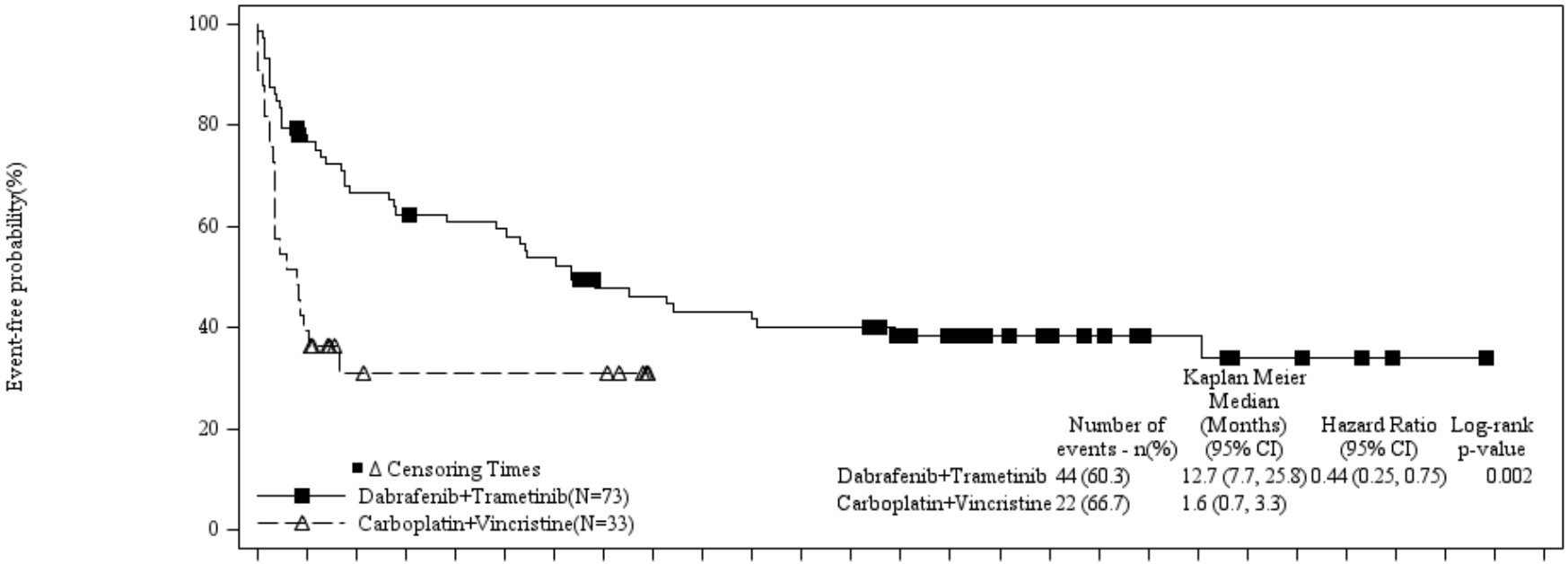
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	63	61	59	56	55	54	46	46	46	43	40	40	35	30	25	20	17	16	13	9	7	5	3	1	0	0
Carboplatin+Vincristine	33	29	18	15	13	12	12	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 9 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Investigations



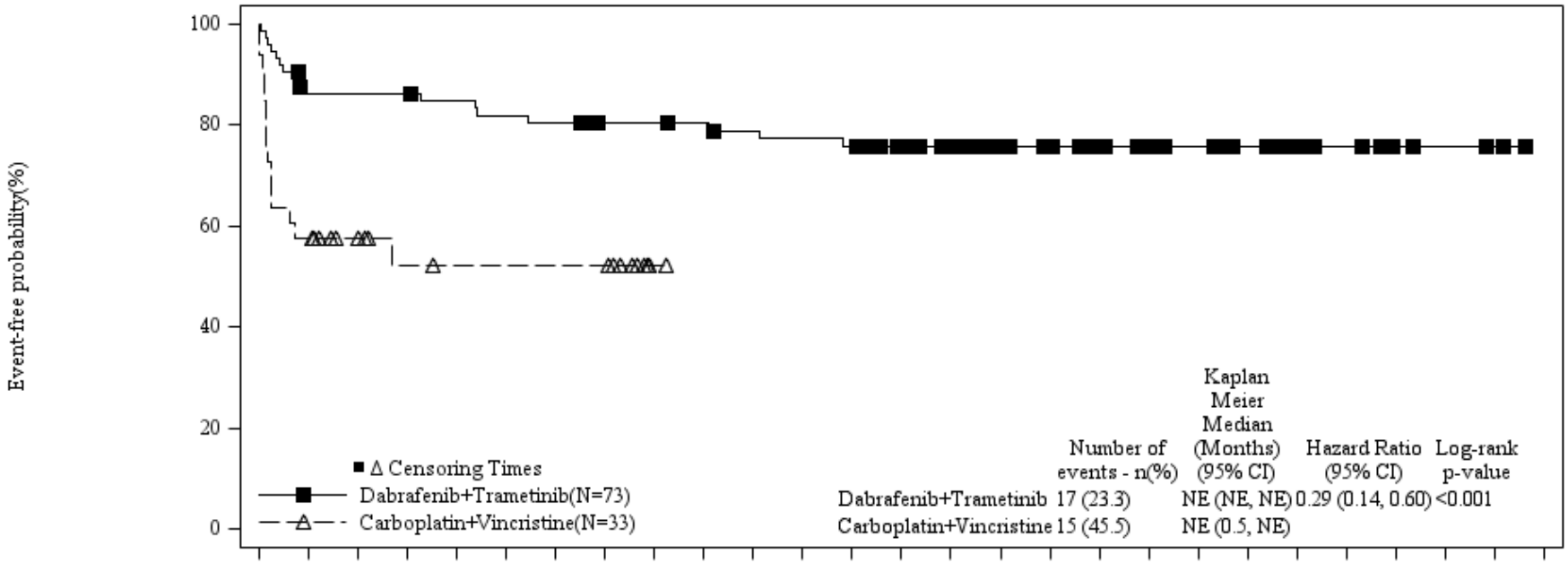
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	55	47	44	42	41	37	31	30	28	28	26	26	21	19	16	14	12	9	9	4	4	3	1	1	0	0
Carboplatin+Vincristine	33	13	6	5	5	5	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 10 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Metabolism and nutrition disorders



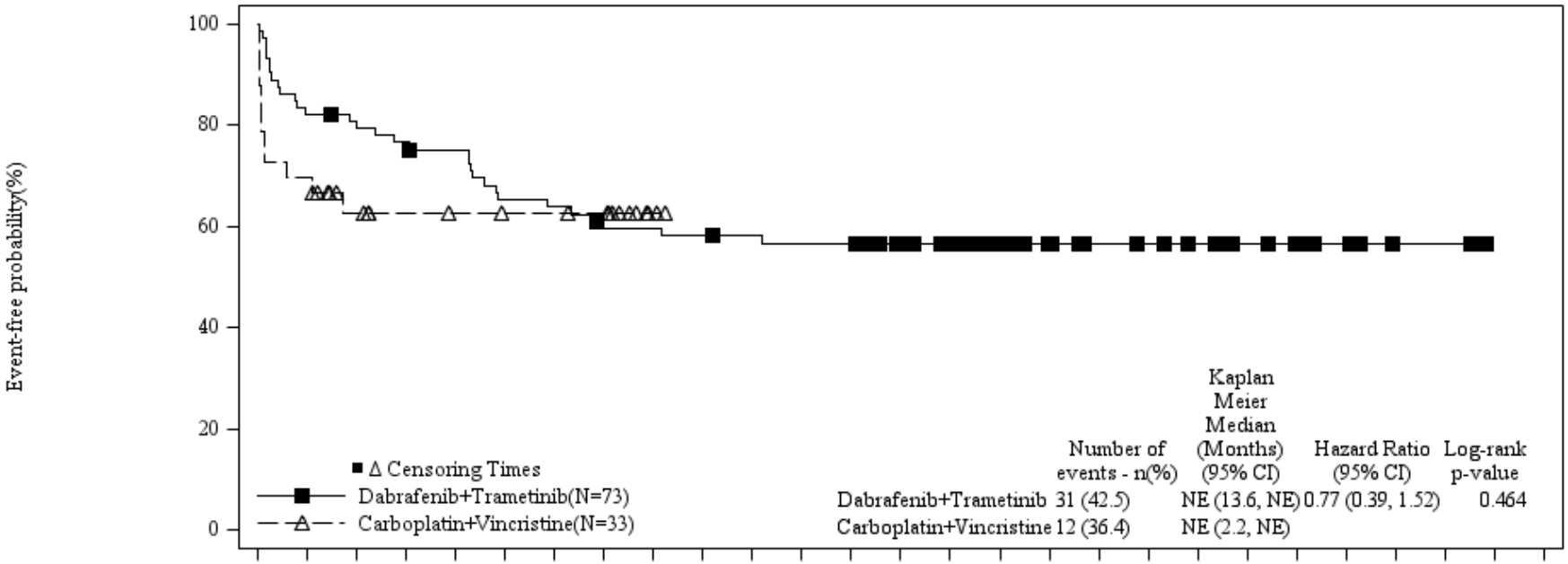
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	61	61	61	59	57	56	53	53	52	50	49	48	43	36	31	27	23	20	18	13	9	7	4	3	2	0
Carboplatin+Vincristine	33	19	14	10	9	9	9	9	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 11 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Musculoskeletal and connective tissue disorders

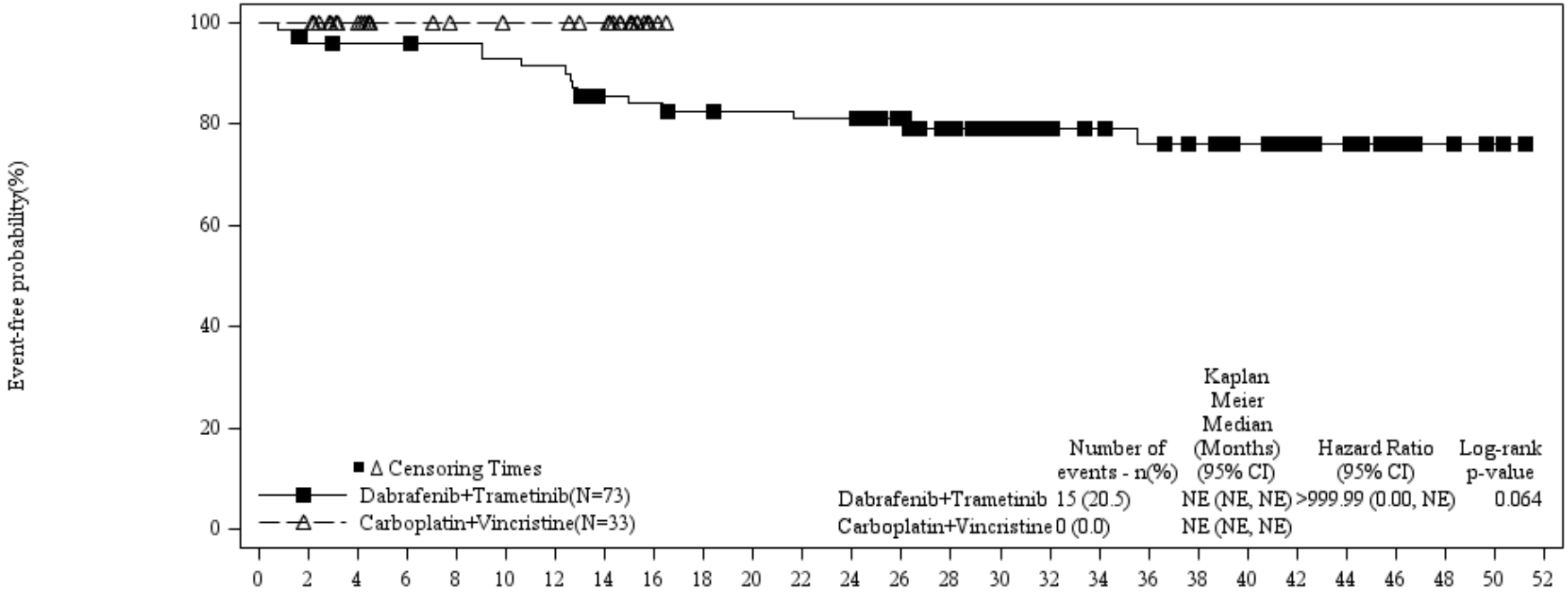


Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	60	57	55	53	46	45	41	41	40	39	38	38	33	28	24	20	17	16	14	9	7	5	2	2	0	0
Carboplatin+Vincristine	33	23	16	13	12	11	11	10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 12 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L
Time to first SOC: Neoplasms benign malignant and unspecified (incl cysts and polyps)



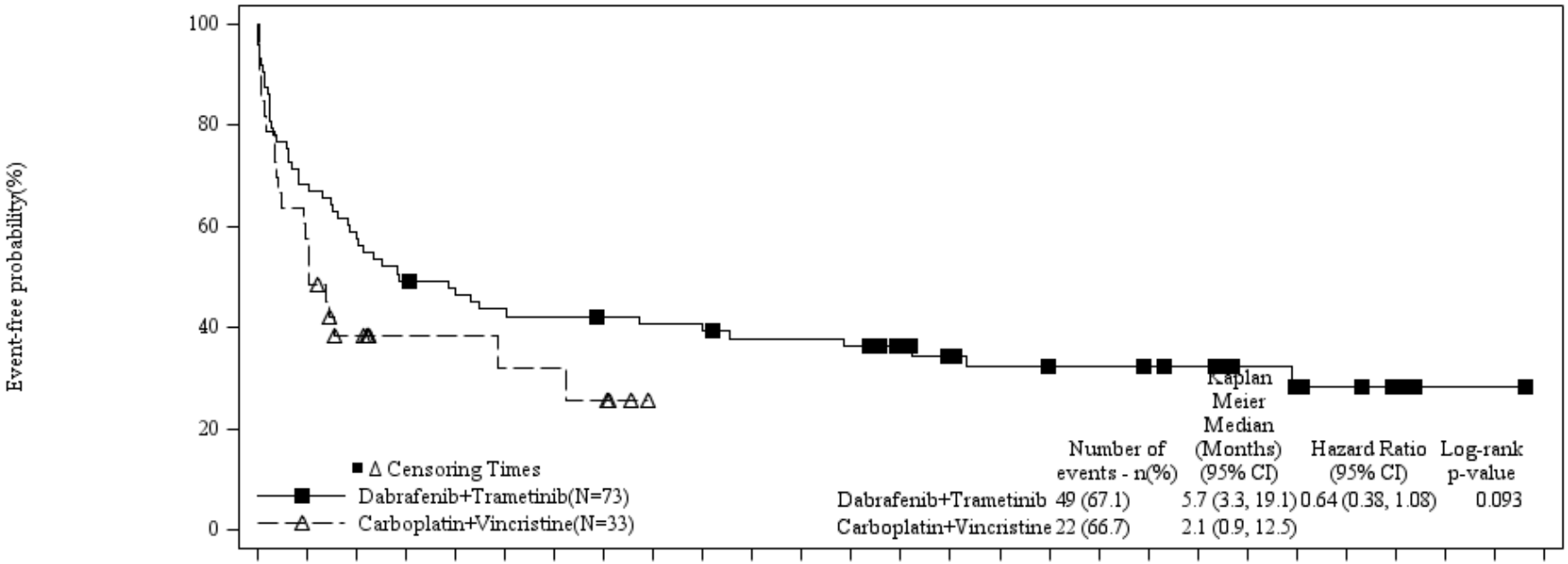
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	67	66	64	63	56	55	53	52	51	51	46	39	34	28	26	24	22	17	14	12	7	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 13 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Nervous system disorders



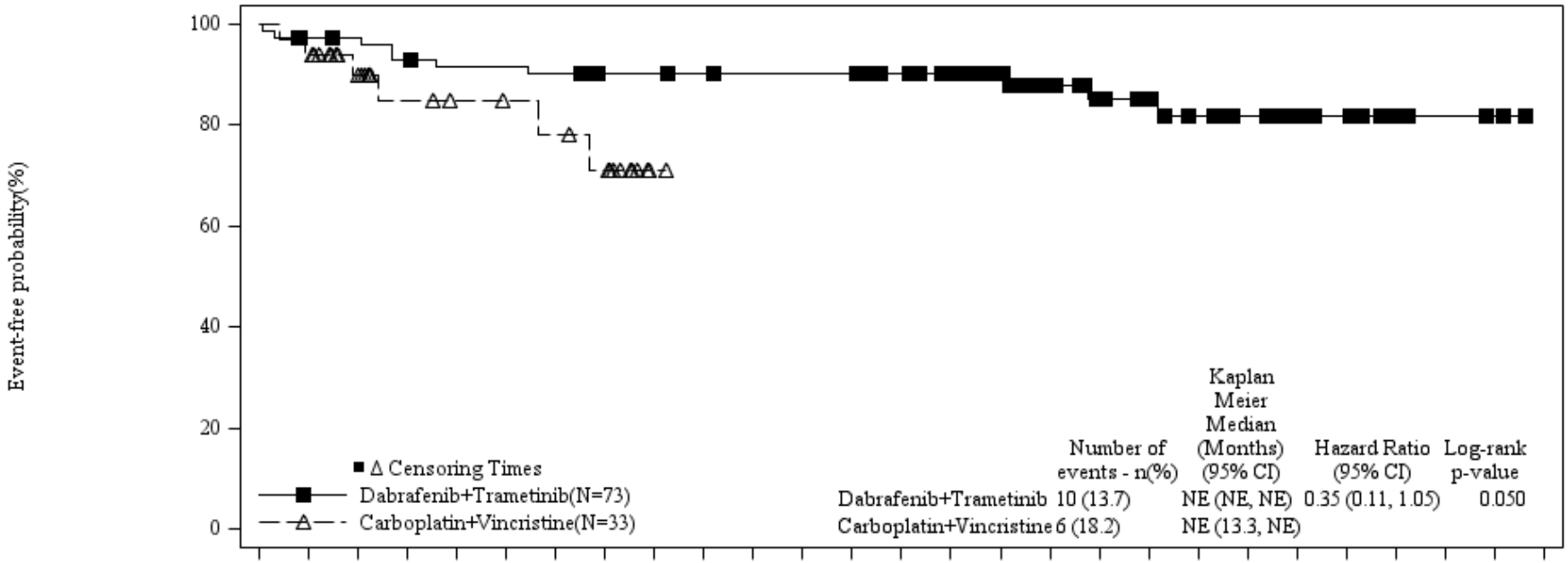
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	50	42	36	34	31	30	29	28	27	25	25	24	21	18	16	15	15	14	13	8	6	5	3	1	1	0
Carboplatin+Vincristine	33	19	10	6	6	5	5	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 14 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Psychiatric disorders



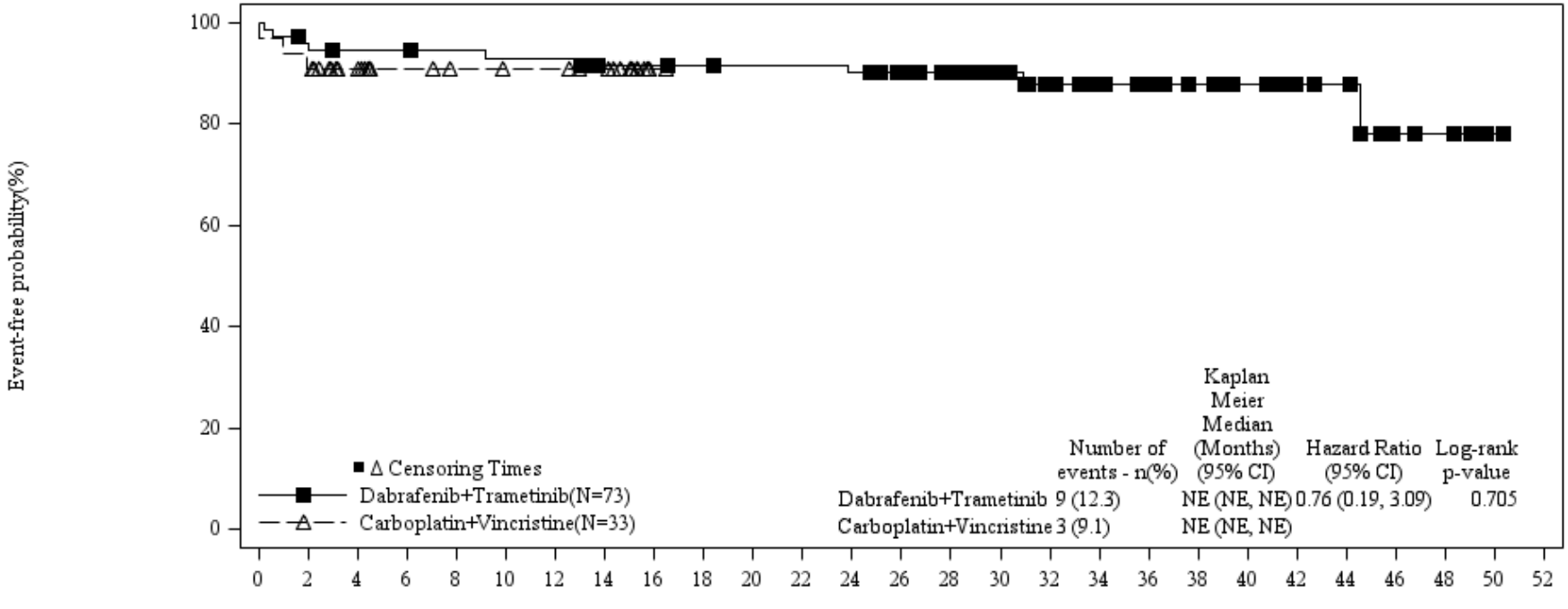
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	68	65	63	63	62	59	59	58	57	57	57	53	48	43	35	29	26	22	15	11	9	4	3	2	0
Carboplatin+Vincristine	33	31	23	16	14	13	12	10	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 15 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Renal and urinary disorders



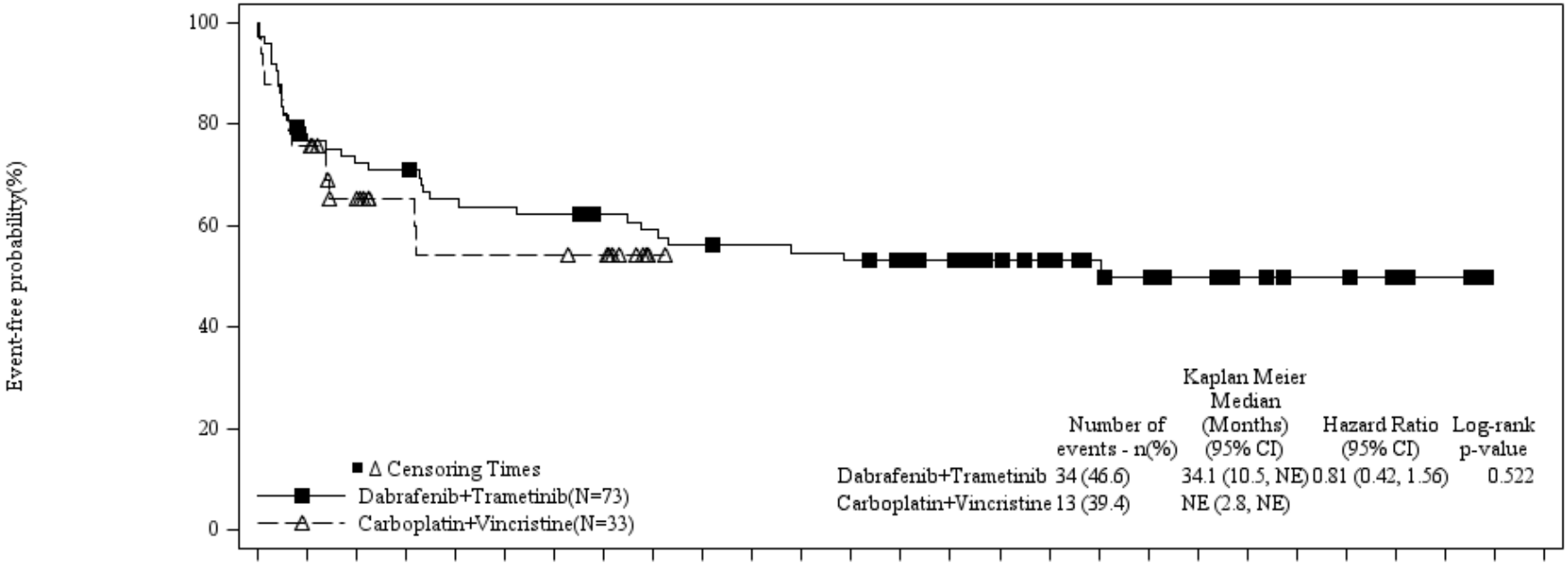
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	67	66	65	65	61	61	60	59	59	58	54	47	41	35	29	26	23	15	11	10	5	4	1	0
Carboplatin+Vincristine	33	30	23	17	15	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 16 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Respiratory thoracic and mediastinal disorders



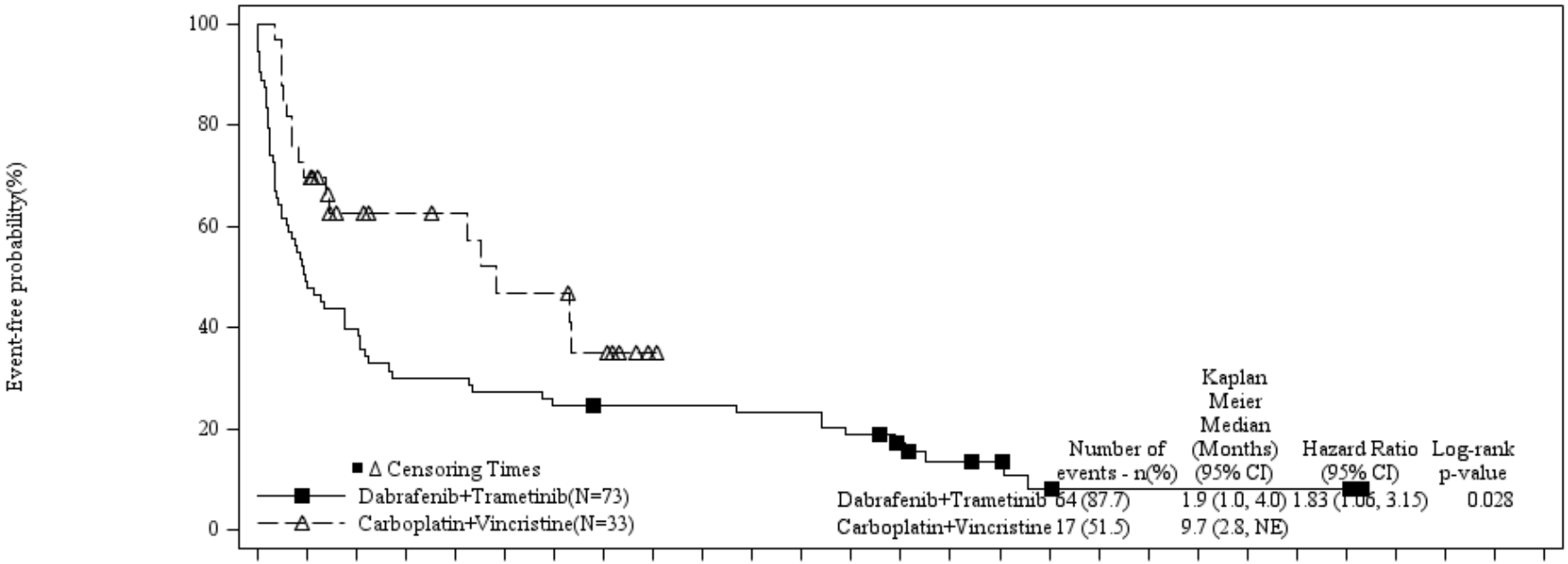
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	55	51	50	45	44	43	41	39	37	36	35	34	32	28	24	20	16	14	12	7	5	5	3	2	0	0
Carboplatin+Vincristine	33	25	17	12	10	10	10	9	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 17 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Skin and subcutaneous tissue disorders



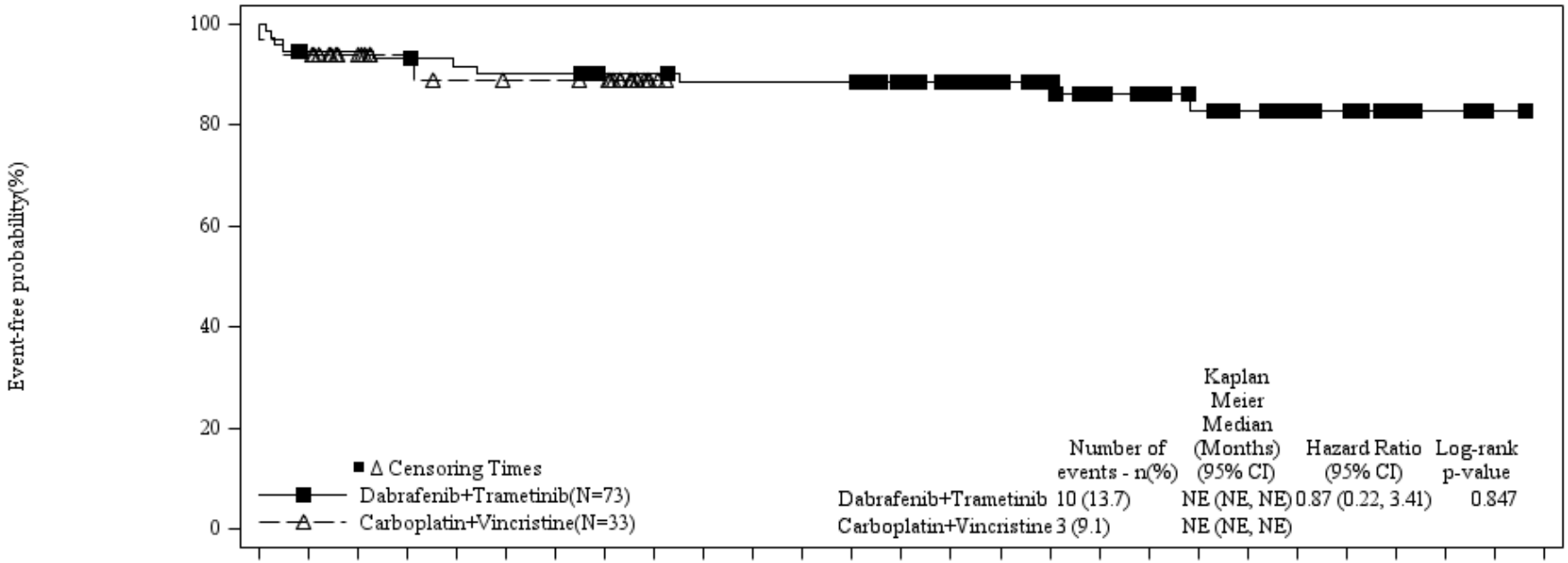
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	36	29	22	22	20	18	17	17	17	16	16	13	10	7	6	3	2	2	2	2	2	2	0	0	0	0
Carboplatin+Vincristine	33	23	15	13	12	9	9	6	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.2 (Page 18 of 18)
Any AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Vascular disorders



Number of patients still at risk

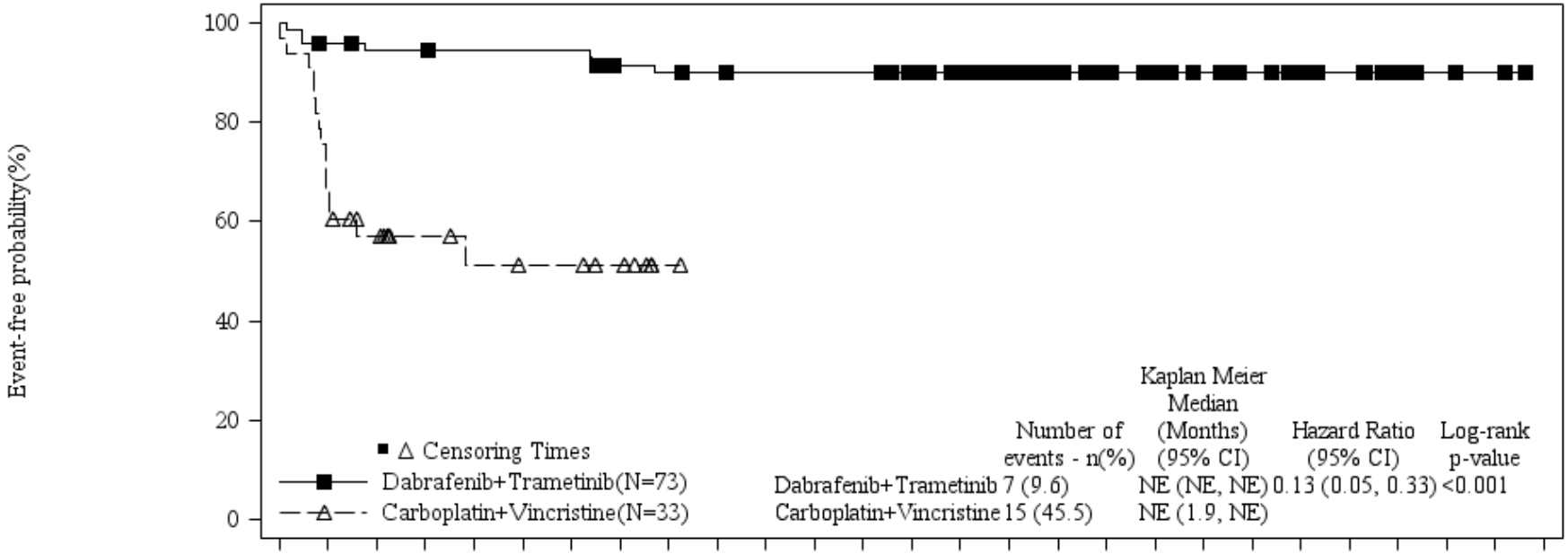
Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	67	66	64	63	63	60	60	58	58	58	58	53	46	41	38	31	28	24	17	13	11	6	3	1	0
Carboplatin+Vincristine	33	31	24	19	17	16	16	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.2. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) nach SOC

Figure 4-2.2 (Page 1 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Blood and lymphatic system disorders



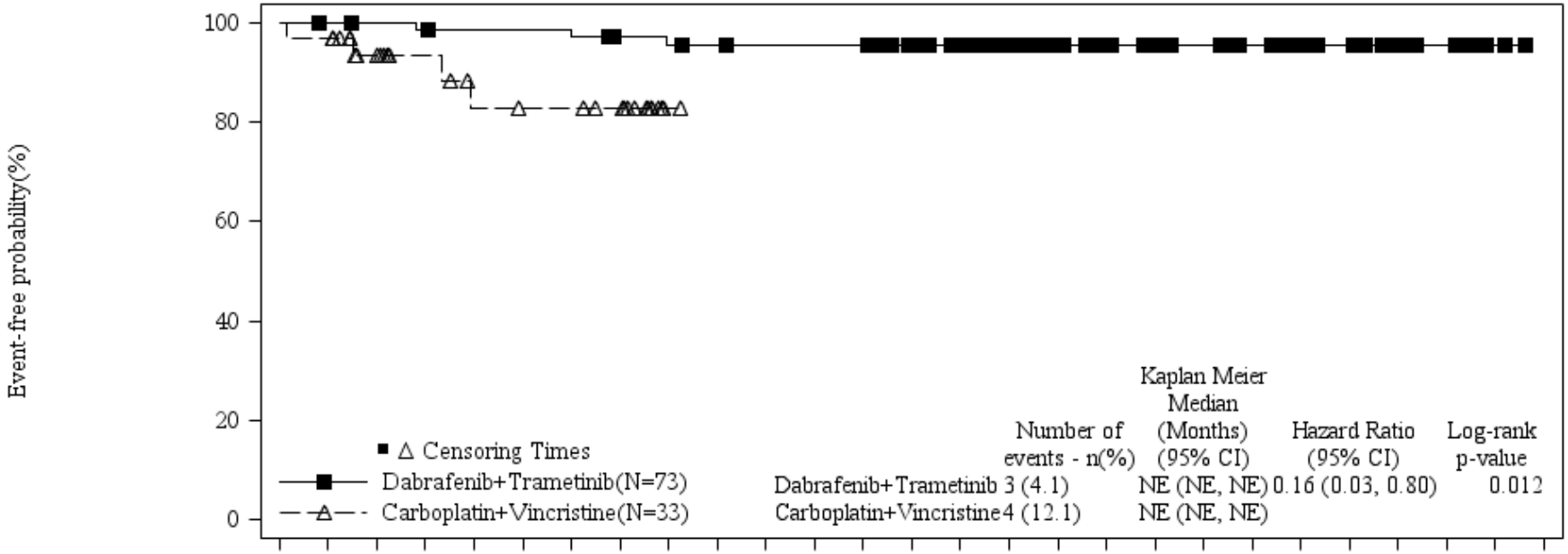
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	66	66	65	65	65	60	59	58	57	57	57	54	47	41	34	28	25	22	15	12	10	6	3	2	0
Carboplatin+Vincristine	33	22	16	11	9	8	8	6	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 2 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Gastrointestinal disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	3 (4.1)	NE (NE, NE)	0.16 (0.03, 0.80)	0.012
Carboplatin+Vincristine	4 (12.1)	NE (NE, NE)		

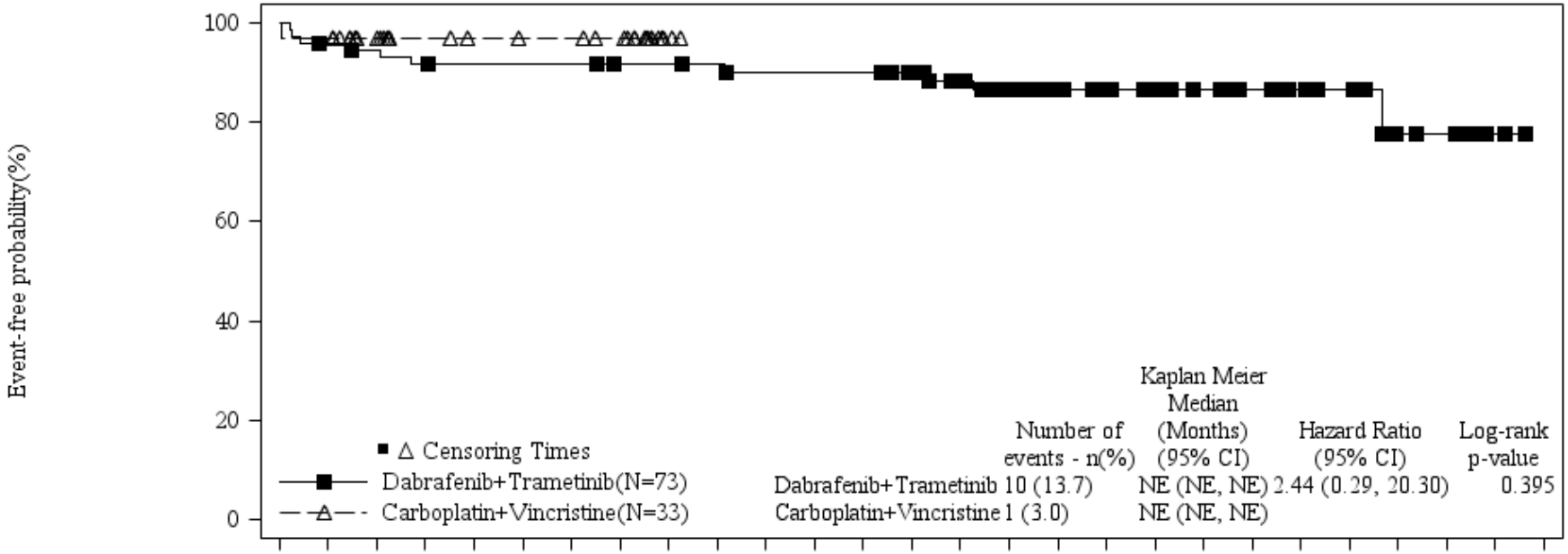
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	69	68	68	67	65	64	63	62	62	62	57	50	44	37	31	28	26	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	24	19	15	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 3 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: General disorders and administration site conditions



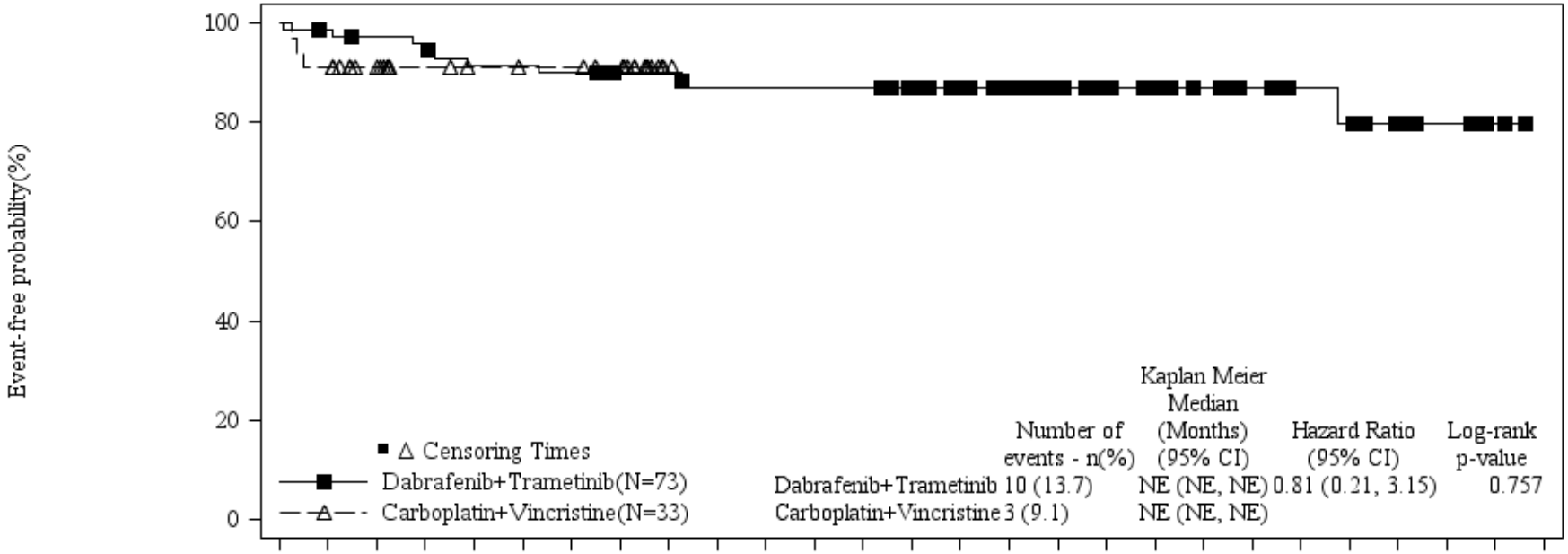
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	65	64	64	64	62	62	61	59	59	59	55	47	41	34	30	27	24	18	15	13	7	5	2	0
Carboplatin+Vincristine	33	32	25	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 4 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Infections and infestations



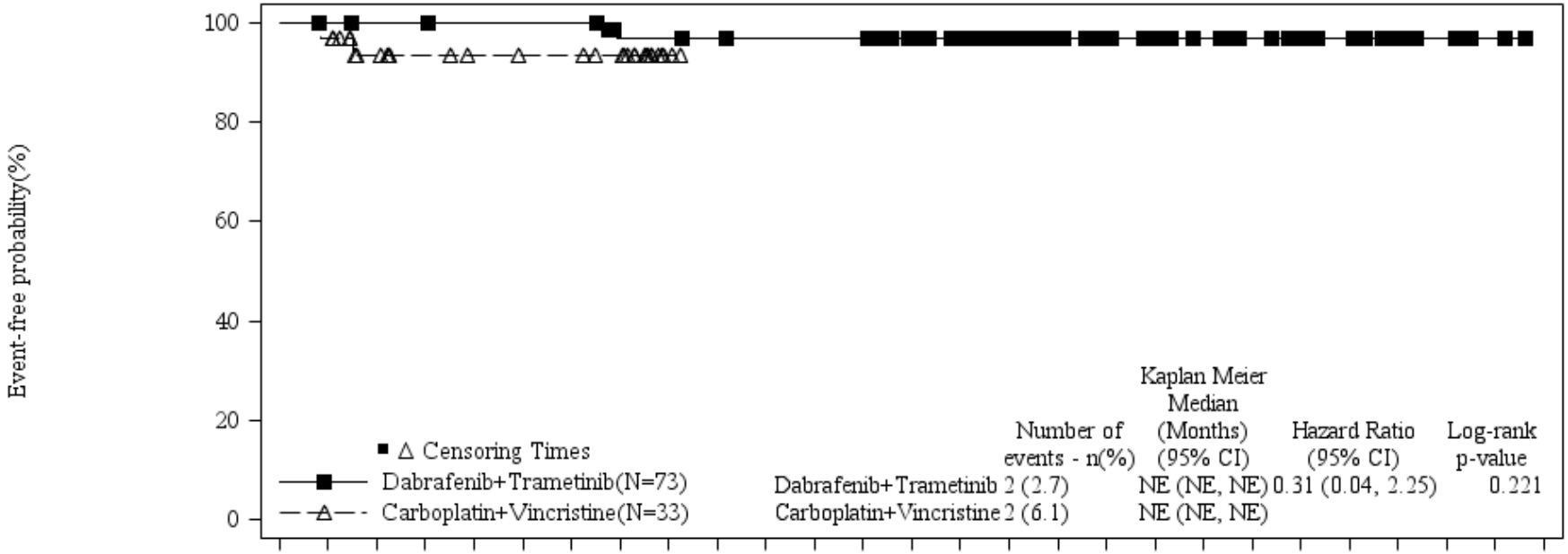
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	68	66	63	63	62	59	59	56	56	56	56	52	46	41	34	29	26	23	15	12	11	7	4	2	0
Carboplatin+Vincristine	33	30	24	18	16	15	15	13	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 5 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Injury poisoning and procedural complications



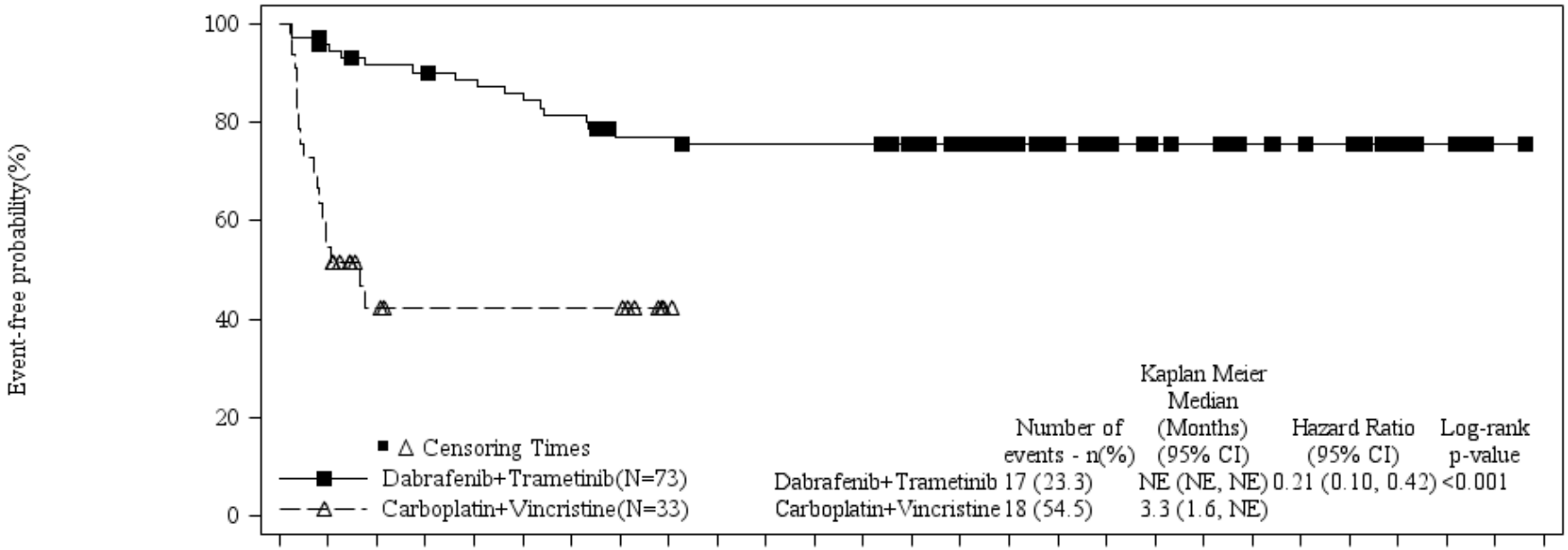
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	64	64	63	62	62	62	57	50	44	37	31	28	25	17	14	12	7	4	2	0
Carboplatin+Vincristine	33	32	24	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 6 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Investigations



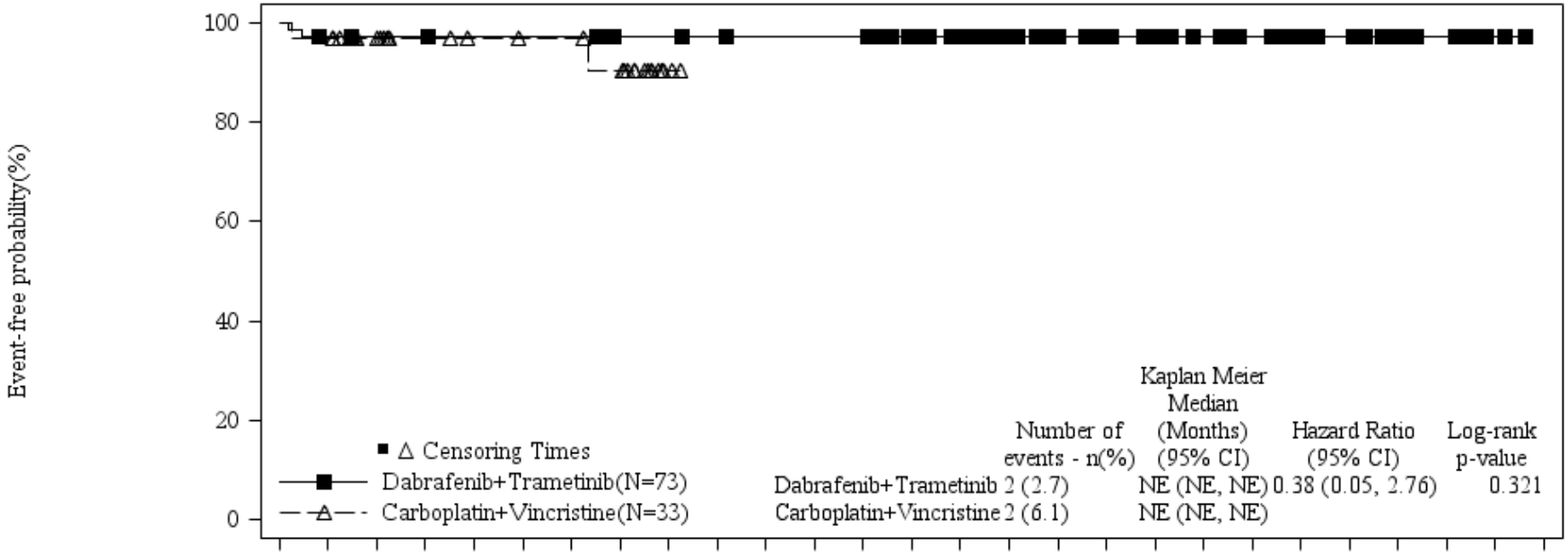
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	64	63	61	59	56	51	51	49	49	49	49	45	39	33	28	24	21	20	14	12	11	6	4	1	0
Carboplatin+Vincristine	33	18	9	7	7	7	7	7	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 7 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Metabolism and nutrition disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	2 (2.7)	NE (NE, NE)	0.38 (0.05, 2.76)	0.321
Carboplatin+Vincristine	2 (6.1)	NE (NE, NE)		

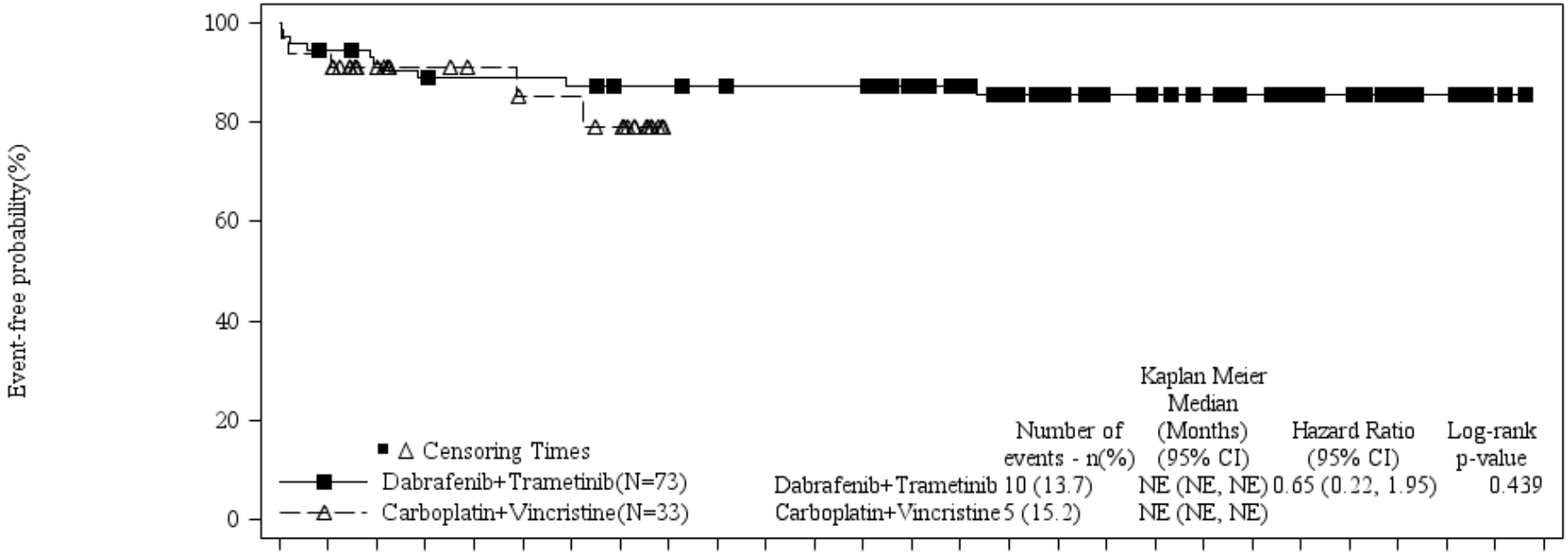
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	68	68	67	67	67	64	64	63	62	62	62	57	50	44	38	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	25	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 8 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Nervous system disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	10 (13.7)	NE (NE, NE)	0.65 (0.22, 1.95)	0.439
Carboplatin+Vincristine	5 (15.2)	NE (NE, NE)		

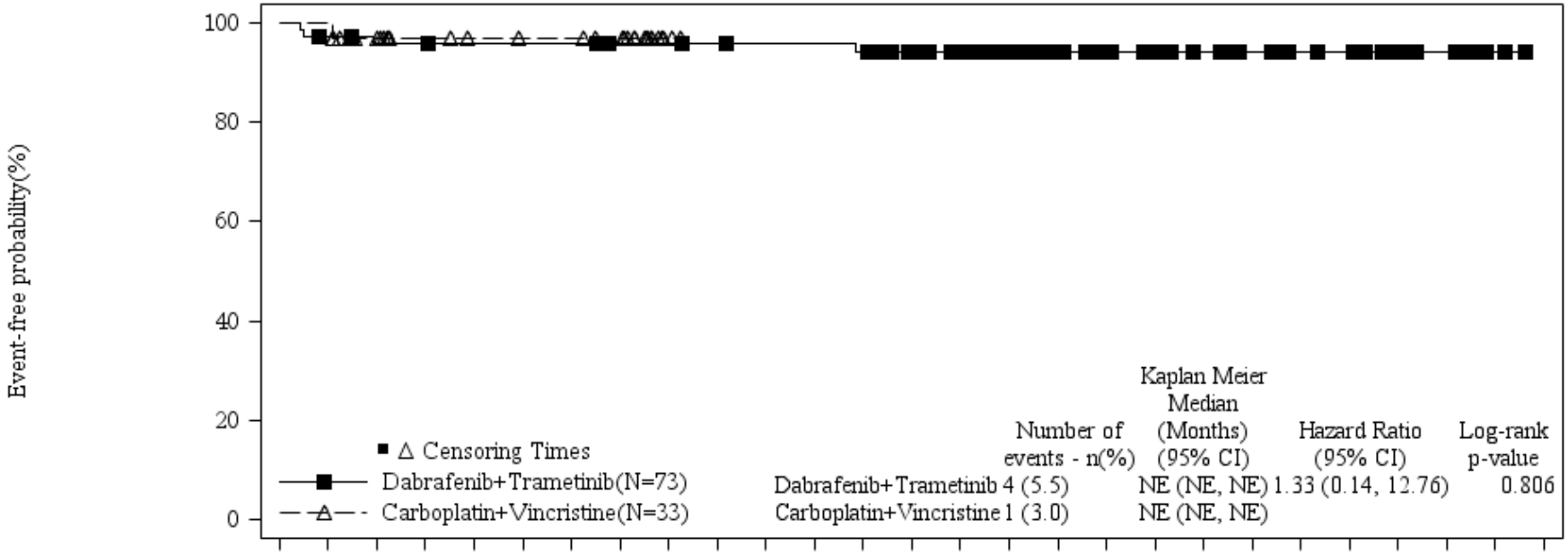
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	65	63	62	62	61	59	59	58	57	57	57	52	45	39	34	30	28	26	18	14	12	7	5	2	0
Carboplatin+Vincristine	33	31	23	18	16	14	14	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 9 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Respiratory thoracic and mediastinal disorders



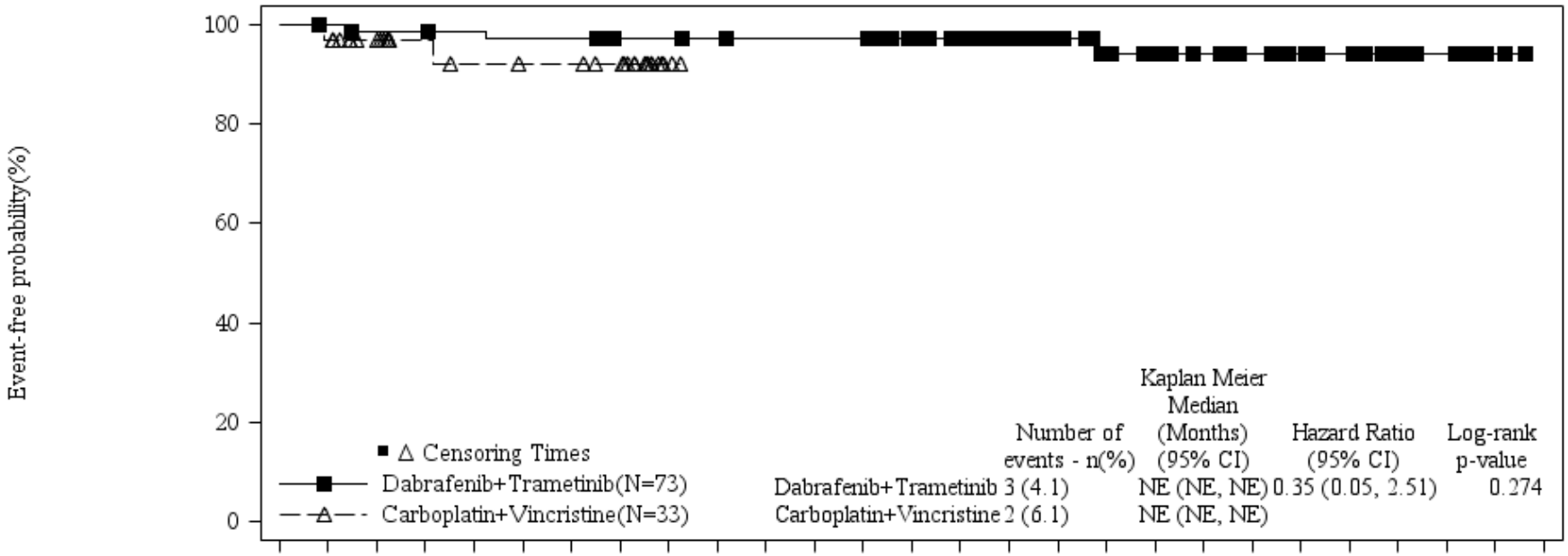
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	67	66	66	66	64	64	63	62	62	61	56	49	43	36	30	27	24	17	14	13	8	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 10 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Skin and subcutaneous tissue disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	3 (4.1)	NE (NE, NE)	0.35 (0.05, 2.51)	0.274
Carboplatin+Vincristine	2 (6.1)	NE (NE, NE)		

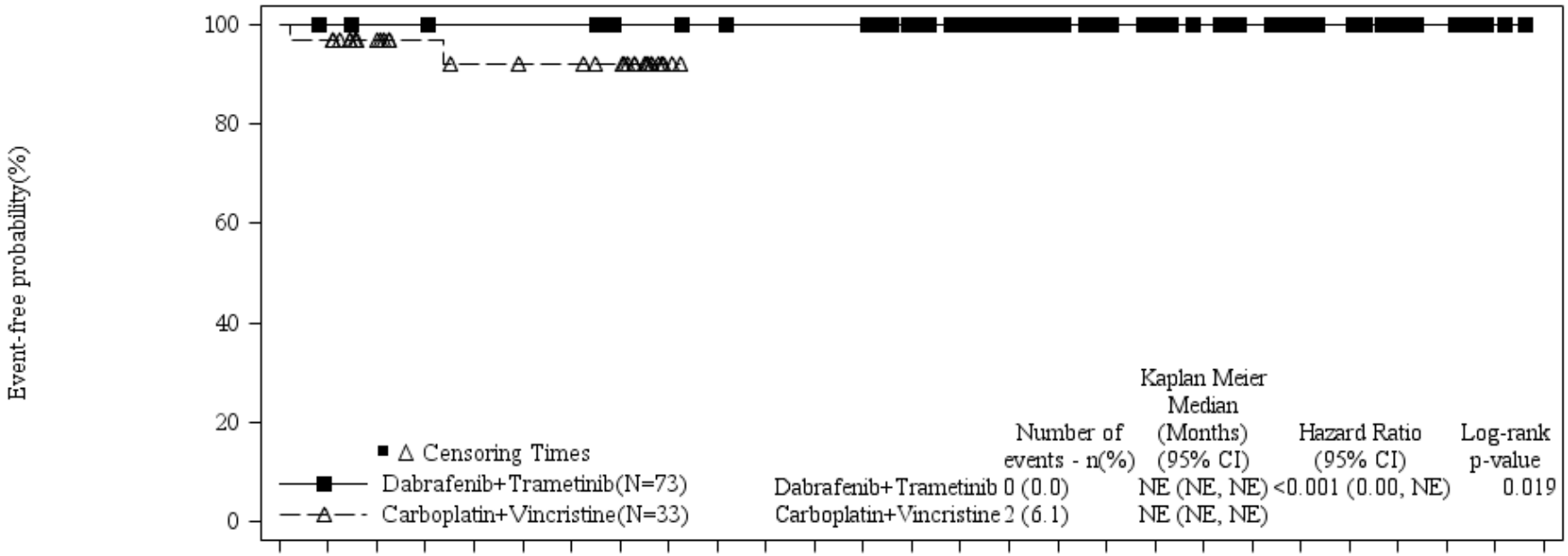
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	69	69	68	67	67	64	64	63	62	62	62	57	50	44	37	30	27	24	17	14	12	7	5	2	0
Carboplatin+Vincristine	33	32	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.2 (Page 11 of 11)
Grade >= 3 AE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Vascular disorders



Number of patients still at risk

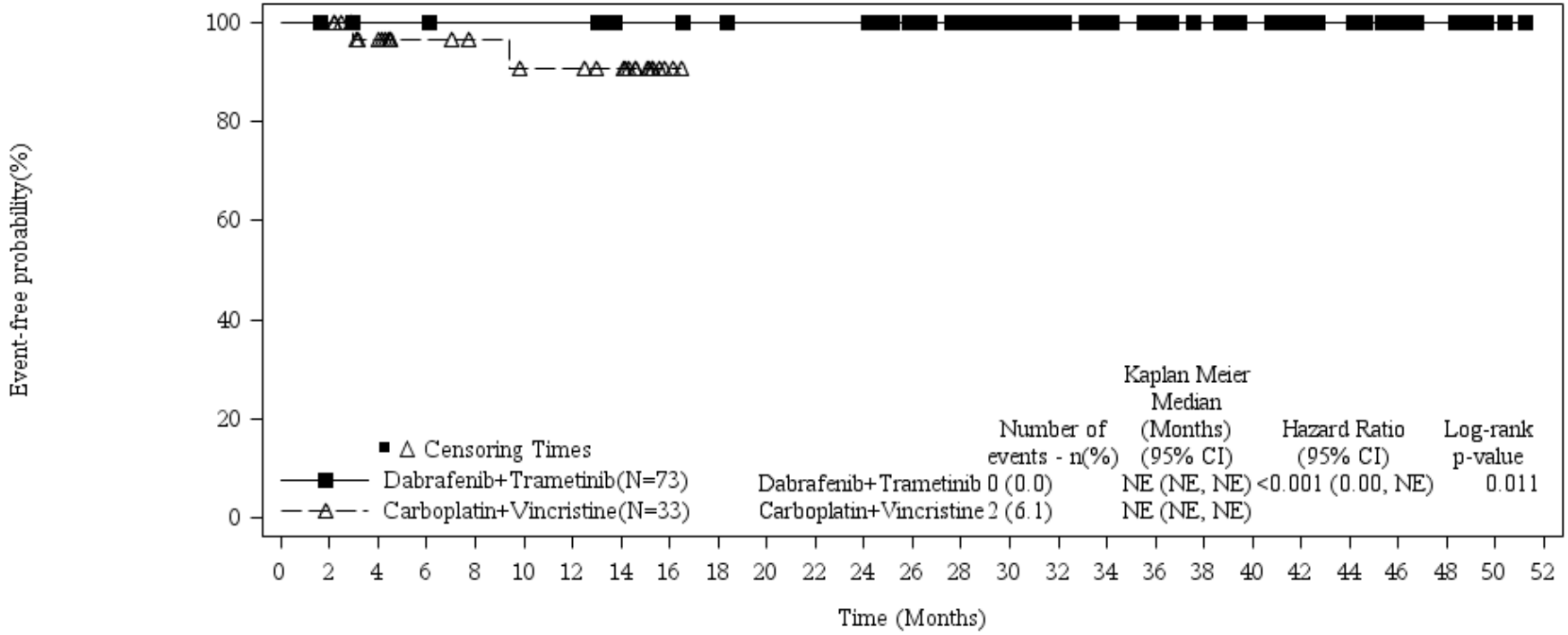
Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	25	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.3. Schwerwiegende unerwünschte Ereignisse nach SOC

Figure 4-3.2 (Page 1 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Blood and lymphatic system disorders



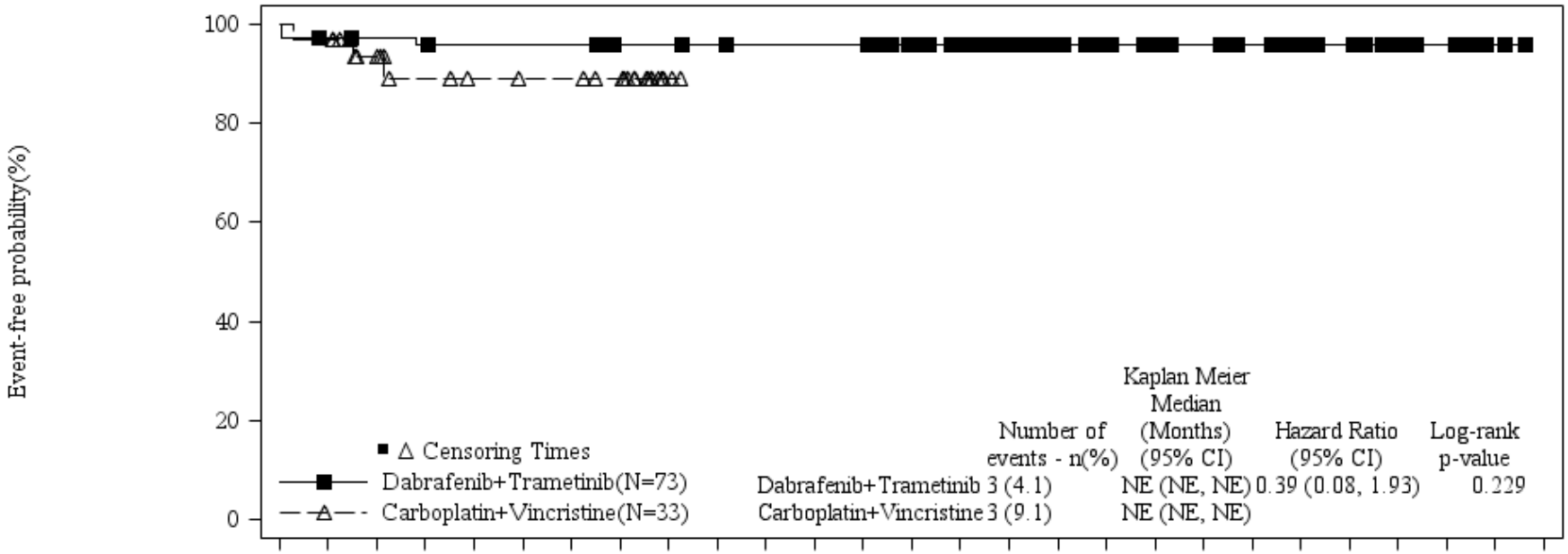
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	33	25	19	17	15	15	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 2 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Gastrointestinal disorders



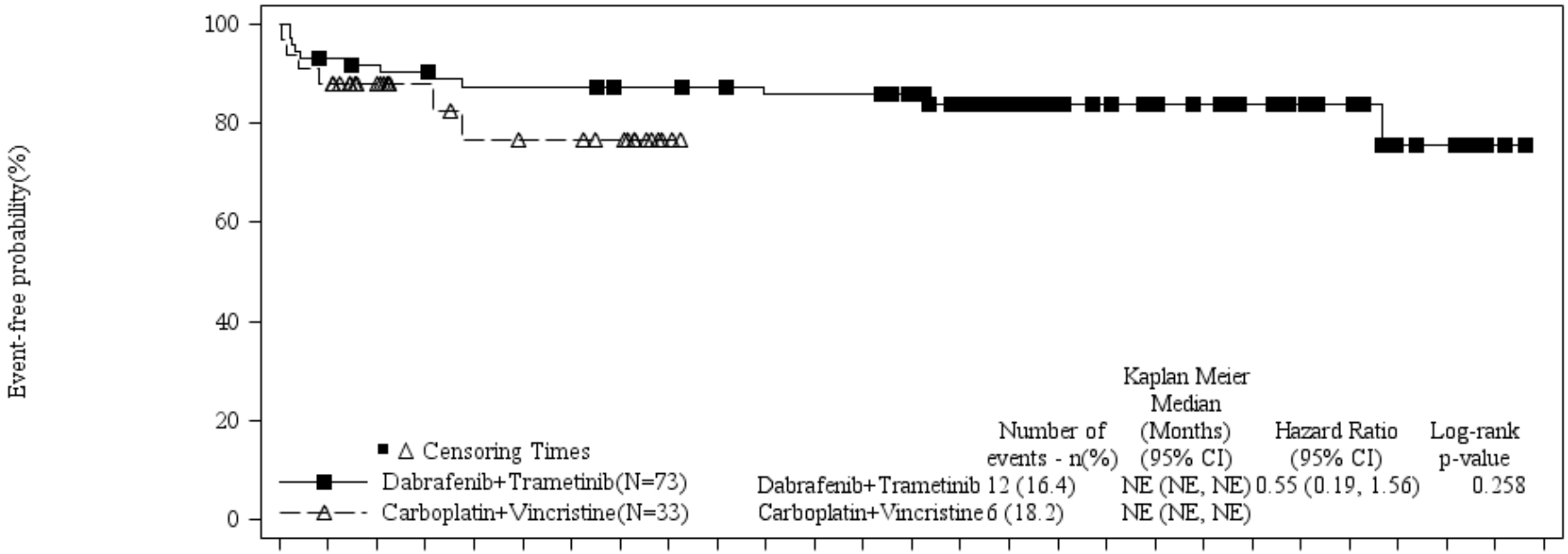
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	68	67	66	66	66	63	63	62	61	61	61	56	49	43	36	31	28	26	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	24	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 3 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: General disorders and administration site conditions



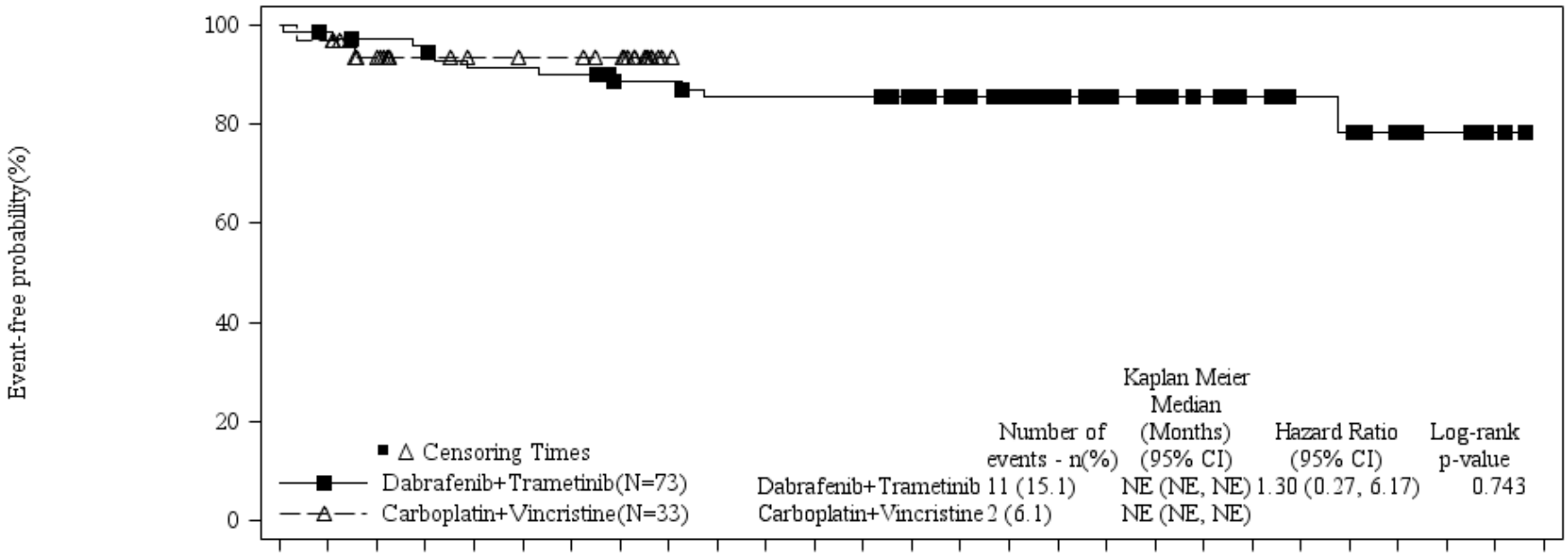
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	66	64	63	60	60	60	58	58	57	55	55	55	51	43	37	30	27	24	22	16	14	12	7	5	2	0
Carboplatin+Vincristine	33	29	22	16	13	12	12	10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 4 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Infections and infestations



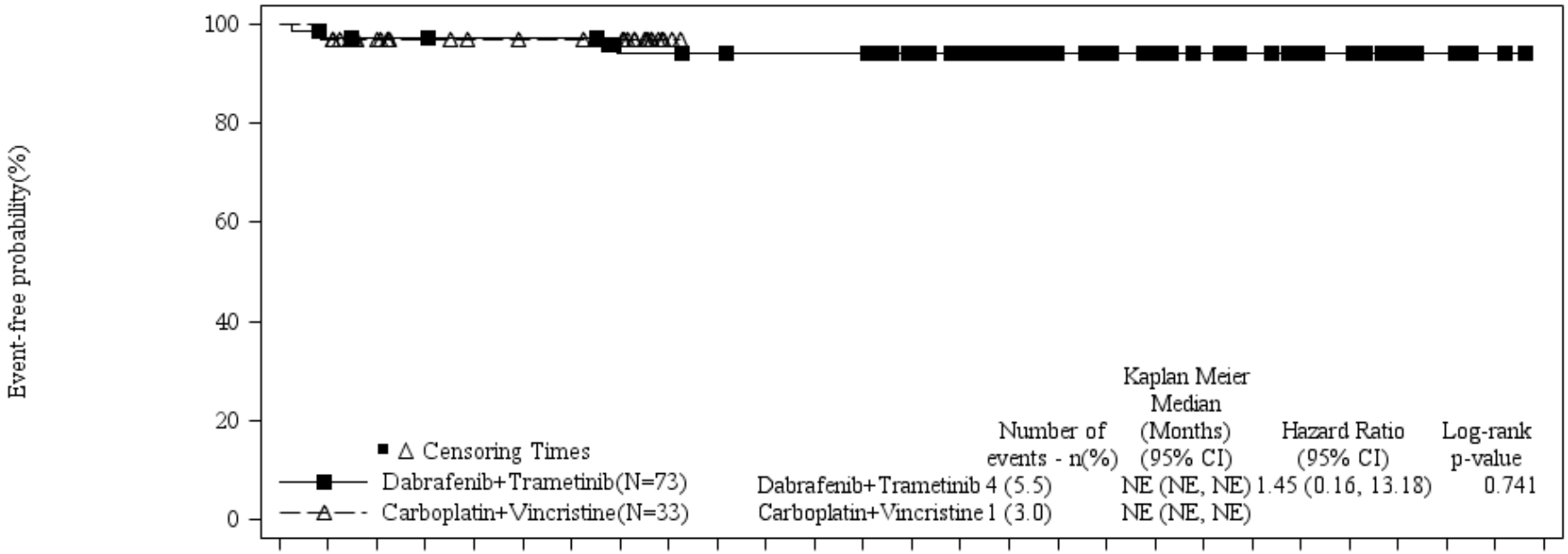
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	68	66	63	63	62	58	58	55	55	55	55	51	45	40	33	28	25	22	15	12	11	7	4	2	0
Carboplatin+Vincristine	33	32	24	18	16	15	15	13	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 5 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Injury poisoning and procedural complications



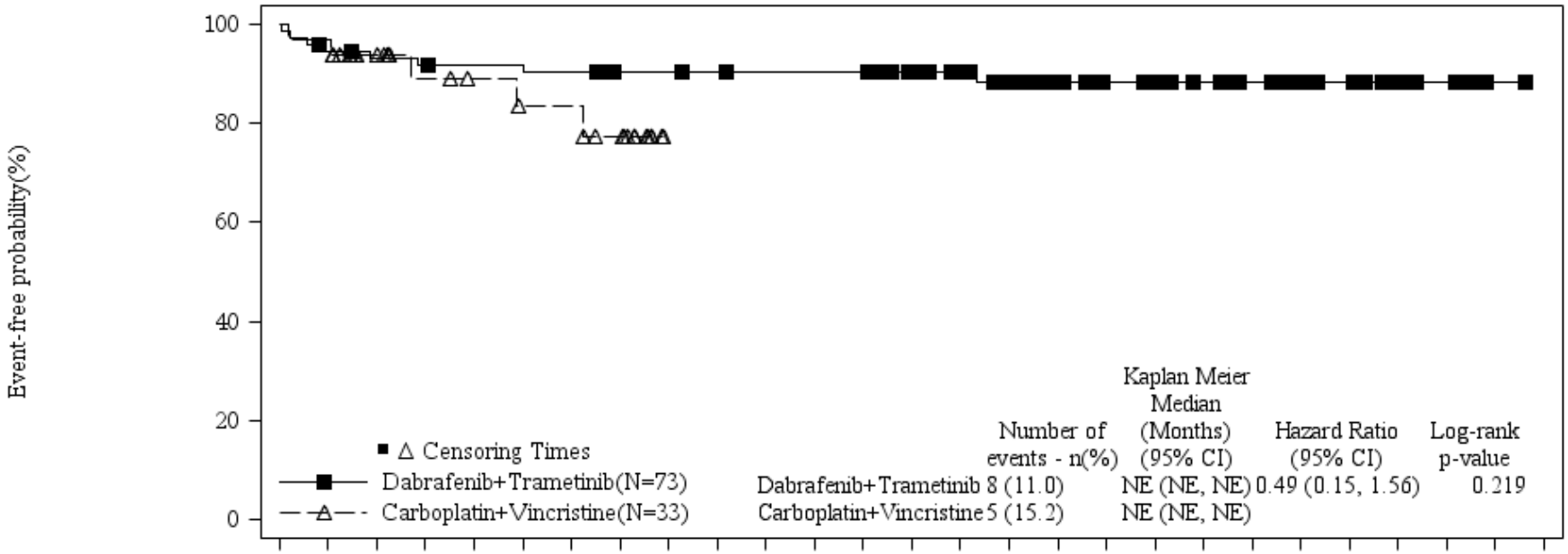
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	68	68	67	67	67	62	62	61	60	60	60	55	48	42	35	31	28	25	17	14	12	7	4	2	0
Carboplatin+Vincristine	33	32	25	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 6 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Nervous system disorders



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	8 (11.0)	NE (NE, NE)	0.49 (0.15, 1.56)	0.219
Carboplatin+Vincristine	5 (15.2)	NE (NE, NE)		

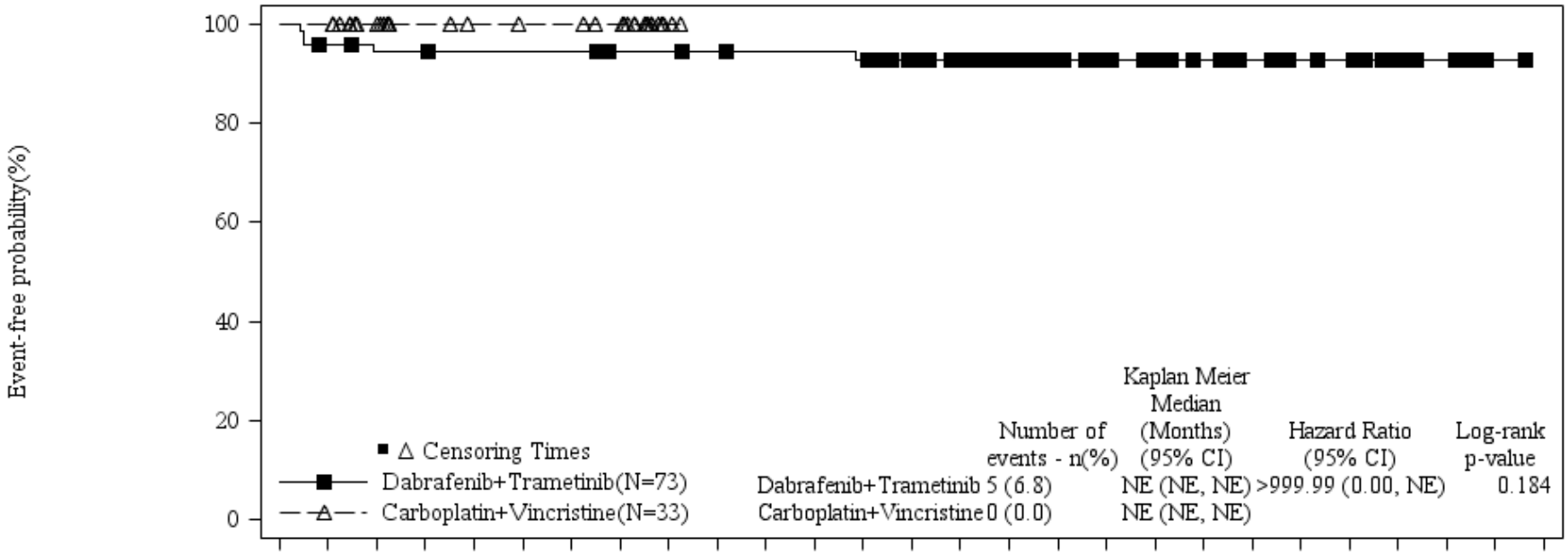
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	66	65	64	64	63	60	60	59	58	58	58	53	46	40	33	29	27	24	17	13	11	6	4	1	0
Carboplatin+Vincristine	33	32	24	18	16	14	14	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-3.2 (Page 7 of 7)
SAE by SOC: Kaplan Meier plot of time to first event
Safety Set - L

Time to first SOC: Respiratory thoracic and mediastinal disorders



Number of patients still at risk

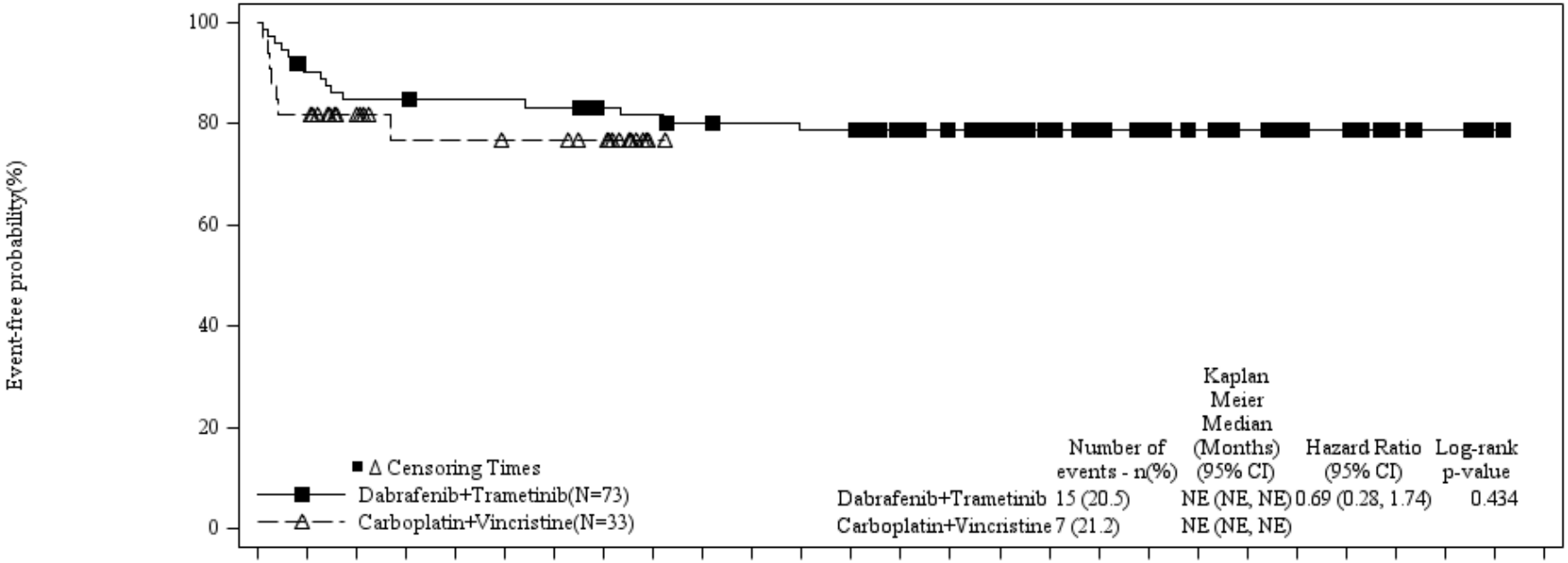
Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	66	66	65	65	65	63	63	62	61	61	60	55	48	42	35	29	26	23	16	13	12	7	4	1	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.4. Unerwünschte Ereignisse nach PT

Figure 4-1.3 (Page 1 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Abdominal pain



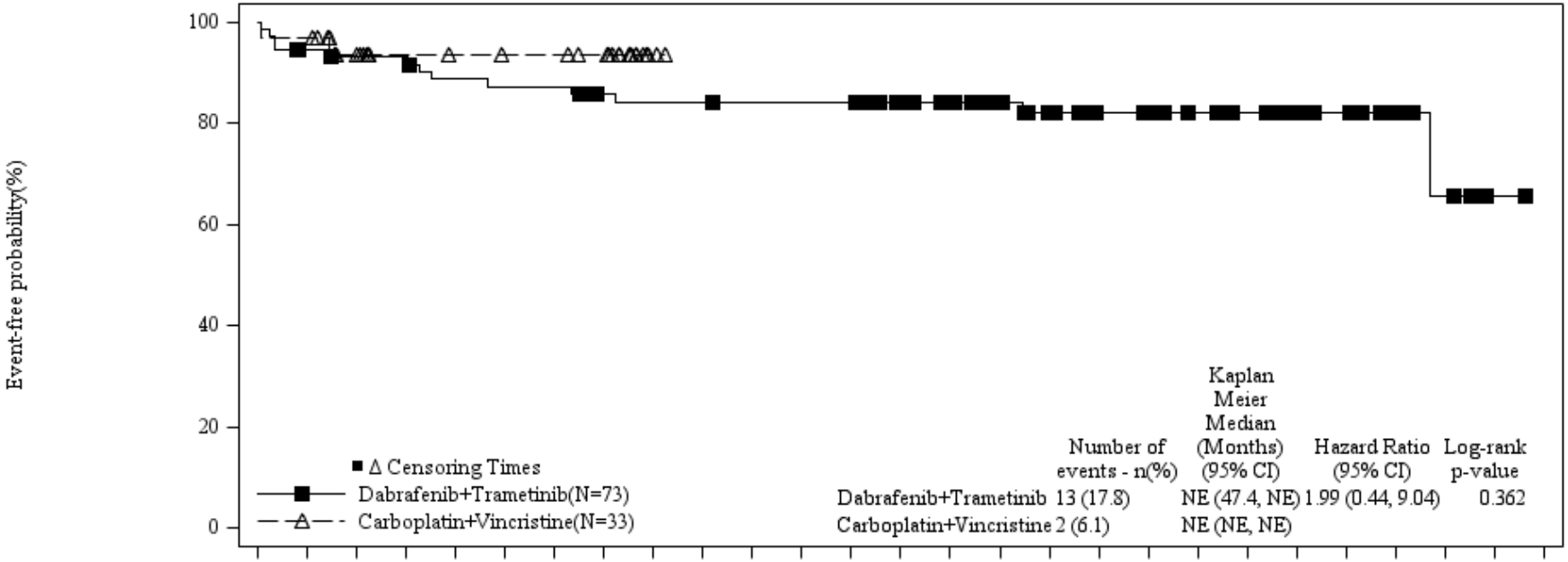
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	64	60	60	59	59	58	55	54	52	51	50	50	45	40	38	32	27	24	21	14	11	10	5	3	1	0
Carboplatin+Vincristine	33	27	20	15	15	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 2 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Abdominal pain upper



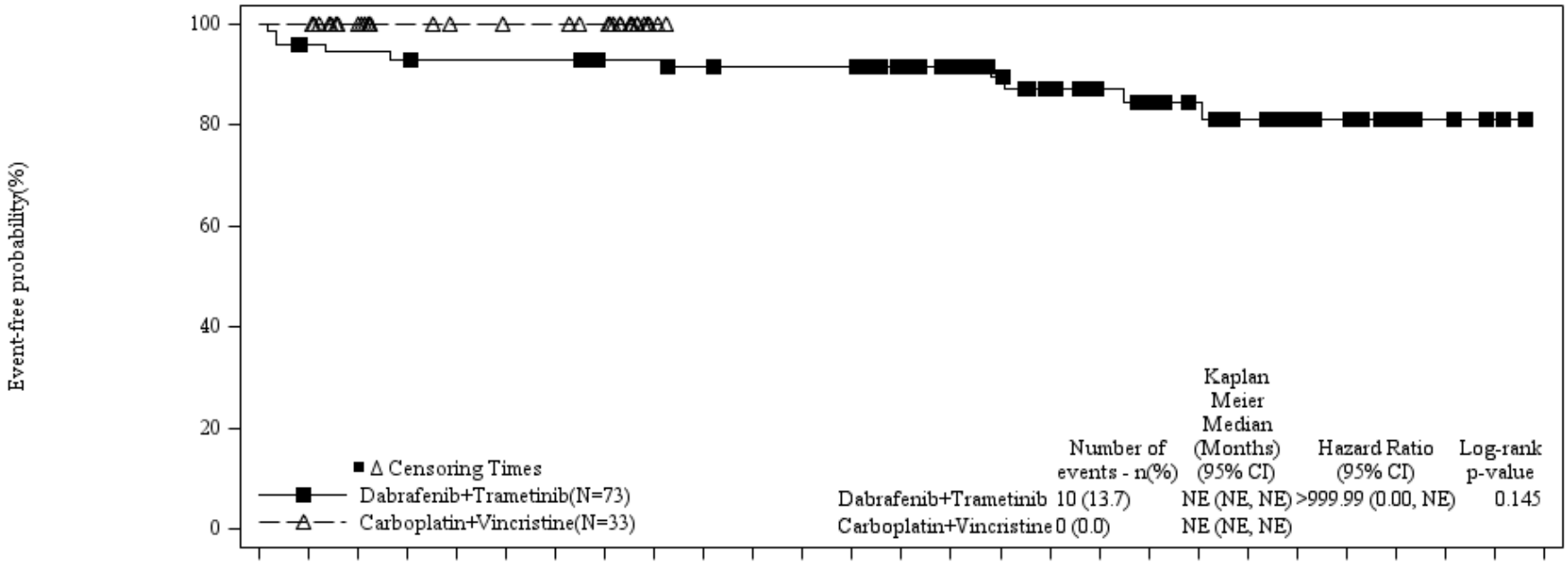
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	65	65	61	60	60	56	55	55	54	54	54	49	43	38	33	28	27	24	18	14	12	7	4	1	0
Carboplatin+Vincristine	33	32	25	19	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 3 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Acne



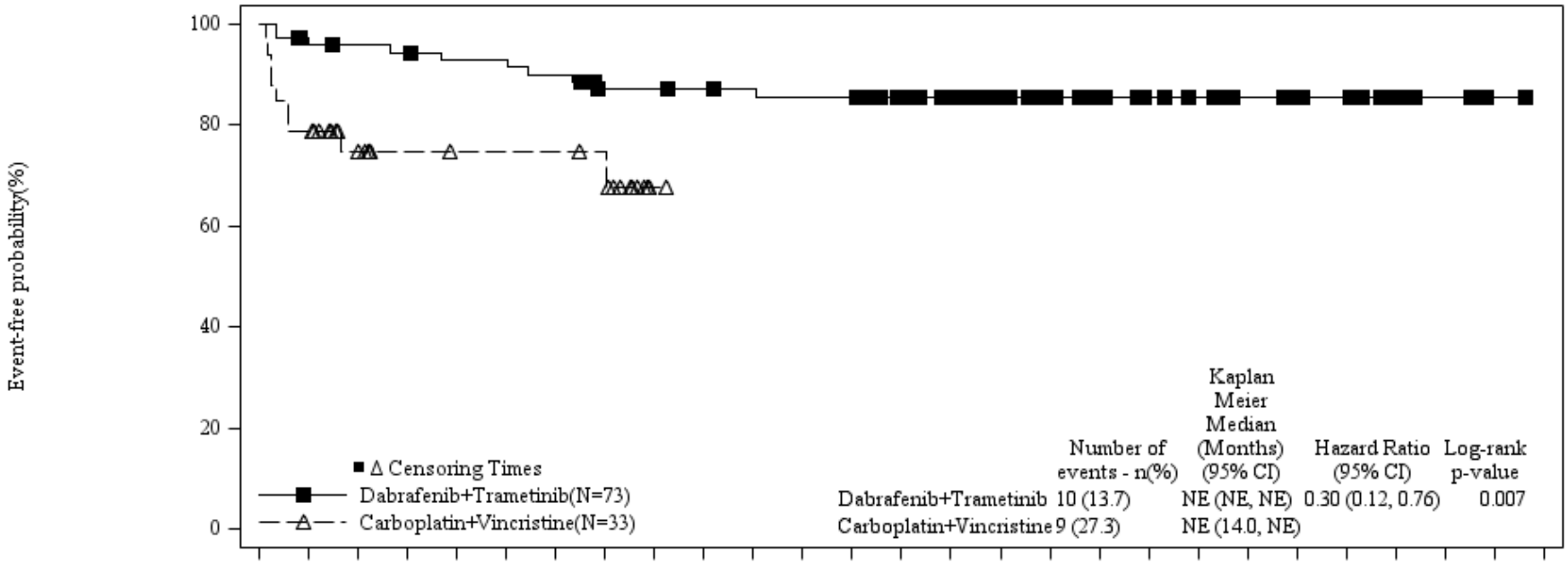
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	66	65	65	65	62	62	60	59	59	59	55	49	43	37	31	28	25	18	14	12	7	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 4 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Alanine aminotransferase increased



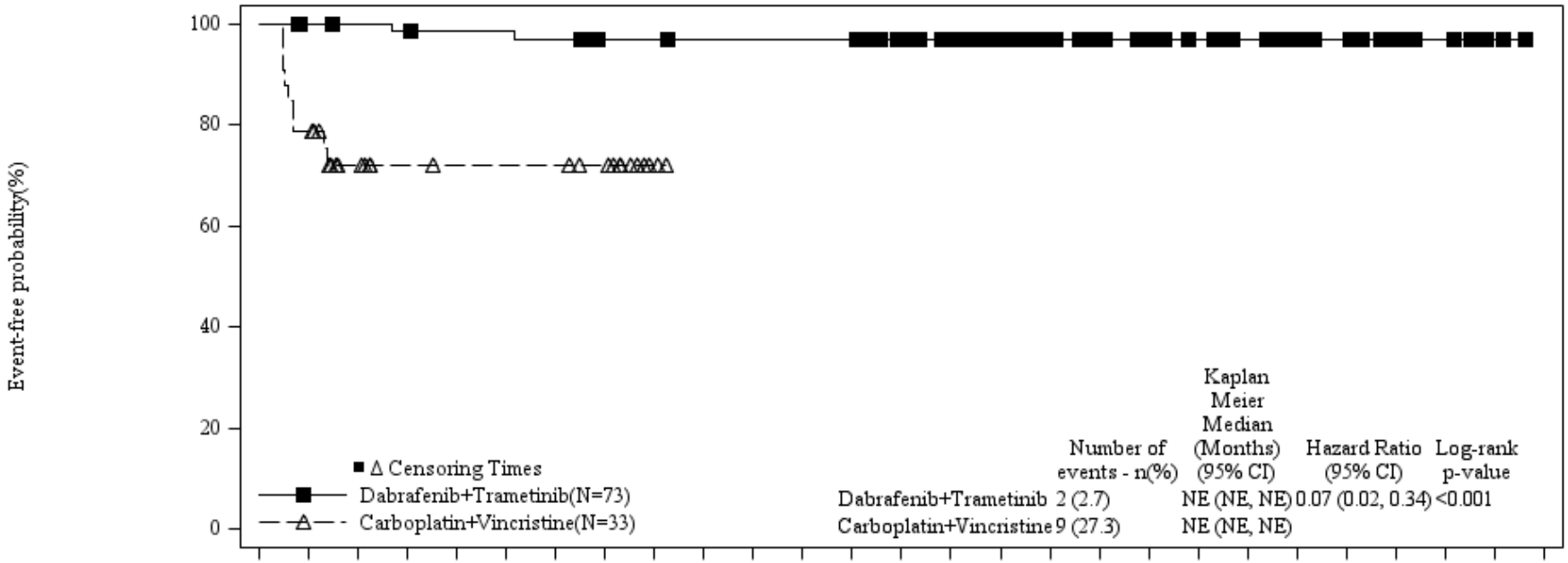
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	66	64	64	62	57	57	56	55	54	54	49	44	38	32	26	23	21	14	12	11	6	3	1	0
Carboplatin+Vincristine	33	26	18	13	12	12	12	11	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 5 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Alopecia



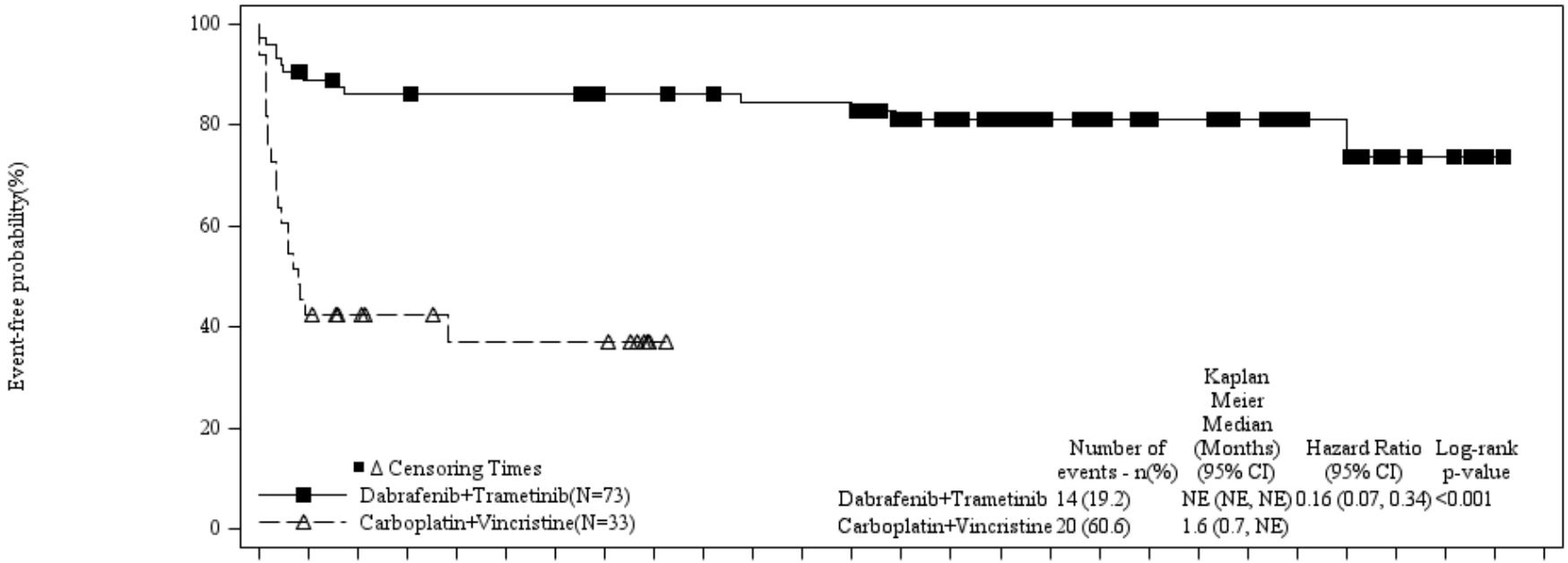
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	69	68	68	67	64	64	63	63	63	63	58	51	45	38	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	26	17	13	12	12	12	10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 6 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Anaemia



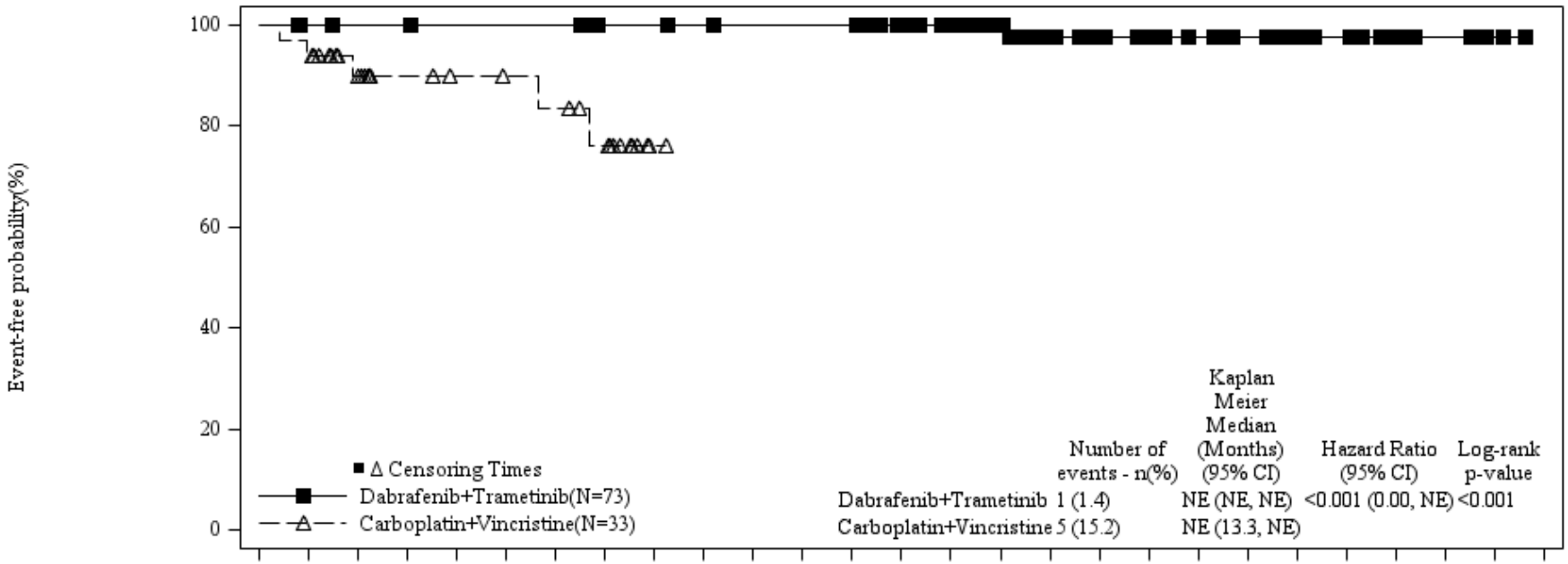
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	63	60	60	59	59	59	56	56	55	53	53	52	46	42	37	31	27	24	23	16	12	10	5	4	1	0
Carboplatin+Vincristine	33	14	11	9	7	7	7	7	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 7 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Anxiety



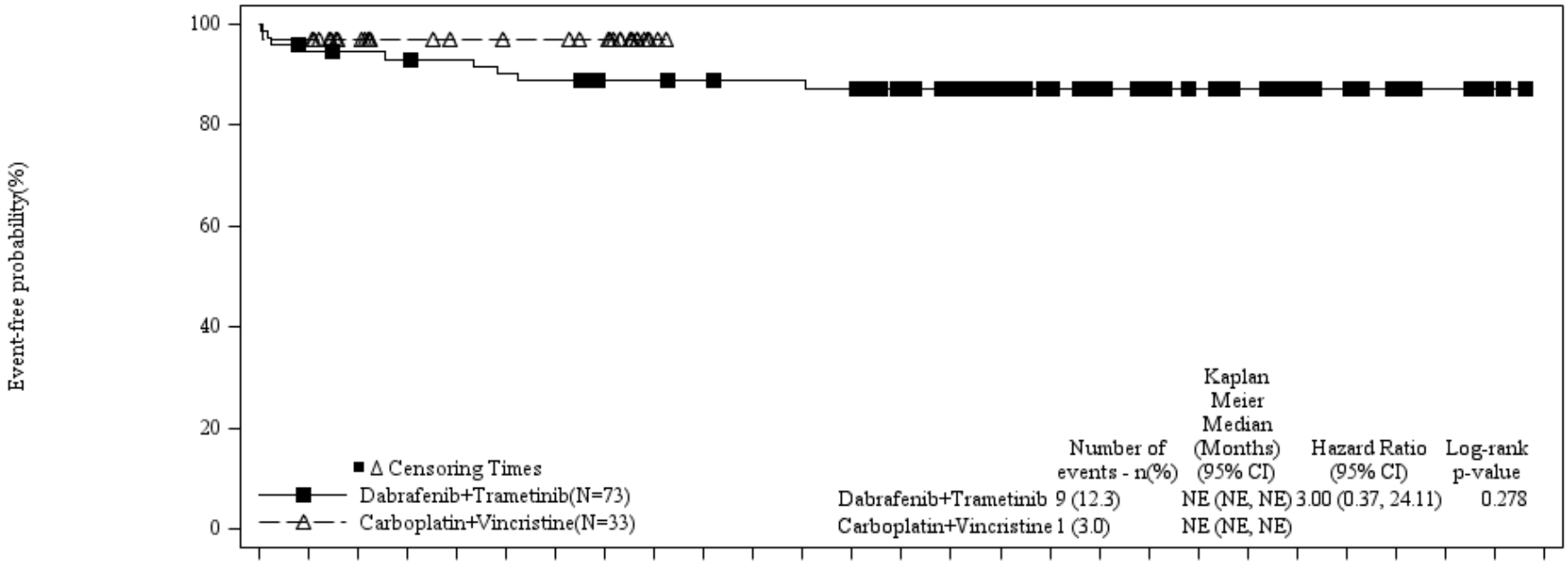
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	38	32	29	26	18	14	12	7	4	2	0
Carboplatin+Vincristine	33	31	23	17	15	14	13	10	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 8 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Arthralgia



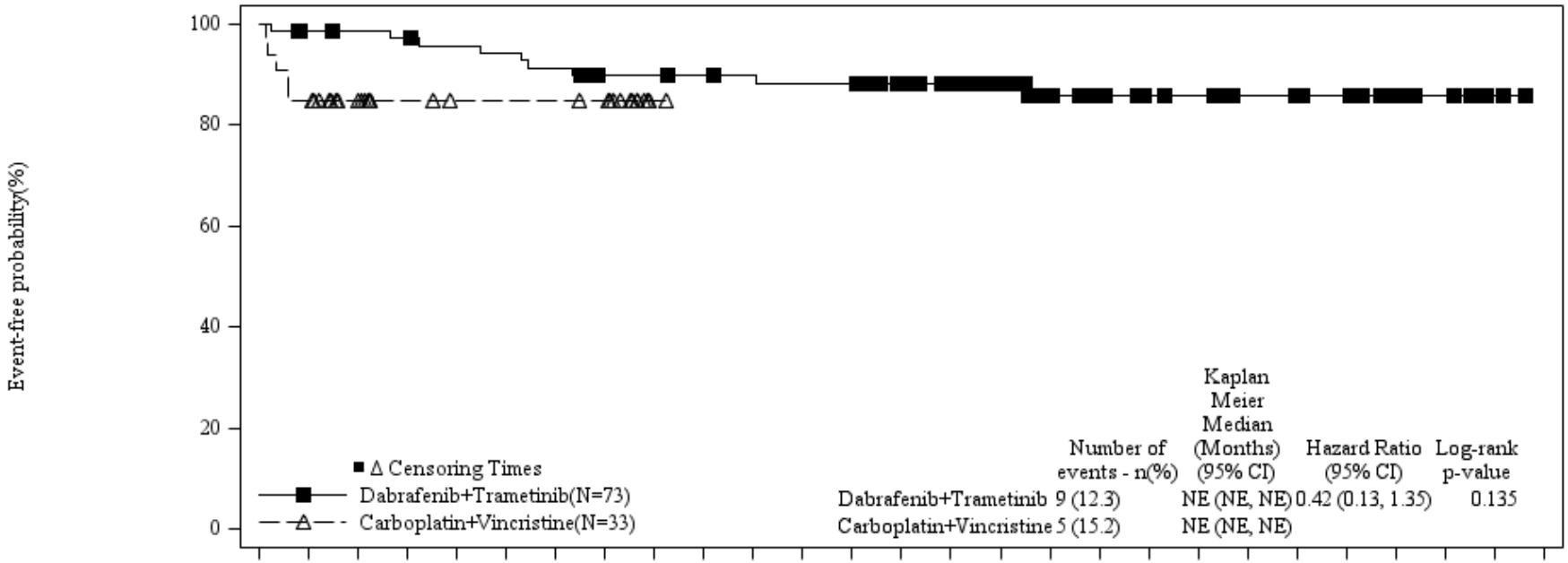
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	66	65	63	62	59	59	58	57	57	56	51	45	40	34	30	27	24	17	13	11	7	4	2	0
Carboplatin+Vincristine	33	32	25	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 9 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Aspartate aminotransferase increased



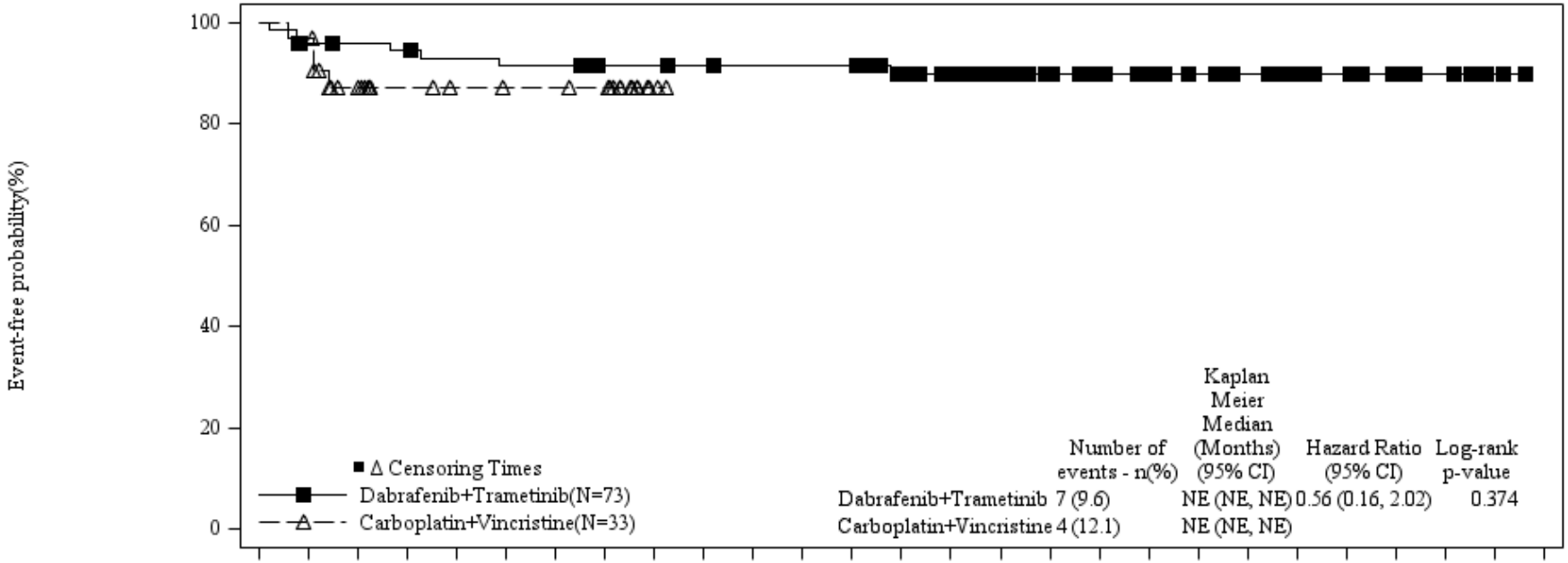
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	69	68	66	65	63	59	59	58	57	56	56	51	45	39	31	26	23	22	14	13	12	8	5	2	0
Carboplatin+Vincristine	33	28	21	15	13	13	13	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 10 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Back pain



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	7 (9.6)	NE (NE, NE)	0.56 (0.16, 2.02)	0.374
Carboplatin+Vincristine	4 (12.1)	NE (NE, NE)		

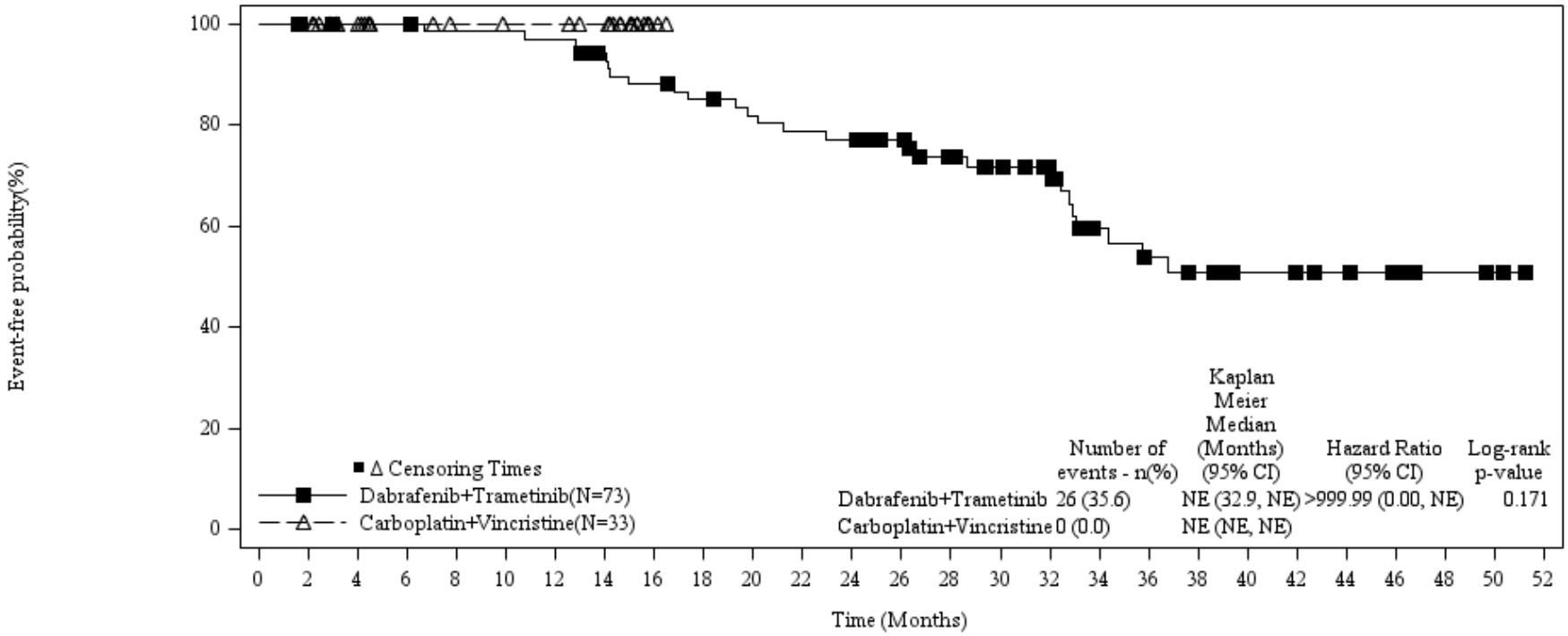
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	66	64	63	63	60	60	59	58	58	58	52	45	39	33	29	26	23	17	14	12	8	5	2	0
Carboplatin+Vincristine	33	32	23	17	15	14	14	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 11 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: COVID-19



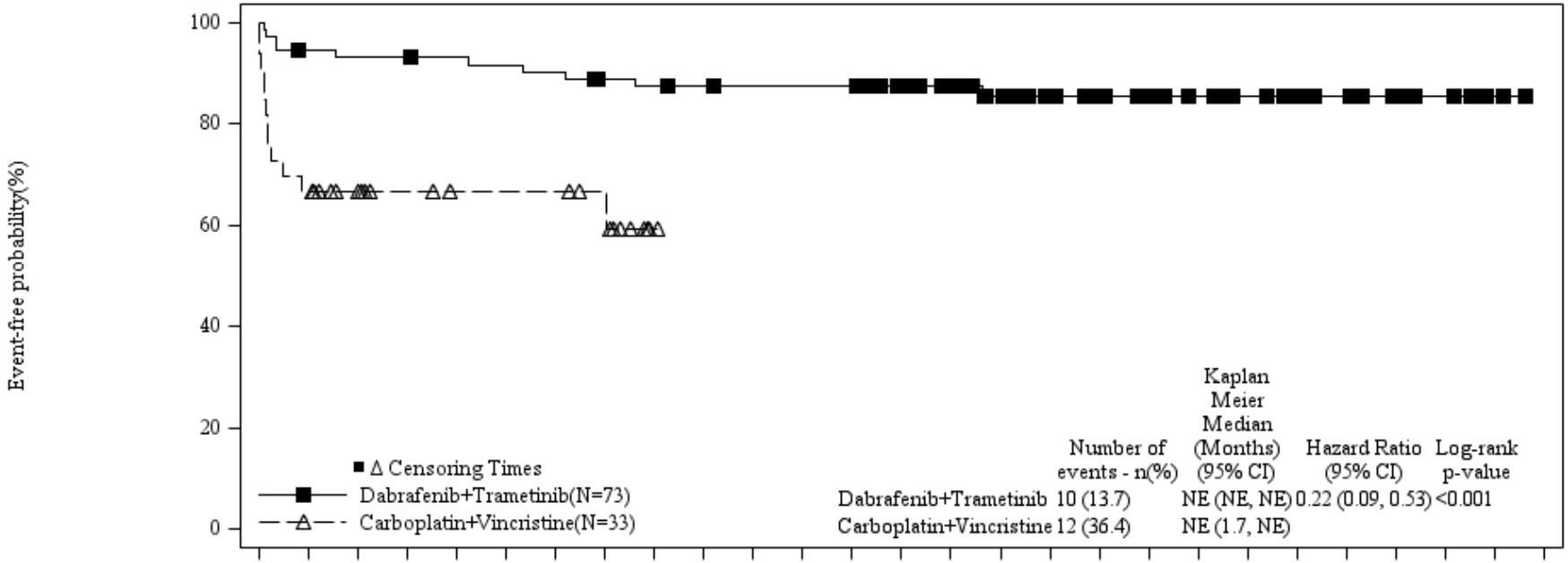
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	68	68	67	62	58	55	52	50	49	45	39	35	30	21	18	16	9	8	7	5	3	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 12 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Constipation



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	10 (13.7)	NE (NE, NE)	0.22 (0.09, 0.53)	<0.001
Carboplatin+Vincristine	12 (36.4)	NE (1.7, NE)		

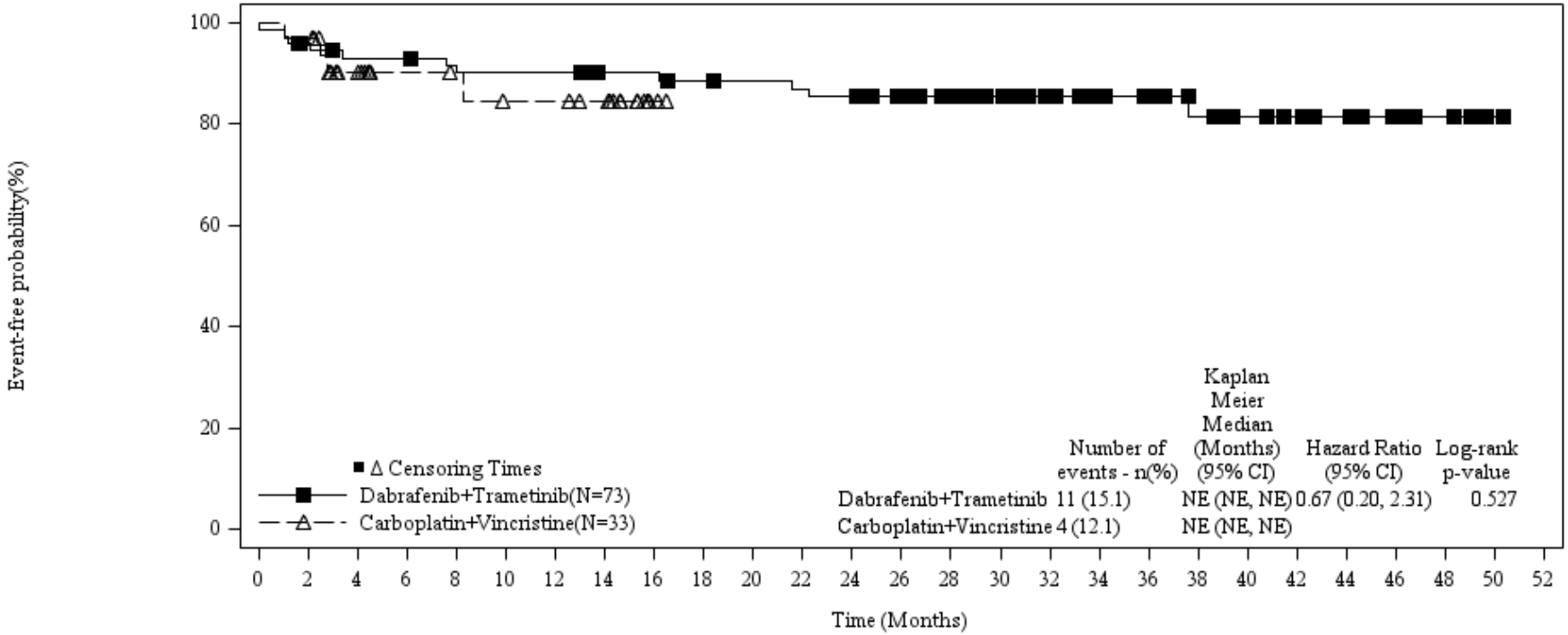
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	67	66	65	64	61	60	59	58	58	58	54	47	41	35	31	28	25	17	14	12	8	5	2	0
Carboplatin+Vincristine	33	22	17	13	11	11	11	9	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 13 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Cough



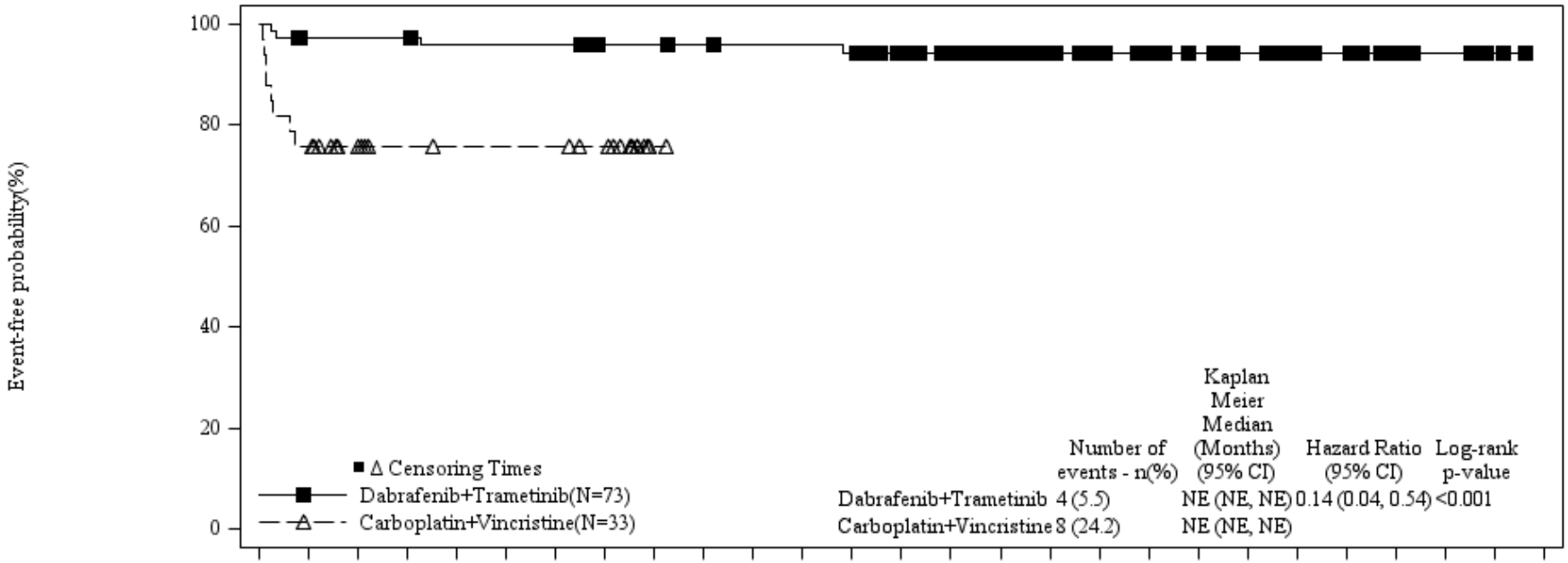
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	65	65	62	62	62	59	59	57	56	55	54	50	43	38	32	26	24	20	13	11	9	6	4	1	0
Carboplatin+Vincristine	33	32	23	17	16	14	14	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 14 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Decreased appetite



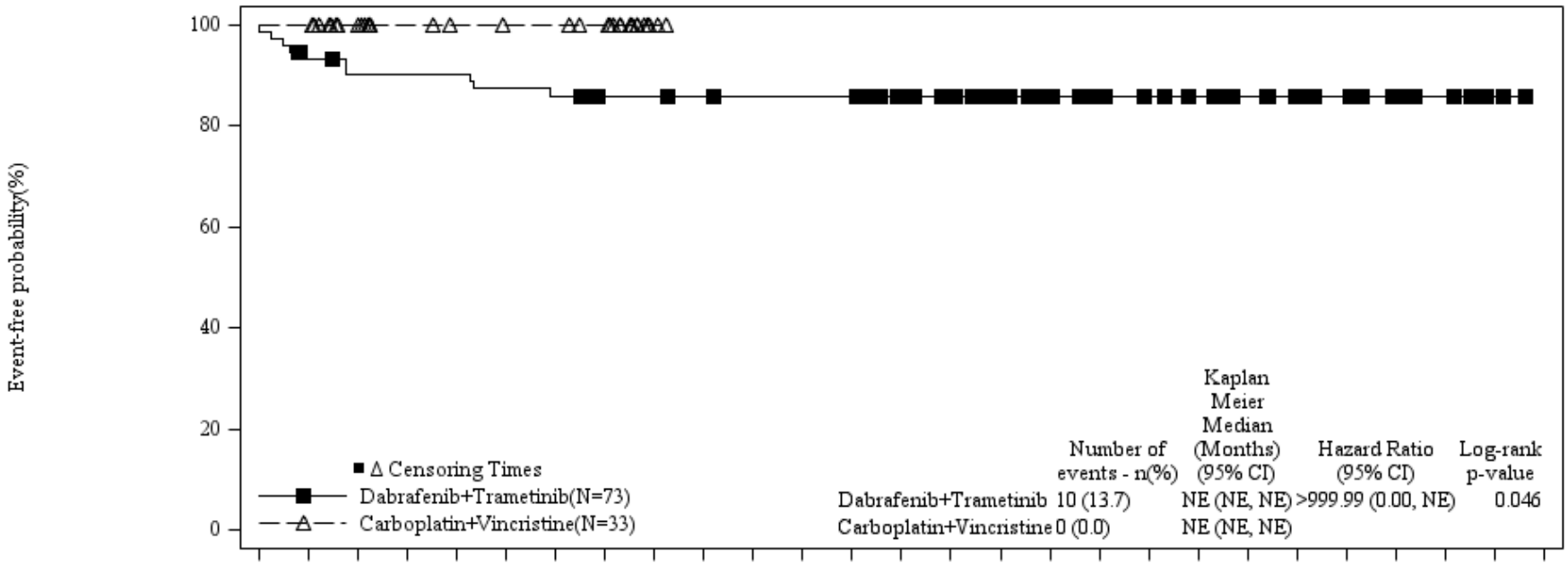
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	69	69	67	67	67	64	64	63	62	62	61	56	49	43	36	31	28	25	17	13	11	6	4	2	0
Carboplatin+Vincristine	33	25	19	15	14	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 15 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Dermatitis acneiform



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	10 (13.7)	NE (NE, NE)	>999.99 (0.00, NE)	0.046
Carboplatin+Vincristine	0 (0.0)	NE (NE, NE)		

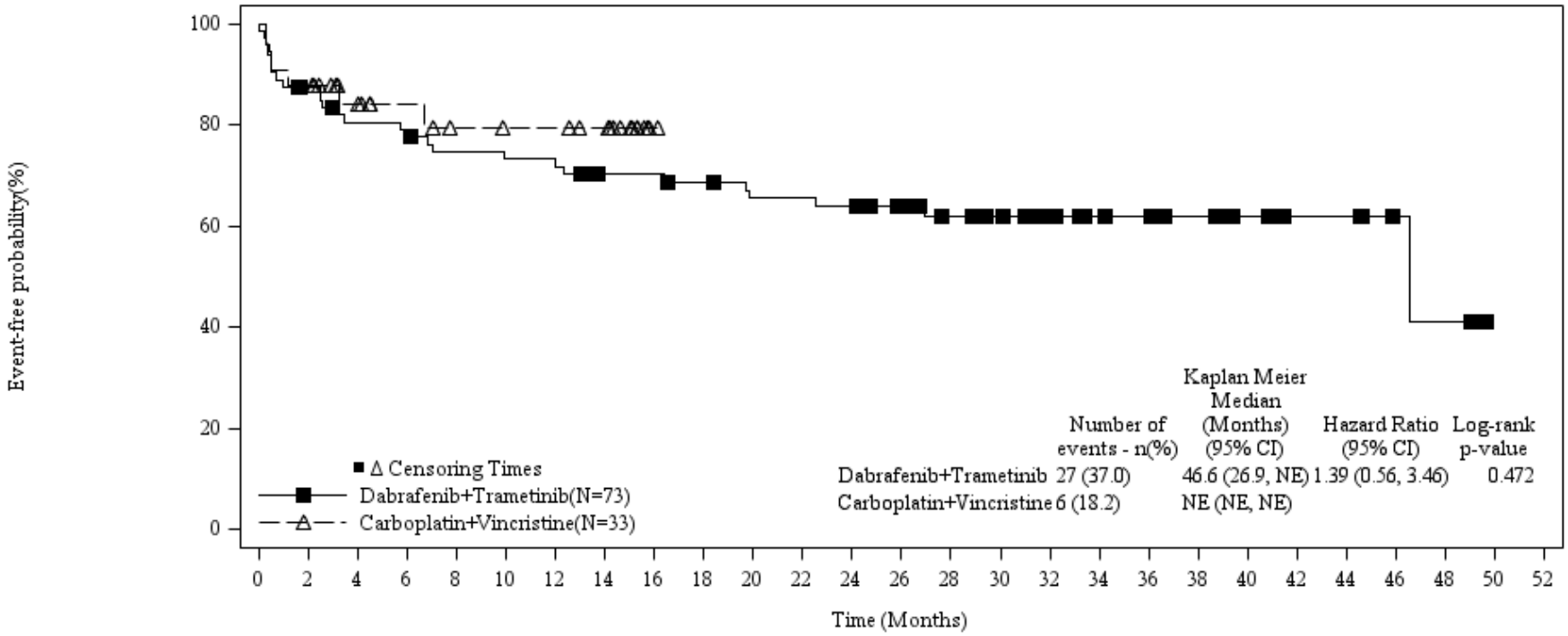
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	66	63	63	63	61	60	57	57	56	55	55	55	50	44	39	33	28	26	24	17	14	12	8	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 16 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Diarrhoea



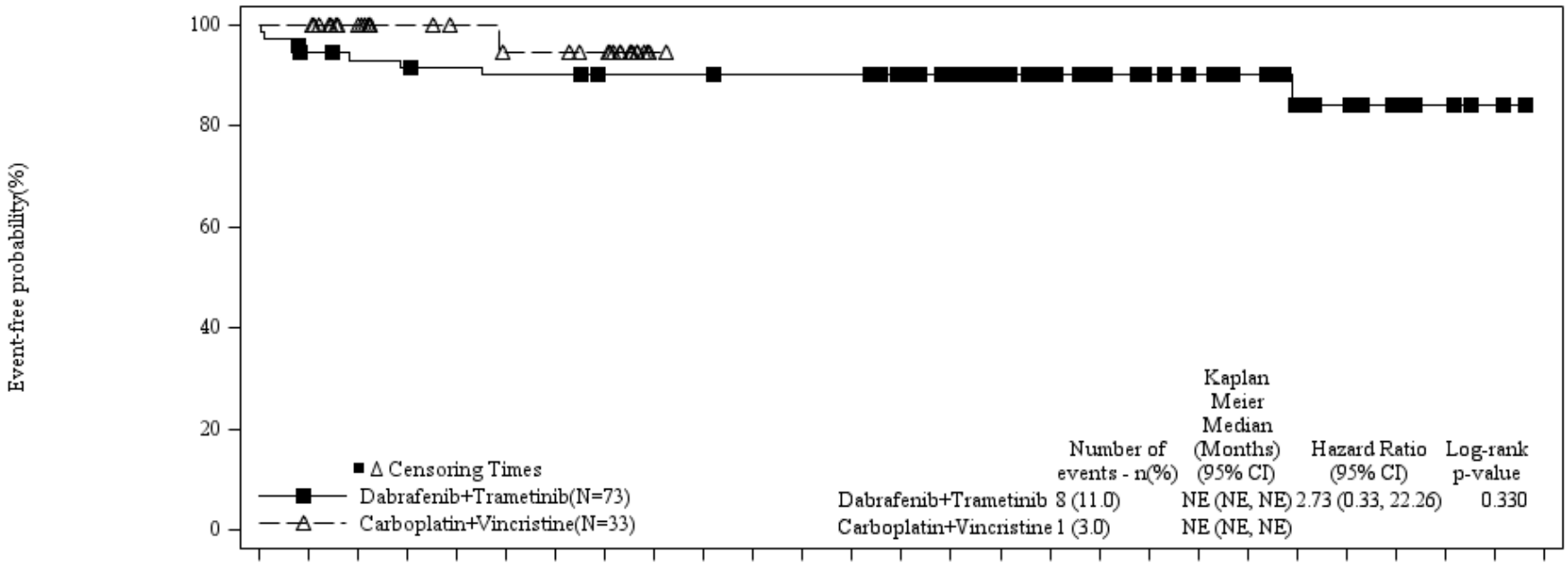
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	62	56	54	51	50	49	45	45	43	40	40	39	36	30	27	22	18	17	15	8	6	6	3	2	0	0
Carboplatin+Vincristine	33	29	22	18	15	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 17 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Dizziness



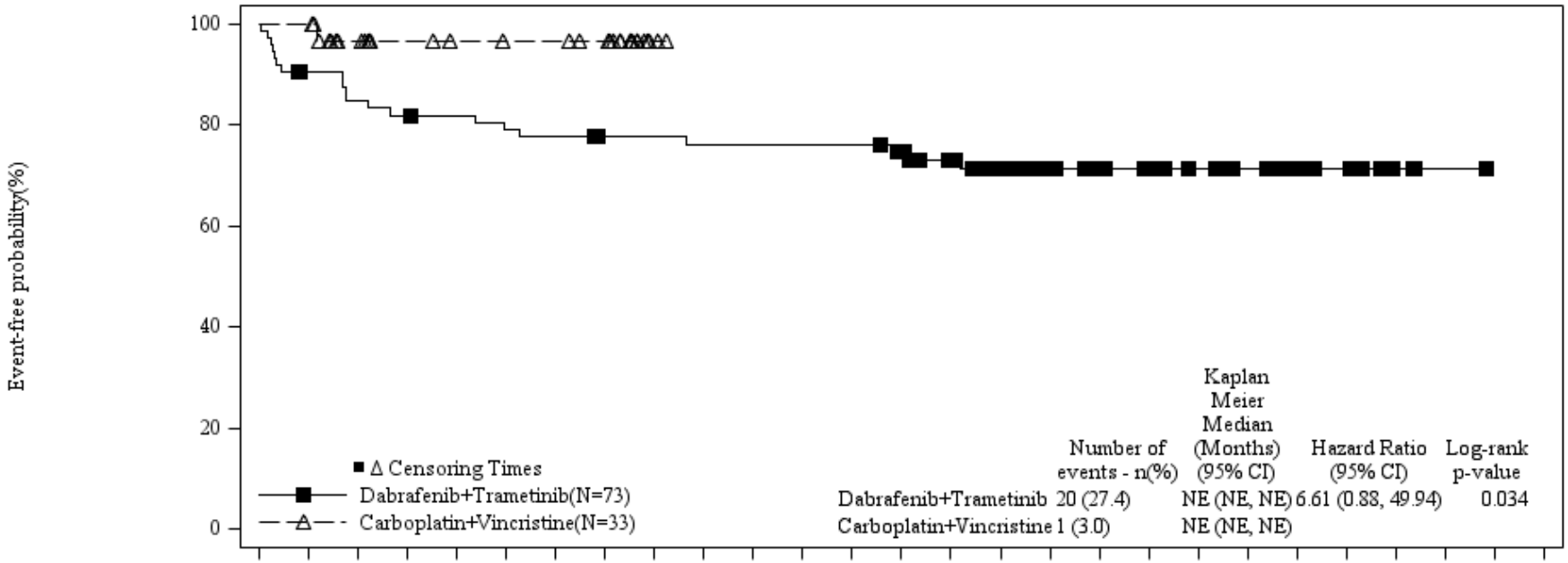
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	65	64	63	62	62	60	60	60	59	59	59	55	48	42	36	31	28	26	18	13	11	7	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	16	16	14	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 18 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Dry skin



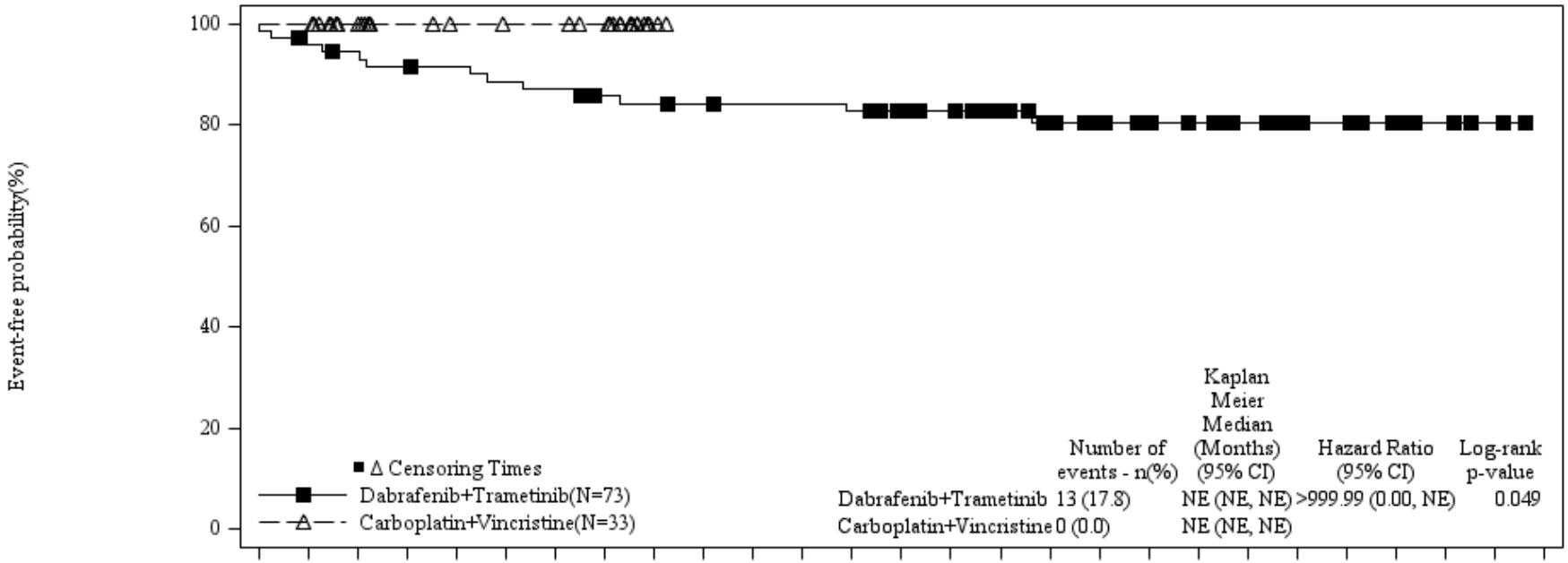
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	64	60	58	57	55	54	52	52	51	51	51	51	48	42	36	29	24	22	19	13	9	7	3	1	0	0
Carboplatin+Vincristine	33	33	25	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 19 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Eczema



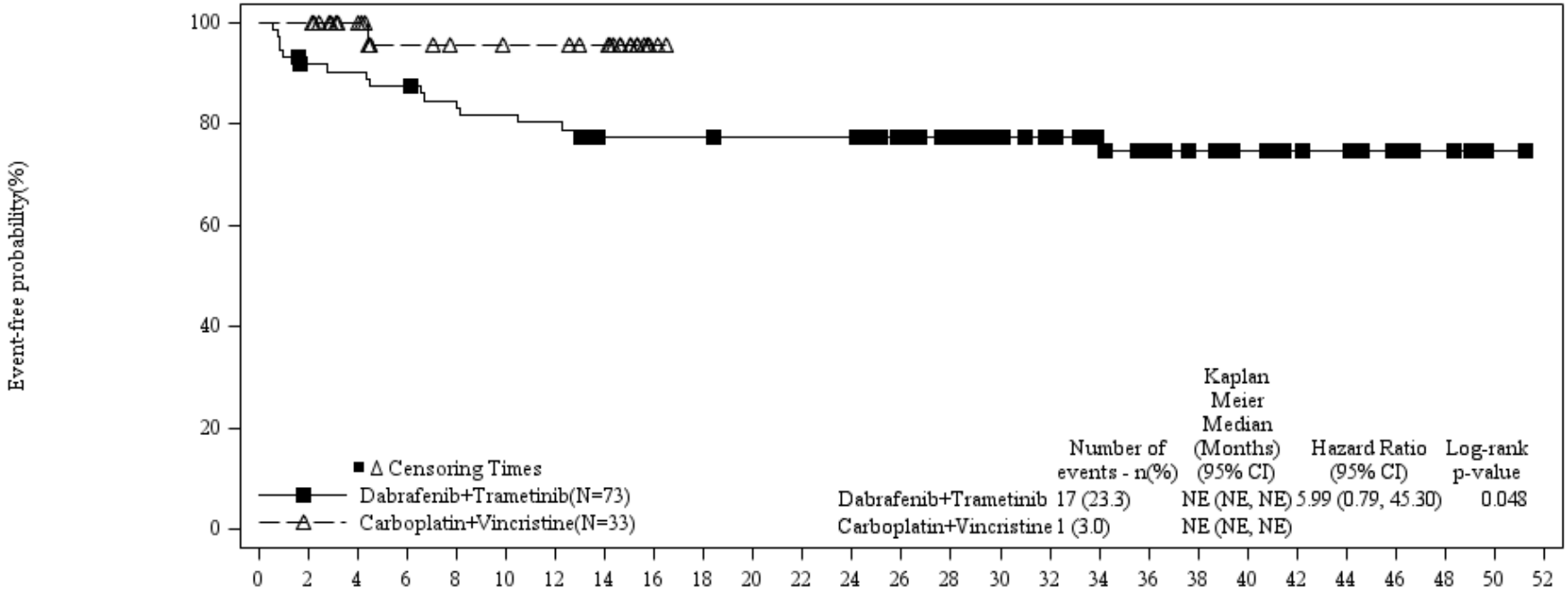
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	66	64	63	61	60	57	56	55	54	54	53	49	44	40	33	28	25	23	16	12	11	7	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 20 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Epistaxis



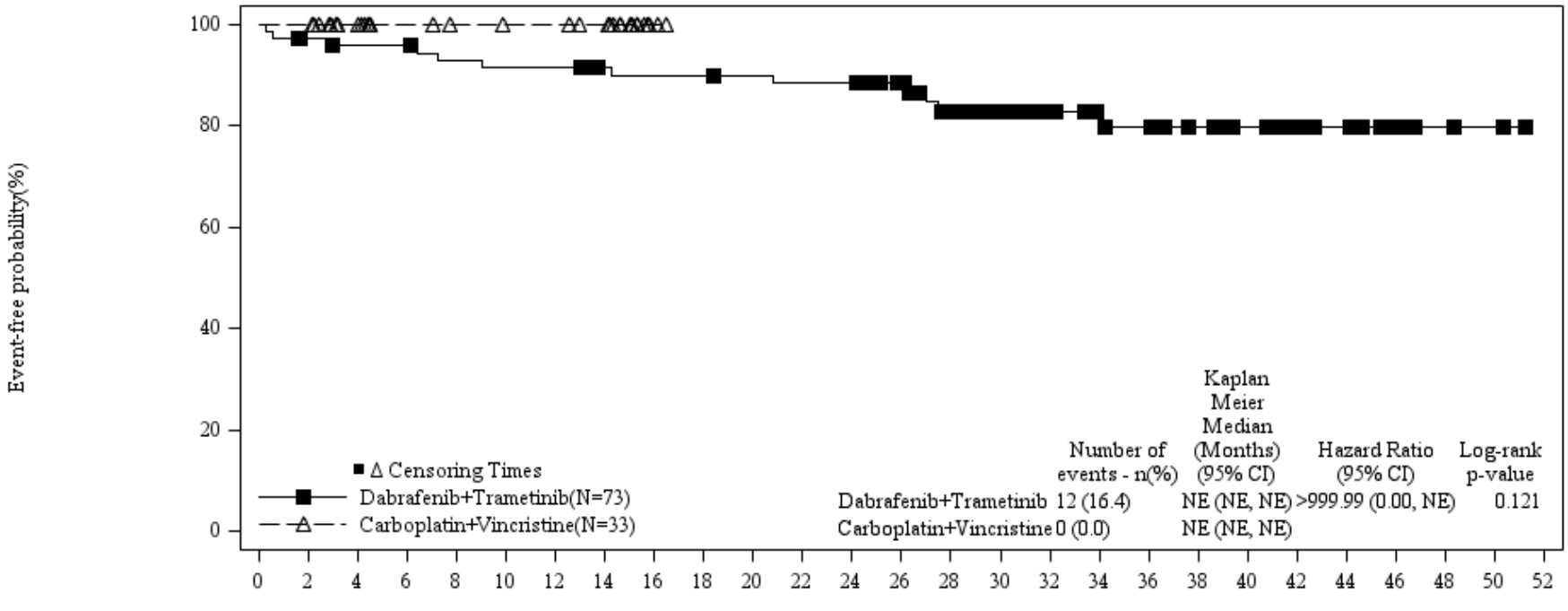
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	65	64	62	59	57	56	51	51	51	50	50	50	46	41	36	32	27	23	20	14	11	10	6	4	1	0
Carboplatin+Vincristine	33	33	26	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 21 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Erythema



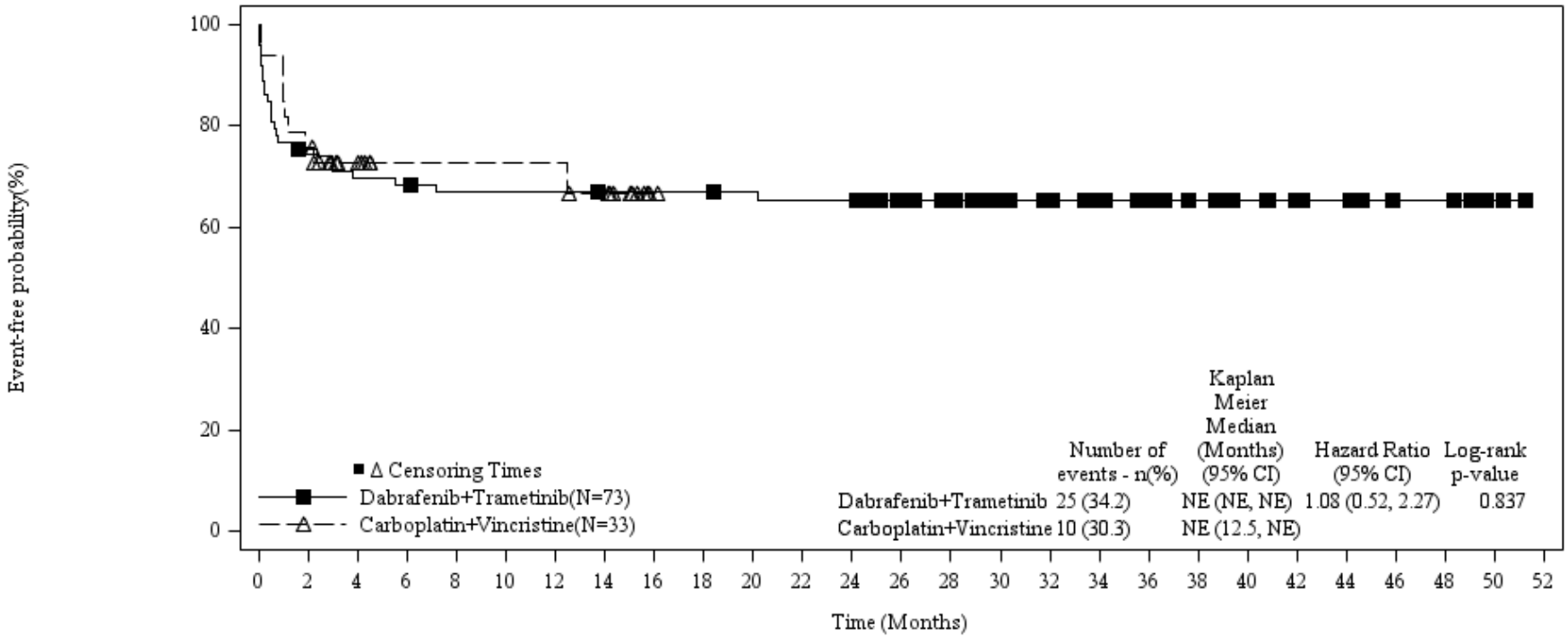
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	67	64	63	63	60	59	59	58	57	57	52	42	37	31	27	25	22	16	12	10	6	3	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 22 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Fatigue



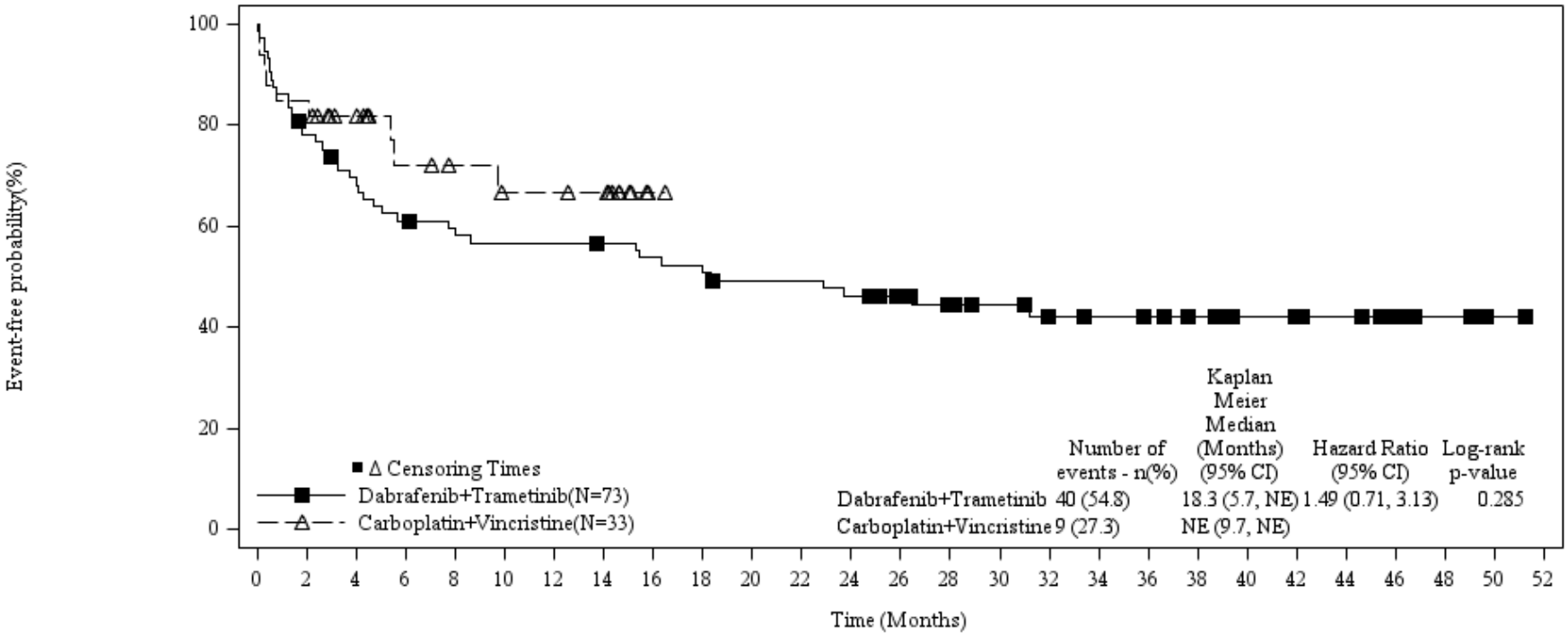
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	54	50	49	47	47	47	46	46	46	45	44	44	40	35	30	26	23	20	17	12	9	8	5	5	2	0
Carboplatin+Vincristine	33	25	17	12	12	12	12	10	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 23 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Headache



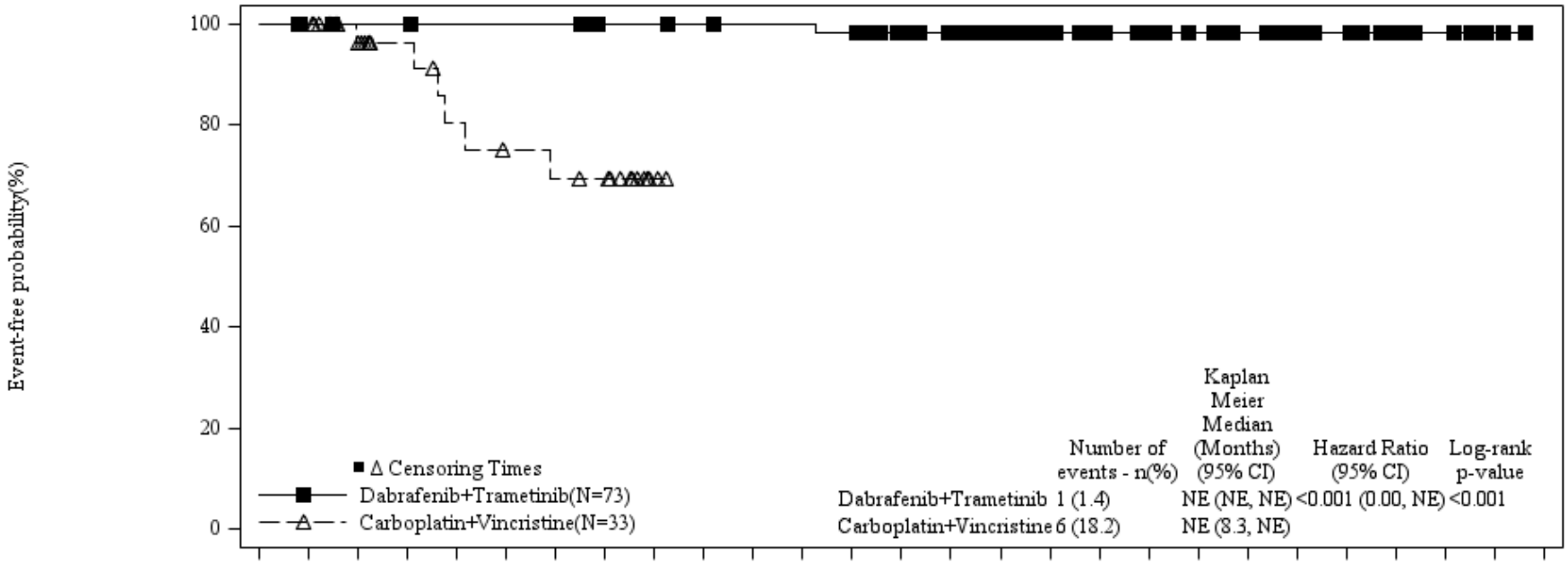
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	56	48	43	41	39	39	38	36	34	32	32	30	27	24	22	19	18	17	15	10	9	8	5	3	1	0
Carboplatin+Vincristine	33	28	22	15	13	11	11	10	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 24 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Hypersensitivity



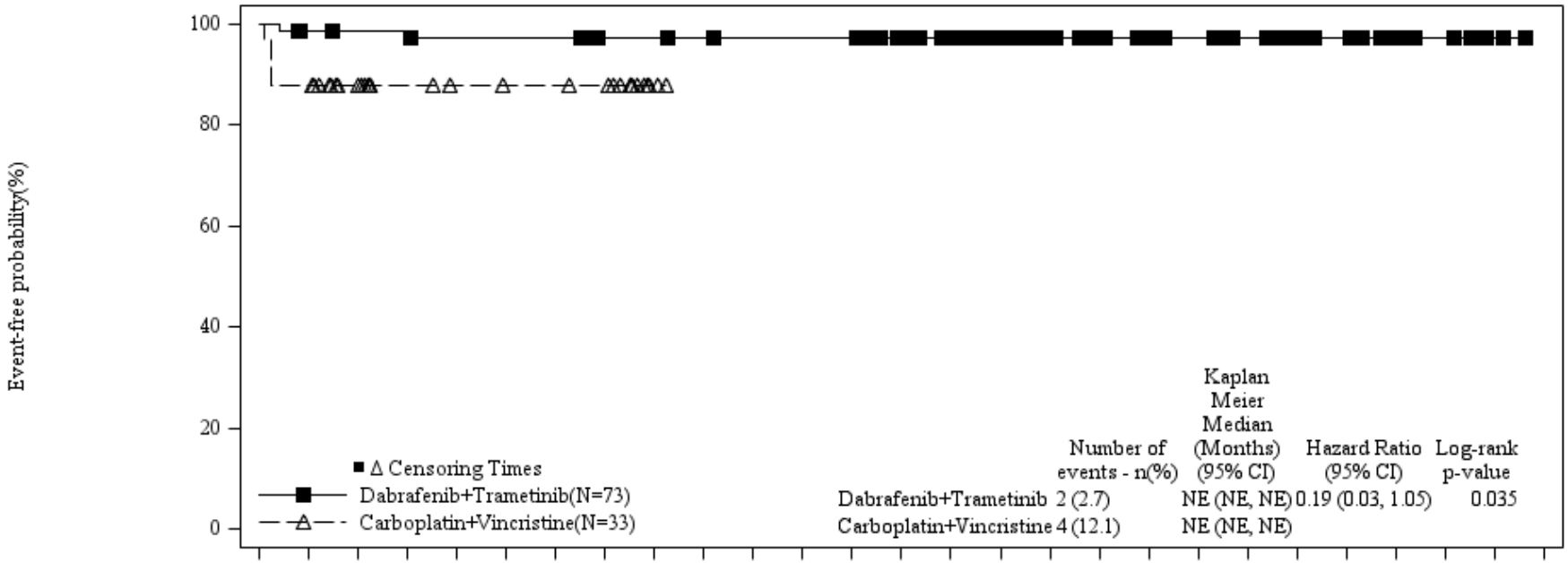
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	63	58	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	33	25	19	15	13	12	11	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 25 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Hypocalcaemia



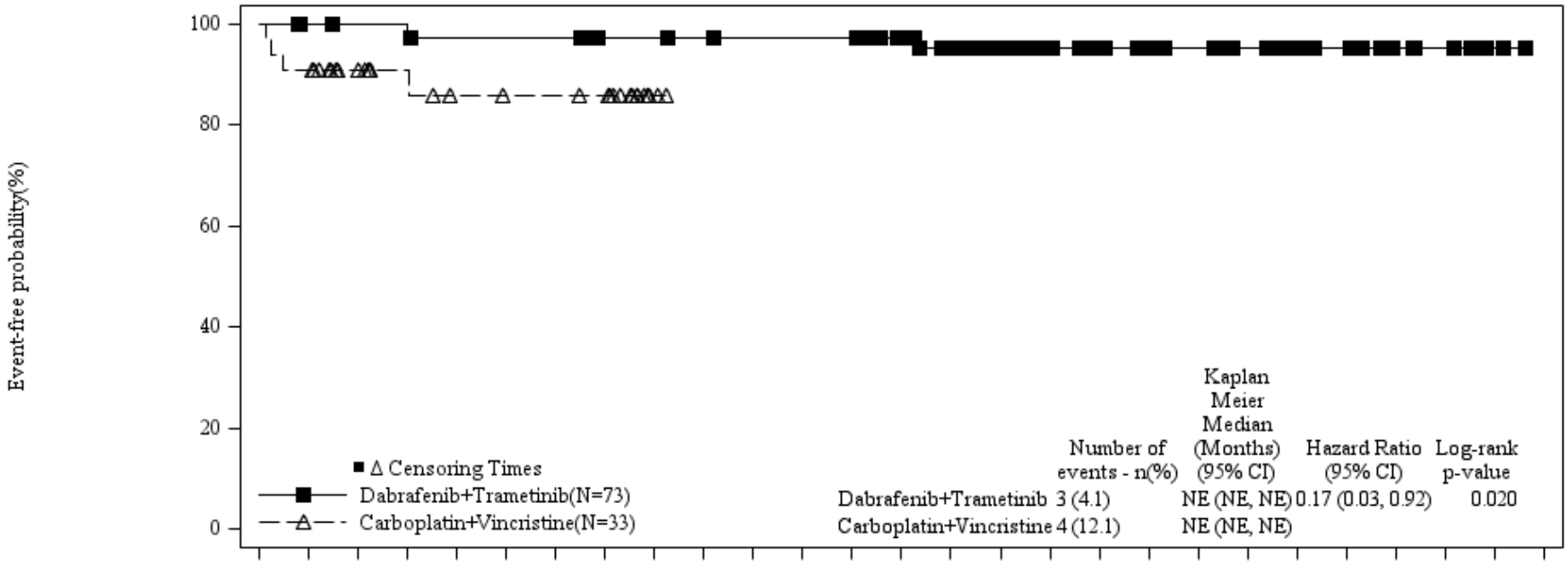
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	69	69	67	67	67	64	64	63	62	62	62	57	50	44	37	31	28	26	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	29	22	16	14	13	13	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 26 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Hypokalaemia



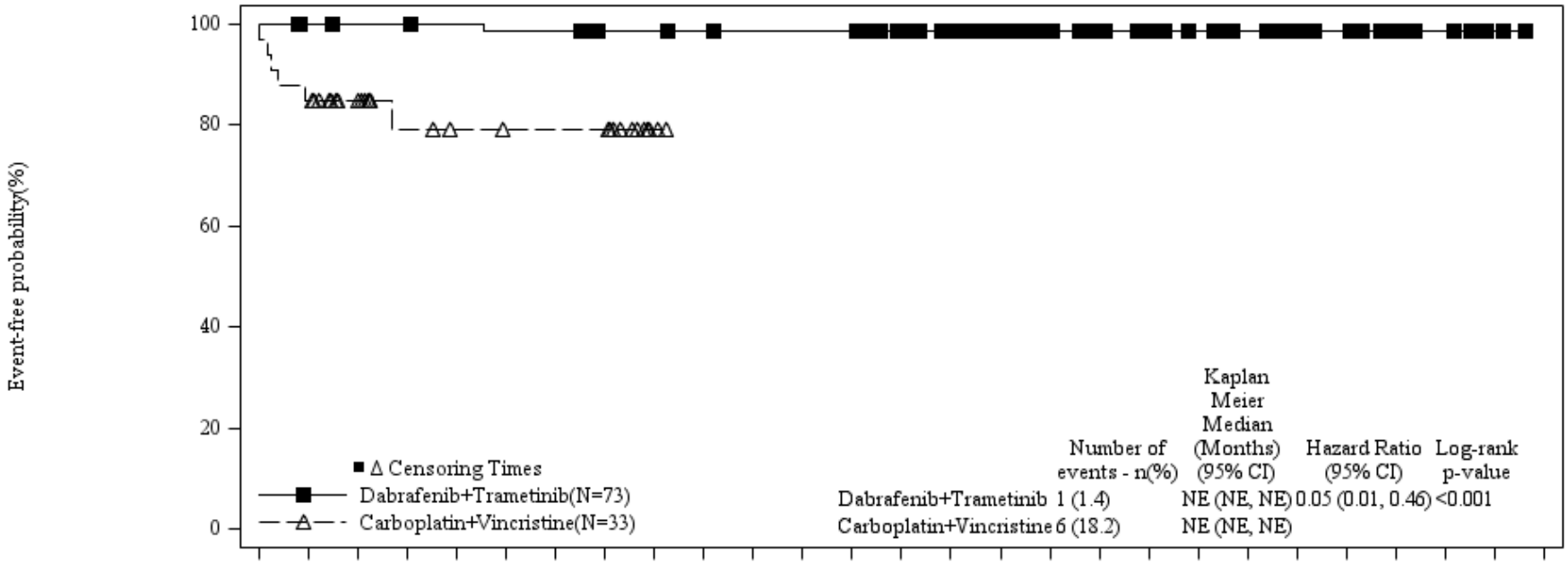
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	69	67	67	67	64	64	63	62	62	62	57	49	43	36	31	28	26	18	14	12	7	5	2	0
Carboplatin+Vincristine	33	30	23	18	15	14	14	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 27 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Hypomagnesaemia



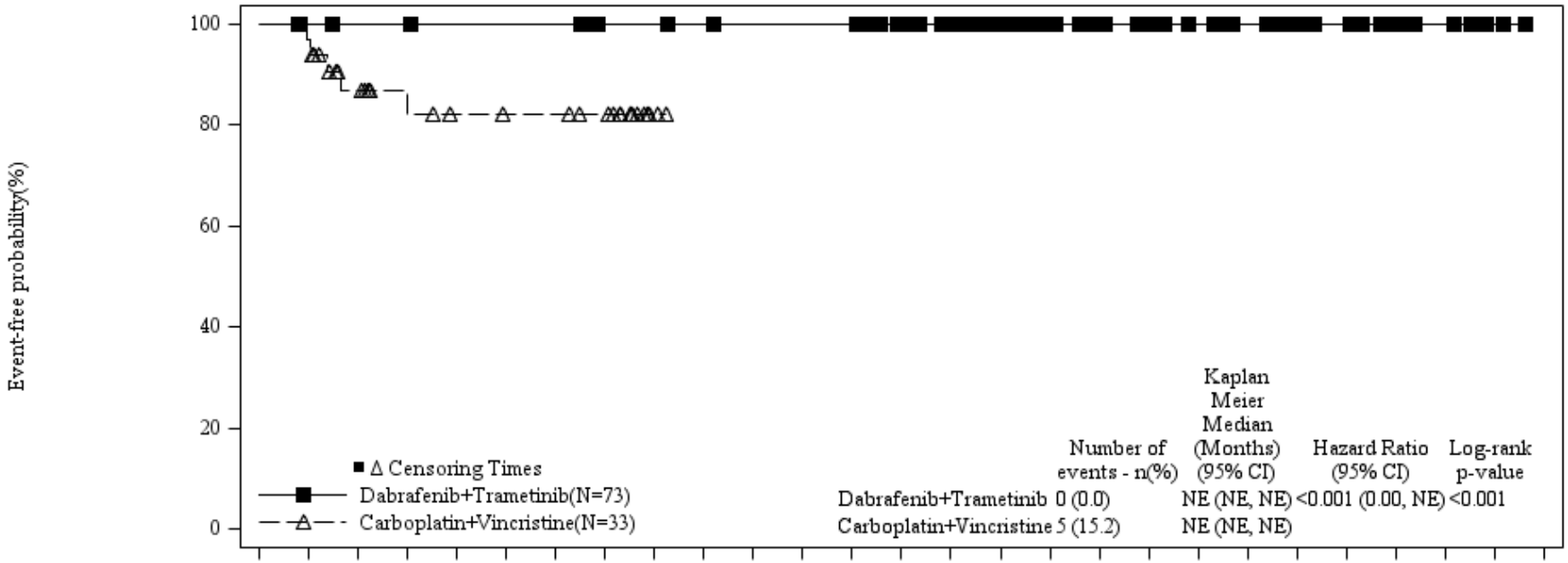
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	68	68	65	65	64	63	63	63	58	51	45	38	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	28	21	14	12	11	11	11	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 28 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Infusion related reaction



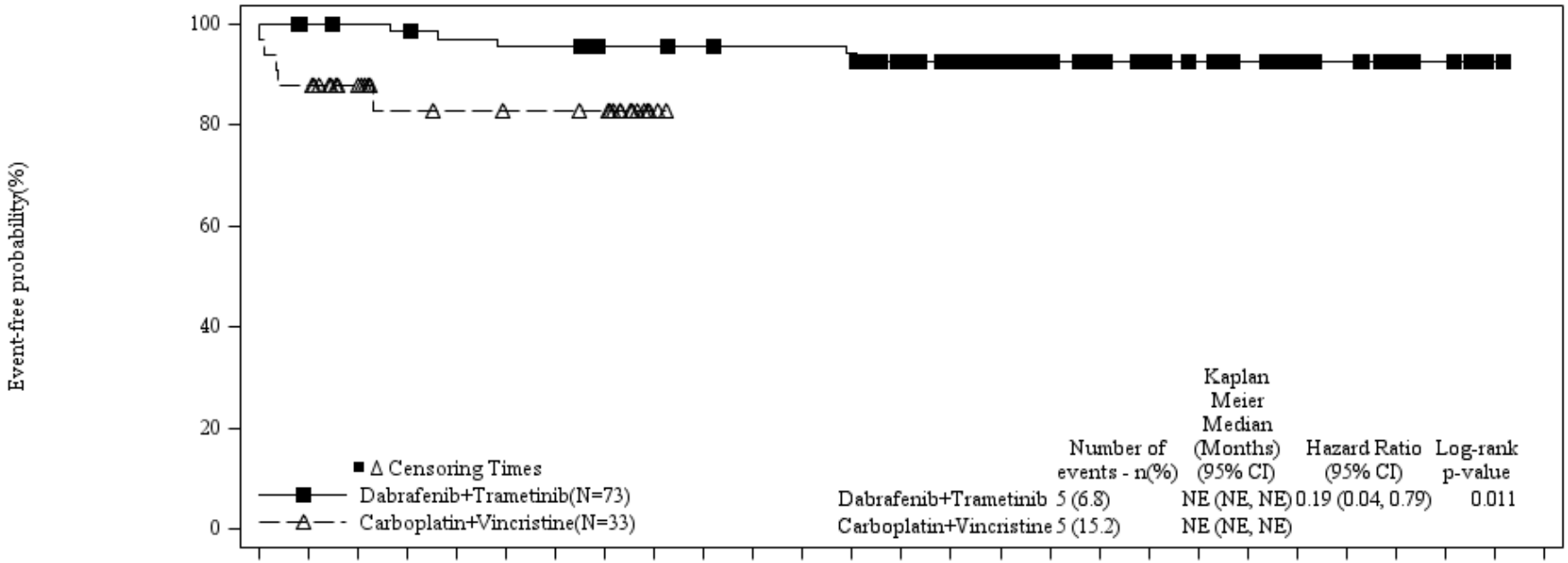
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	23	19	16	15	15	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 29 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Lymphocyte count decreased



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	5 (6.8)	NE (NE, NE)	0.19 (0.04, 0.79)	0.011
Carboplatin+Vincristine	5 (15.2)	NE (NE, NE)		

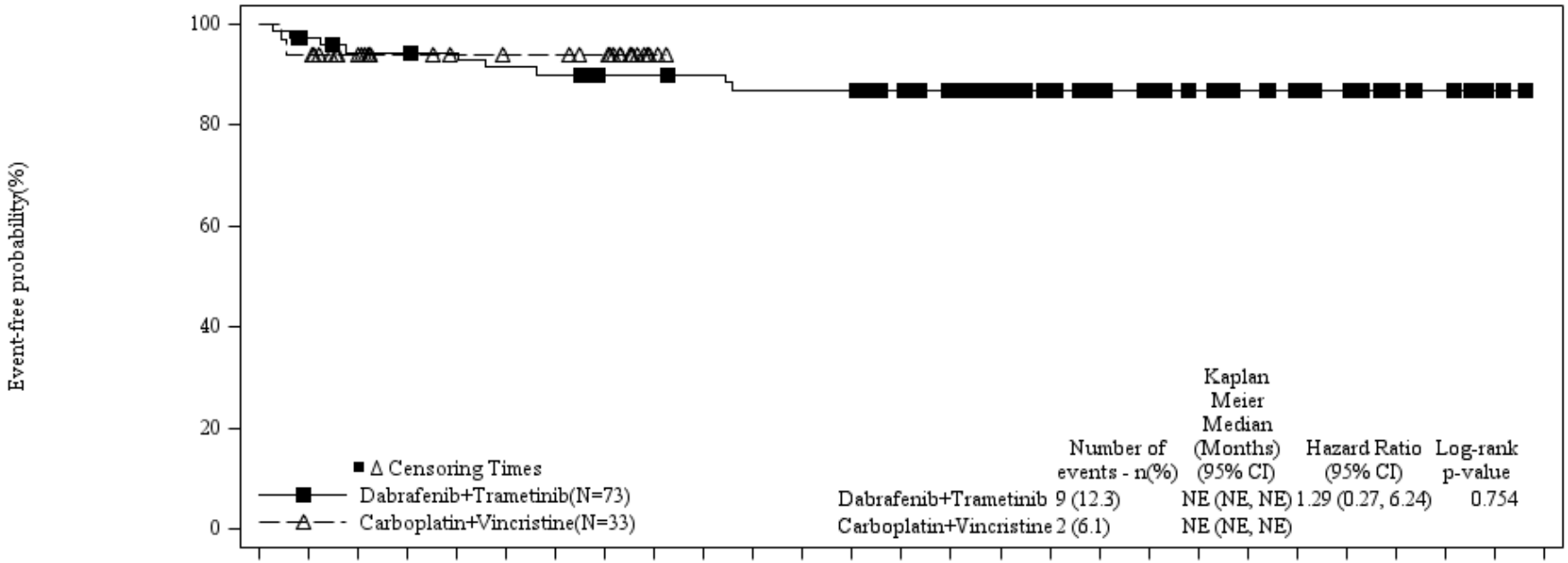
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	69	67	66	66	63	63	62	61	61	60	54	48	42	35	30	27	24	16	12	10	6	4	1	0
Carboplatin+Vincristine	33	29	22	16	15	14	14	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 30 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Nasopharyngitis



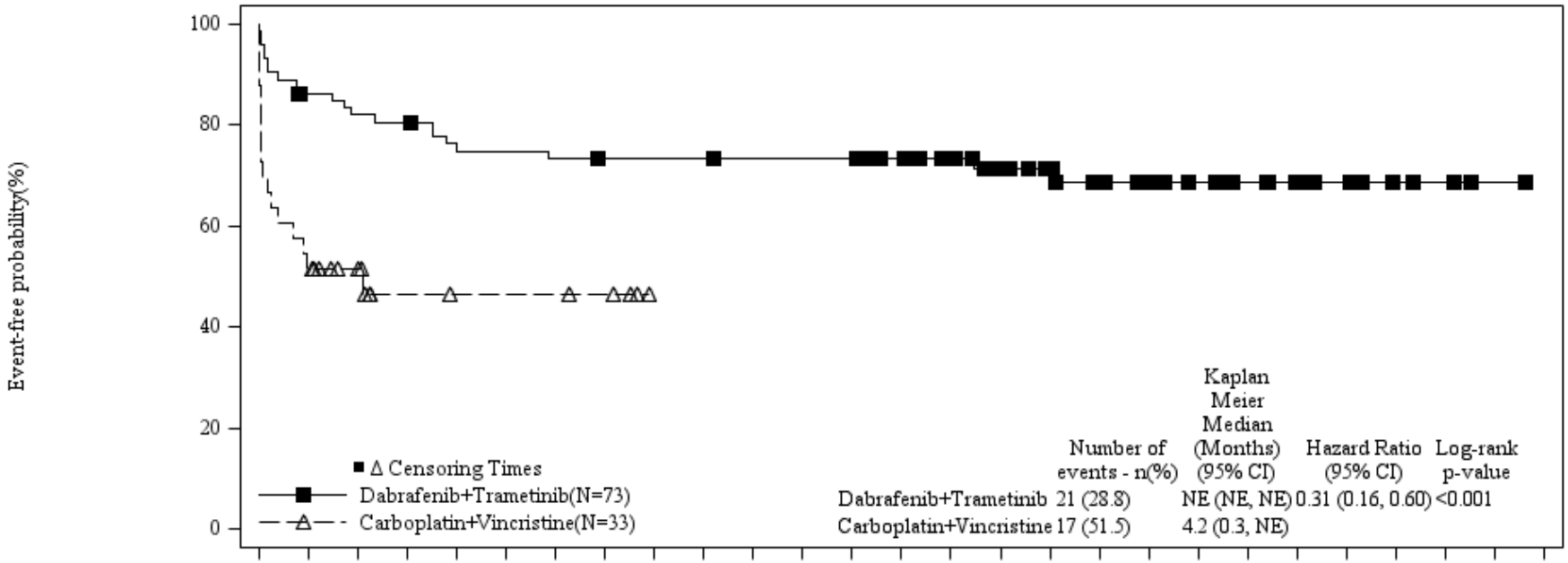
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	66	66	65	63	62	59	59	58	56	56	56	52	46	40	34	29	27	24	17	14	12	7	5	2	0
Carboplatin+Vincristine	33	31	25	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 31 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Nausea



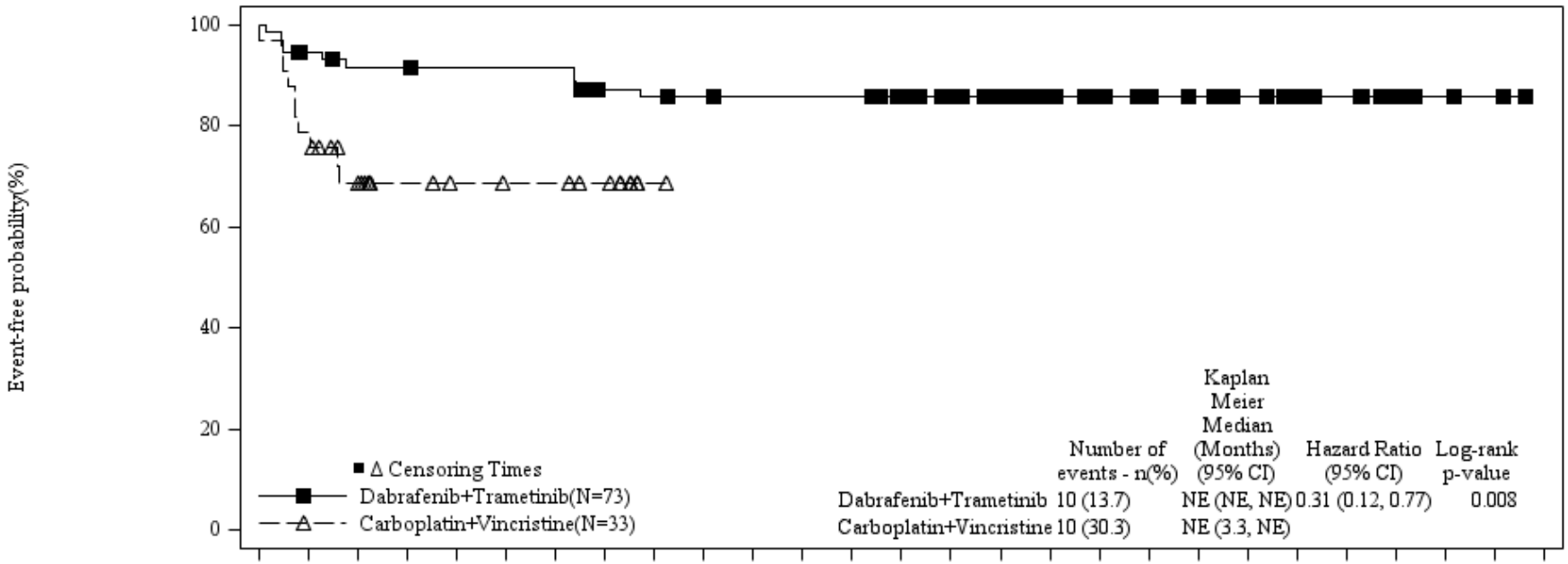
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	61	58	57	53	52	51	50	50	50	49	49	49	45	38	32	27	23	21	18	12	9	7	4	3	1	0
Carboplatin+Vincristine	33	17	12	6	5	5	5	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 32 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Neutropenia



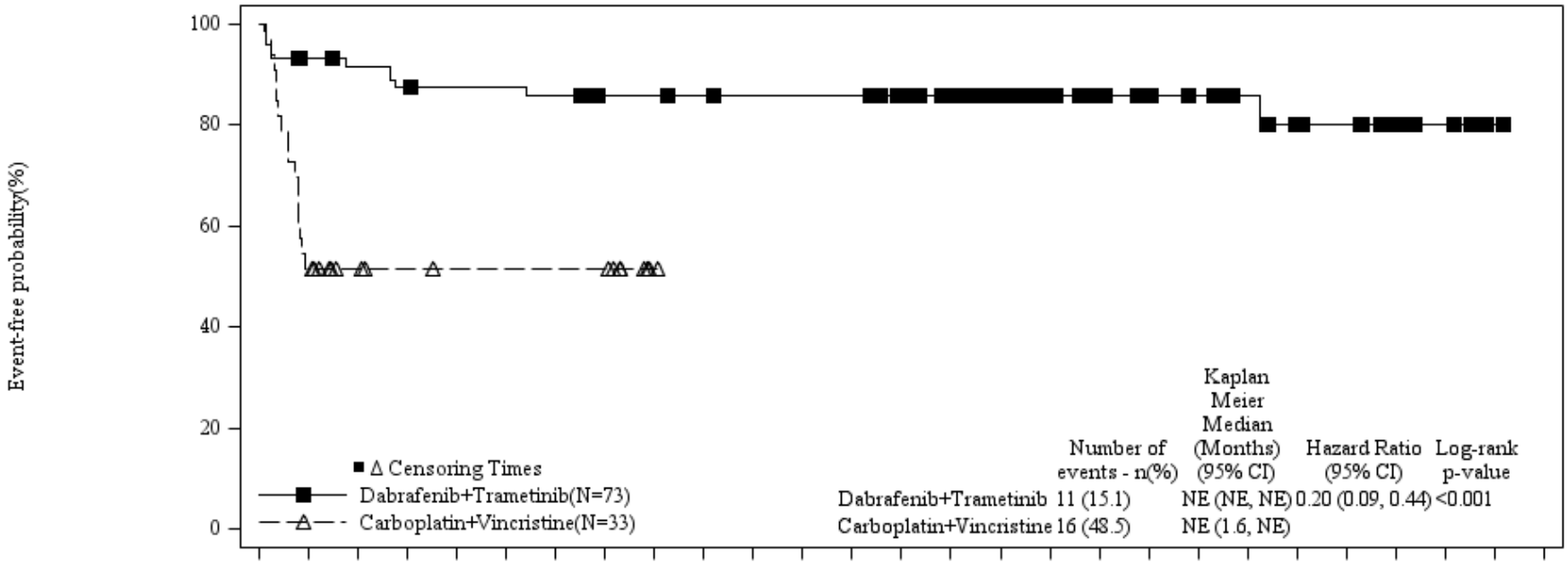
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	64	64	63	63	63	57	56	55	54	54	54	51	44	39	32	27	24	22	15	12	10	6	3	2	0
Carboplatin+Vincristine	33	26	19	13	11	10	10	8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 33 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Neutrophil count decreased



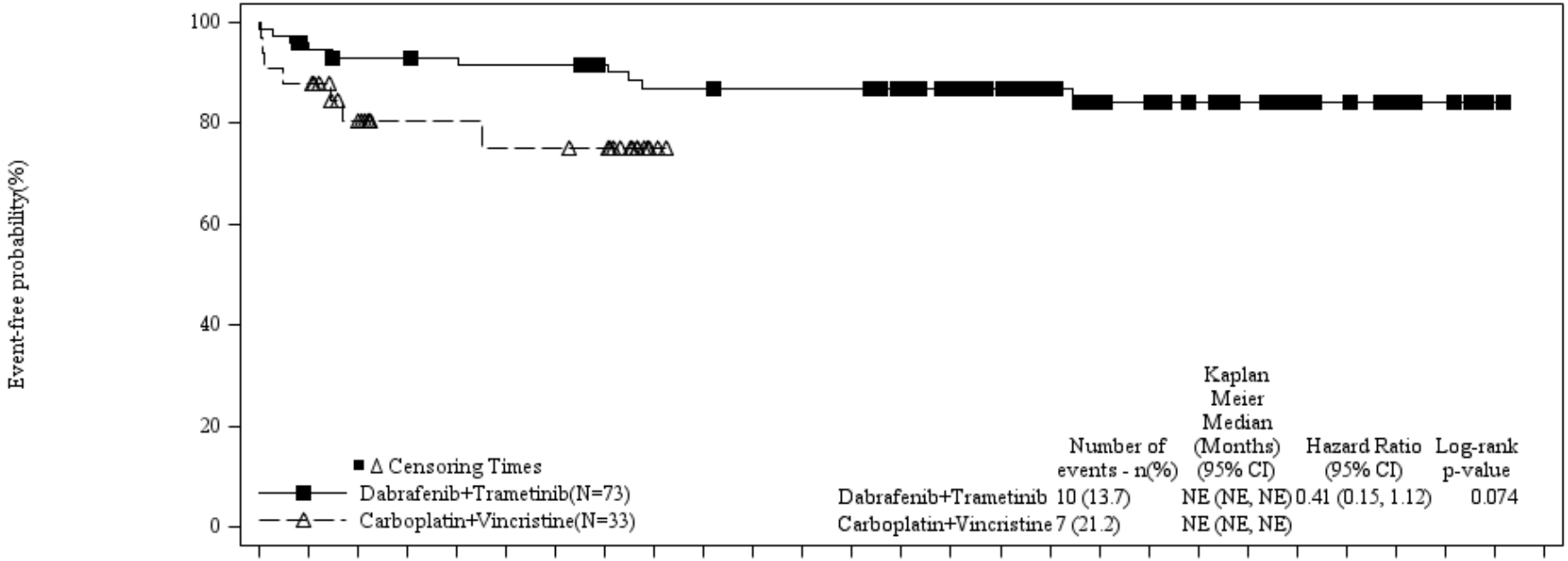
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	66	64	61	60	60	59	56	56	55	54	54	54	50	45	39	34	28	25	23	15	11	10	6	4	1	0
Carboplatin+Vincristine	33	17	11	9	8	8	8	8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 34 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Oropharyngeal pain



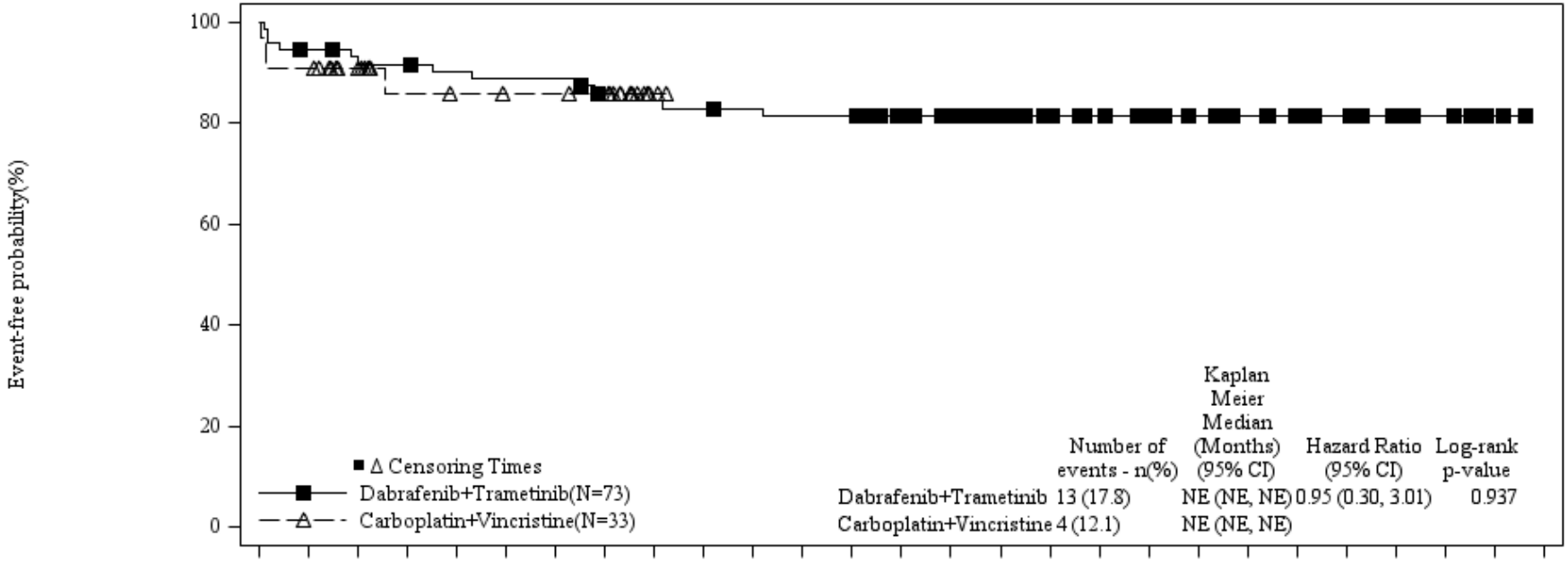
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	65	65	64	63	63	60	57	57	56	56	56	52	45	40	33	27	26	23	16	12	10	7	4	1	0
Carboplatin+Vincristine	33	29	21	15	15	14	14	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 35 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pain in extremity



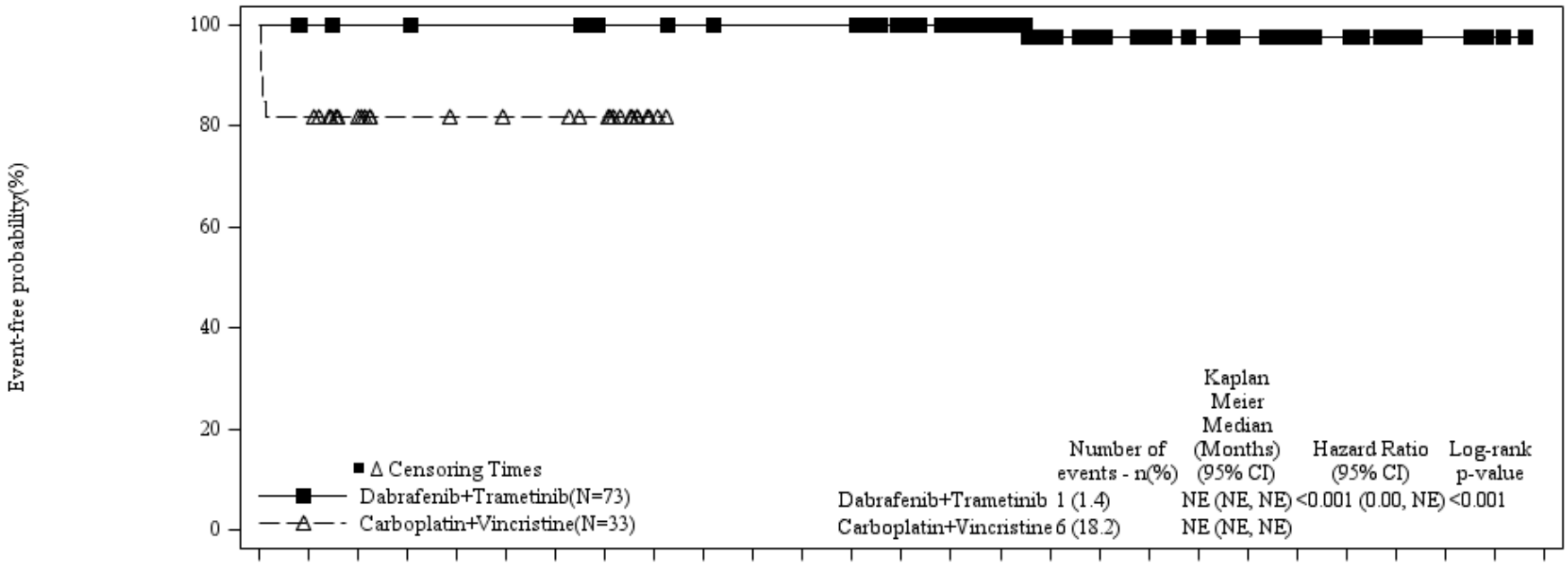
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	65	65	63	62	62	57	57	56	55	54	54	49	43	37	31	28	25	22	16	13	11	7	5	2	0
Carboplatin+Vincristine	33	30	24	17	16	15	15	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 36 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pain in jaw



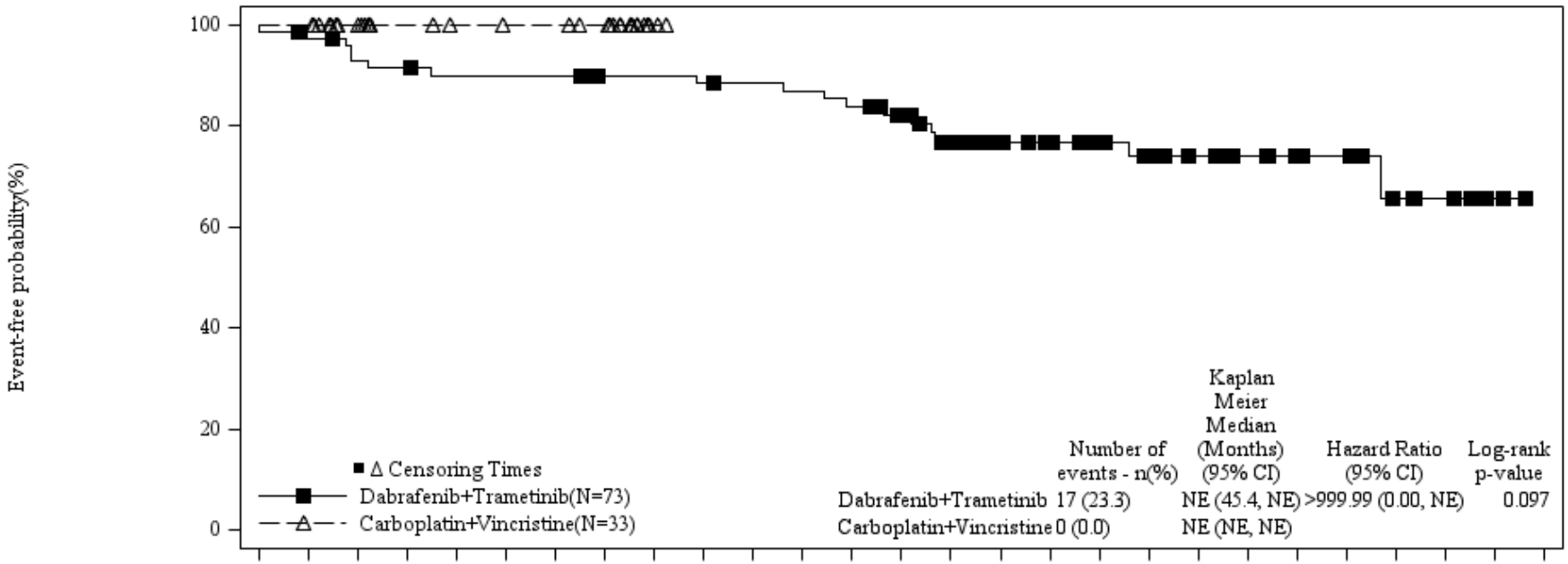
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	38	32	29	26	18	14	12	7	4	2	0
Carboplatin+Vincristine	33	27	21	16	15	14	14	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 37 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Paronychia



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	17 (23.3)	NE (45.4, NE)	>999.99 (0.00, NE)	0.097
Carboplatin+Vincristine	0 (0.0)	NE (NE, NE)		

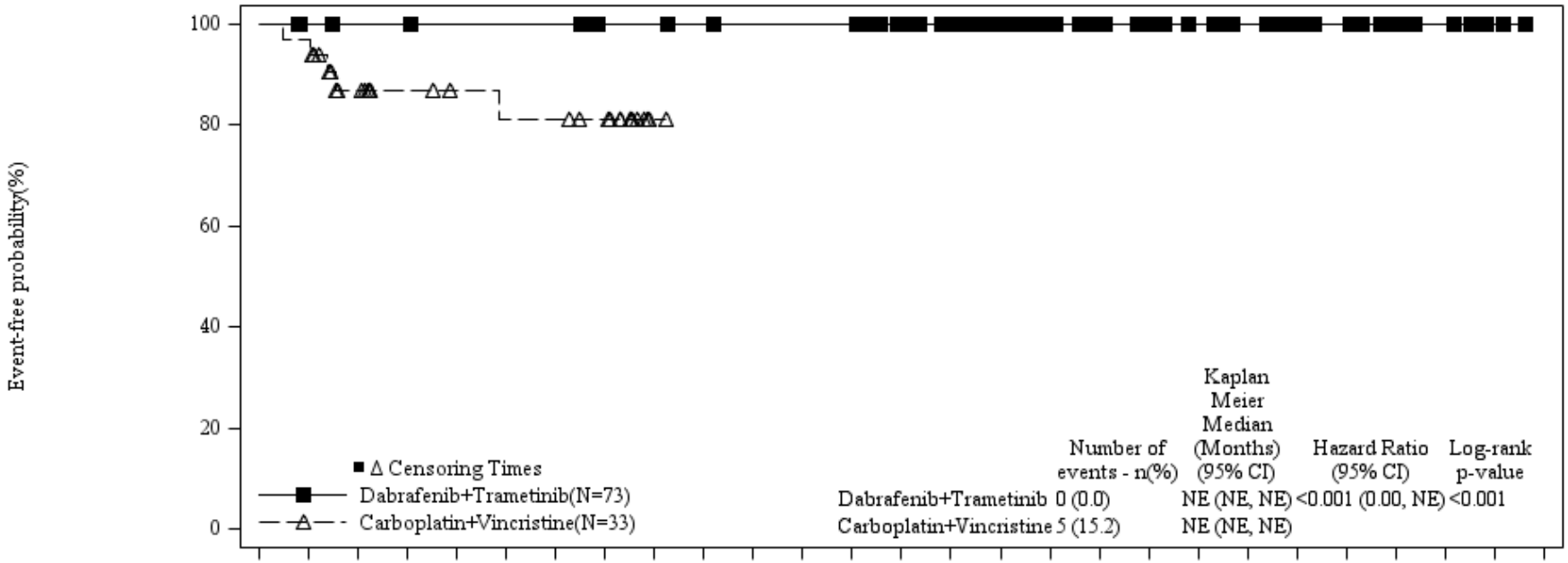
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	65	64	62	62	62	59	59	58	57	56	54	50	42	36	32	27	24	21	16	13	12	7	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 38 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Peripheral motor neuropathy



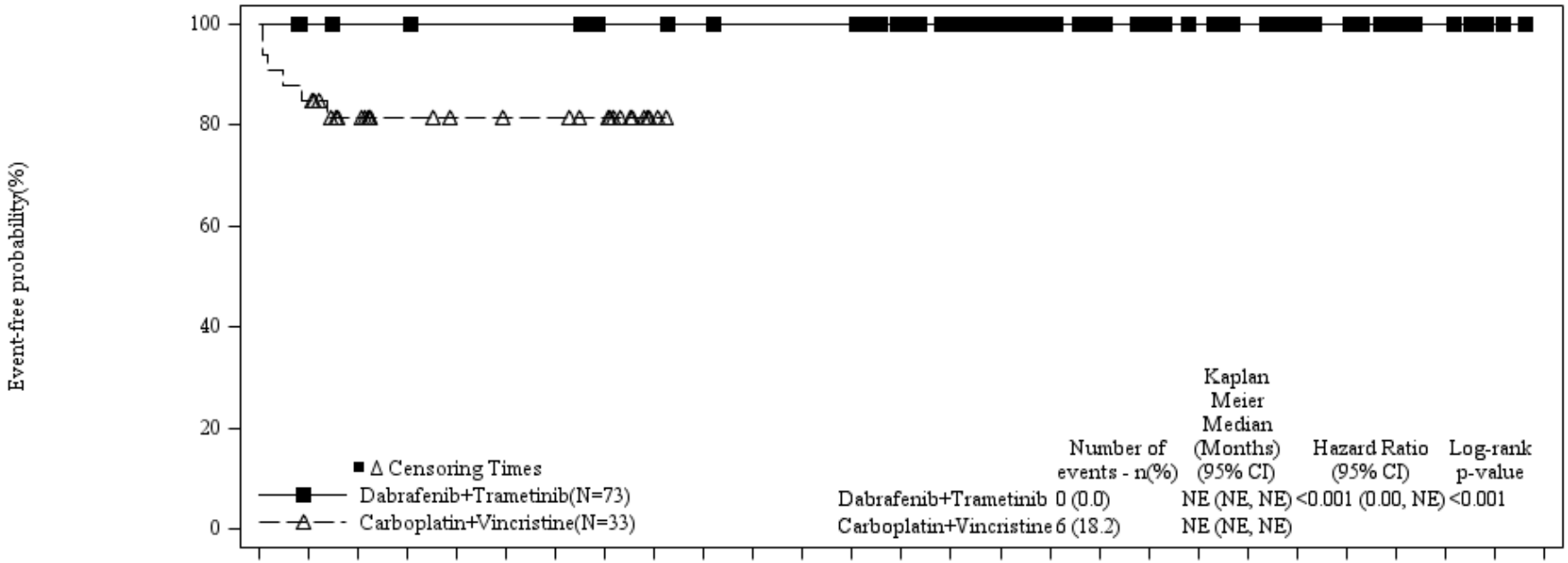
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	22	17	15	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 39 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Peripheral sensory neuropathy



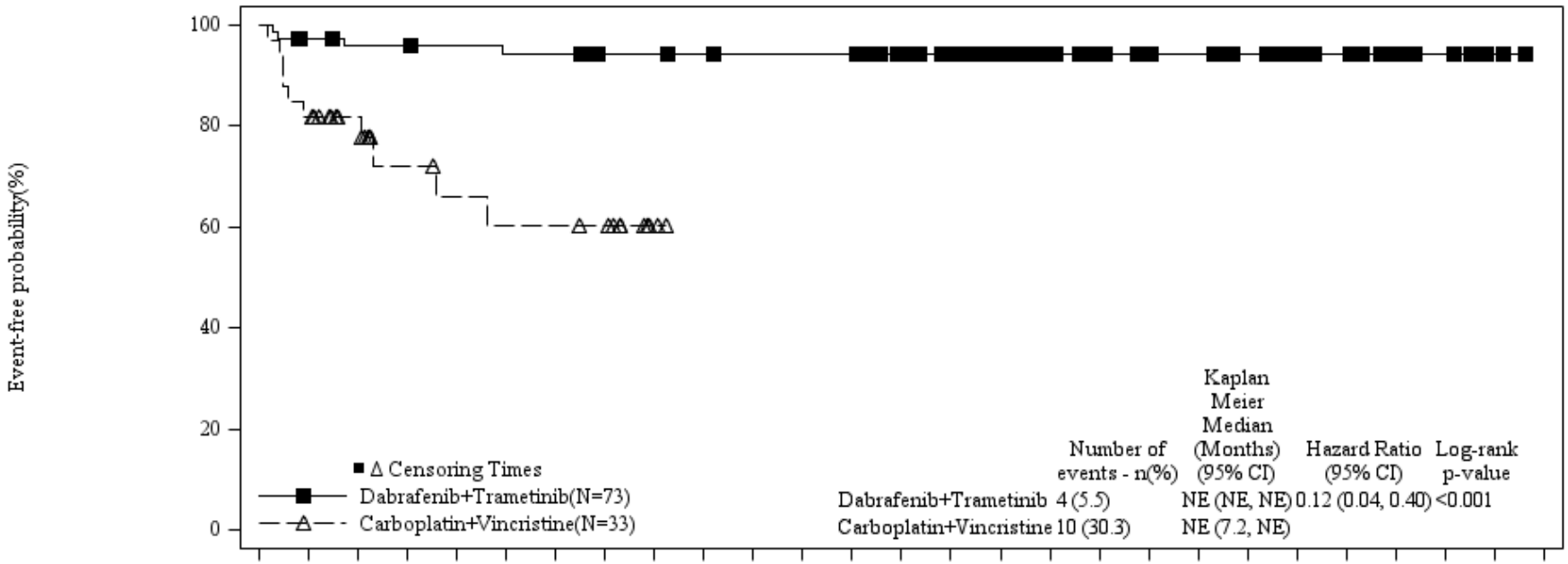
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	28	21	16	14	13	13	11	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 40 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Platelet count decreased



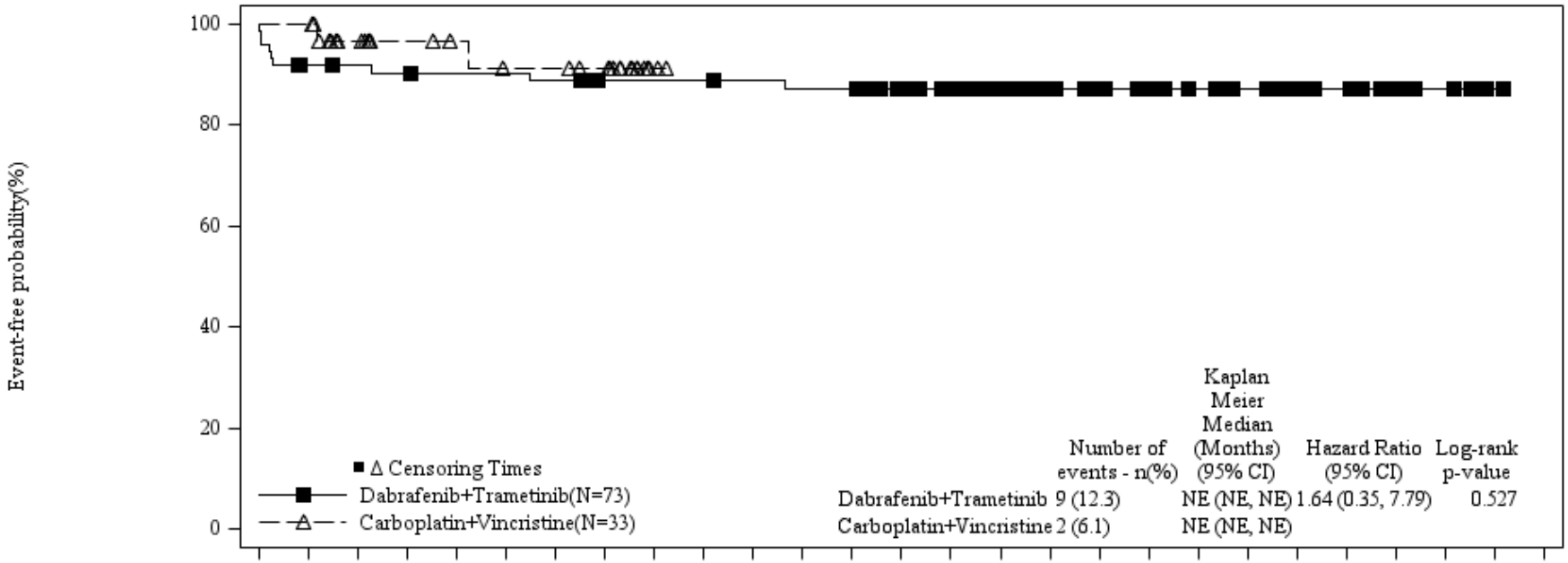
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	67	66	65	65	62	62	61	60	60	60	55	49	43	37	31	28	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	27	20	13	11	10	10	9	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 41 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pruritus



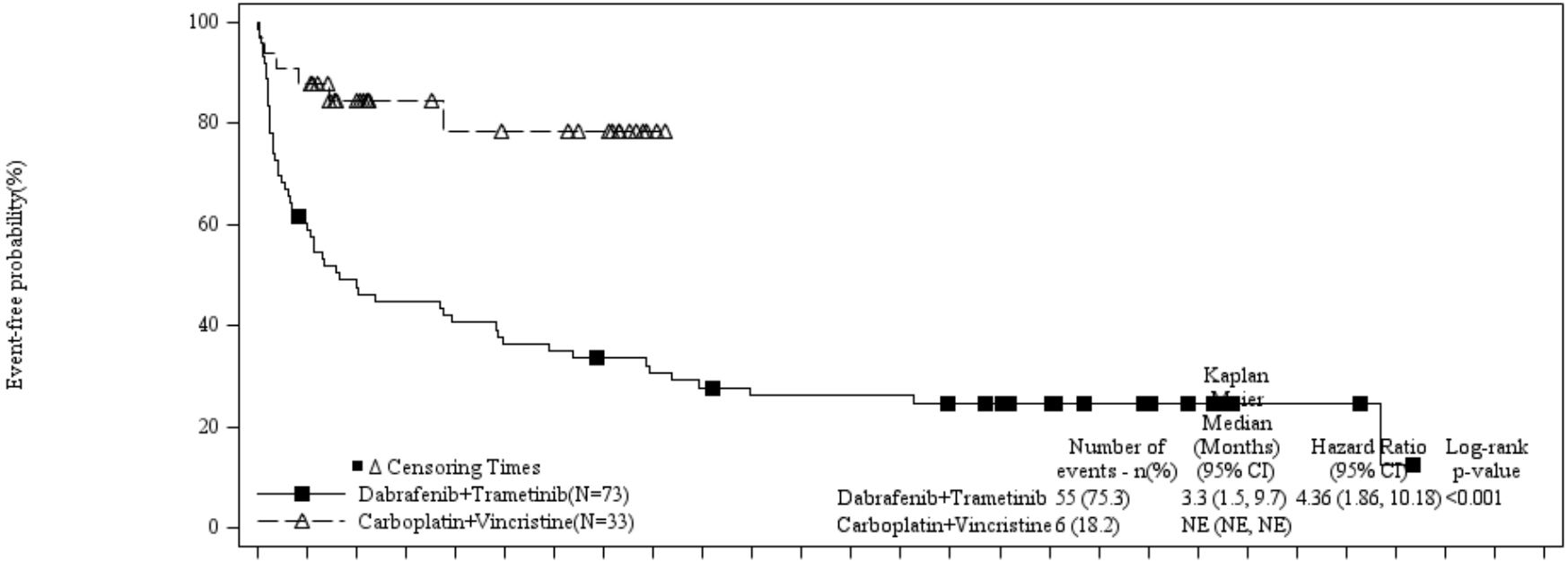
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	65	64	63	62	62	61	58	58	58	57	56	56	51	44	40	33	28	25	22	16	12	10	6	4	1	0
Carboplatin+Vincristine	33	33	25	20	18	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 42 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pyrexia



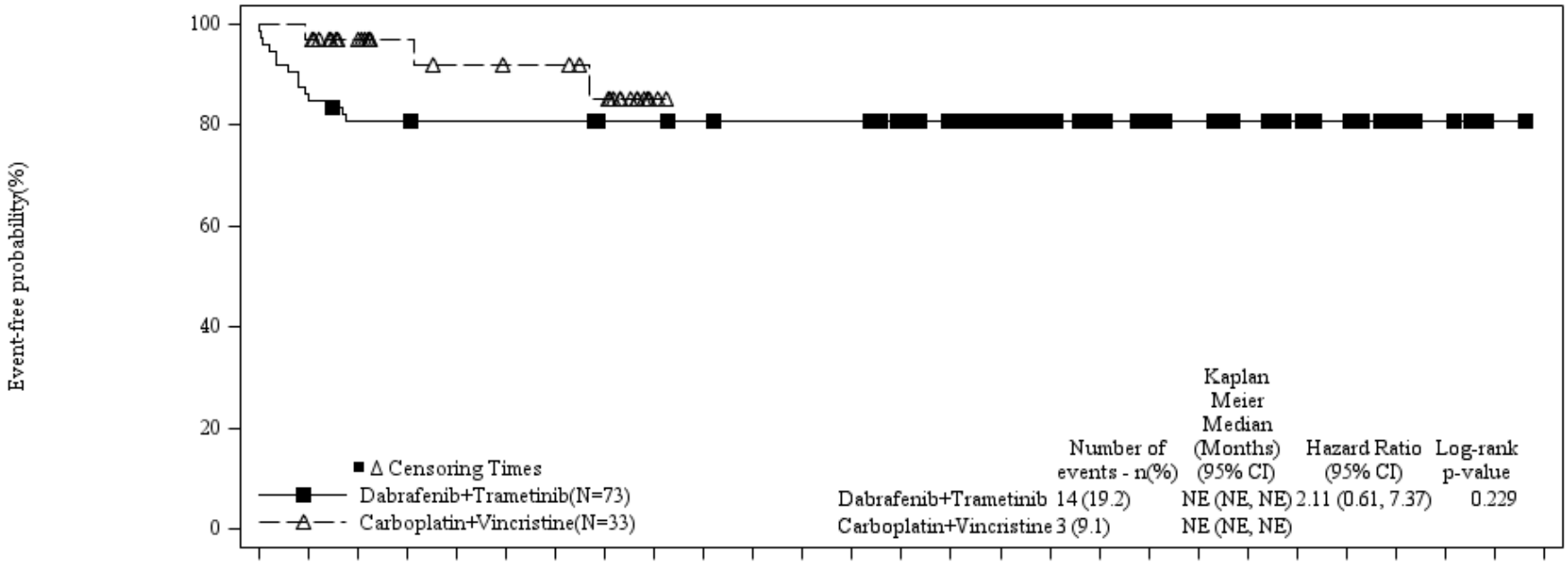
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	43	35	32	29	26	25	23	21	19	17	17	17	17	15	14	12	9	8	6	3	3	3	1	0	0	0
Carboplatin+Vincristine	33	29	21	15	13	12	12	10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 43 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Rash



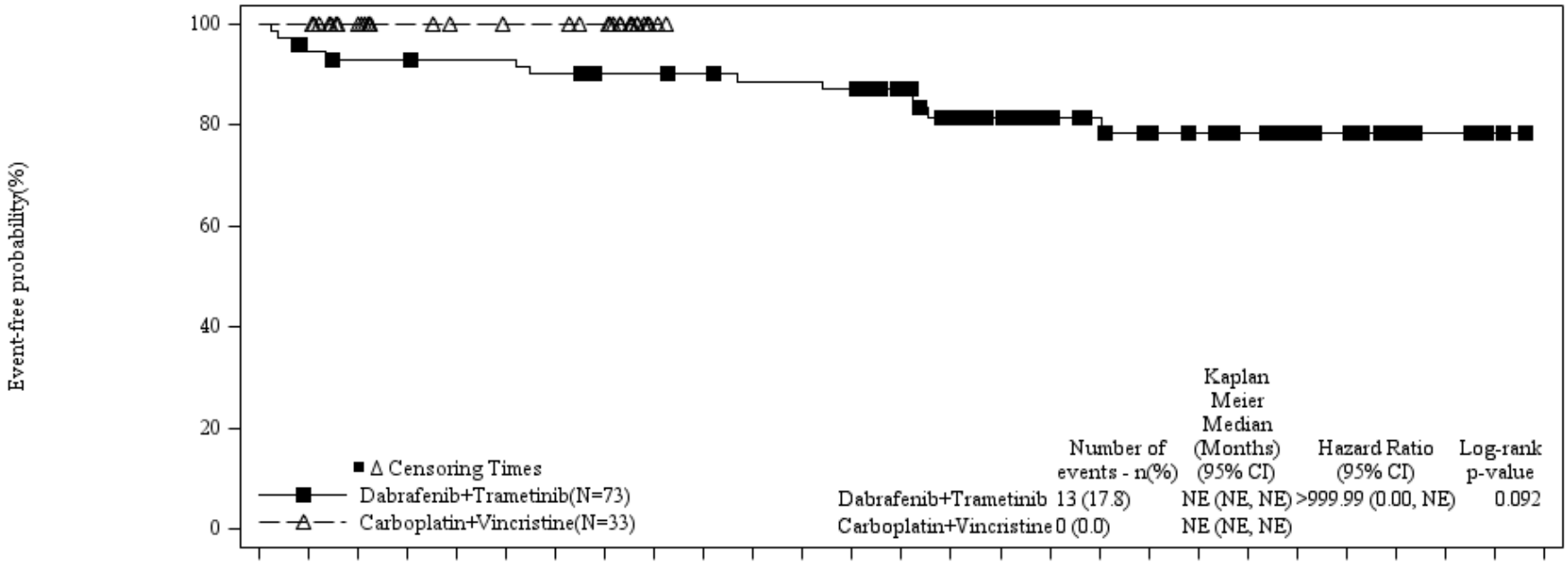
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	63	58	58	57	57	57	55	55	54	53	53	53	50	44	38	32	27	25	23	15	13	11	7	4	1	0
Carboplatin+Vincristine	33	32	25	19	17	16	16	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 44 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Rash maculo-papular



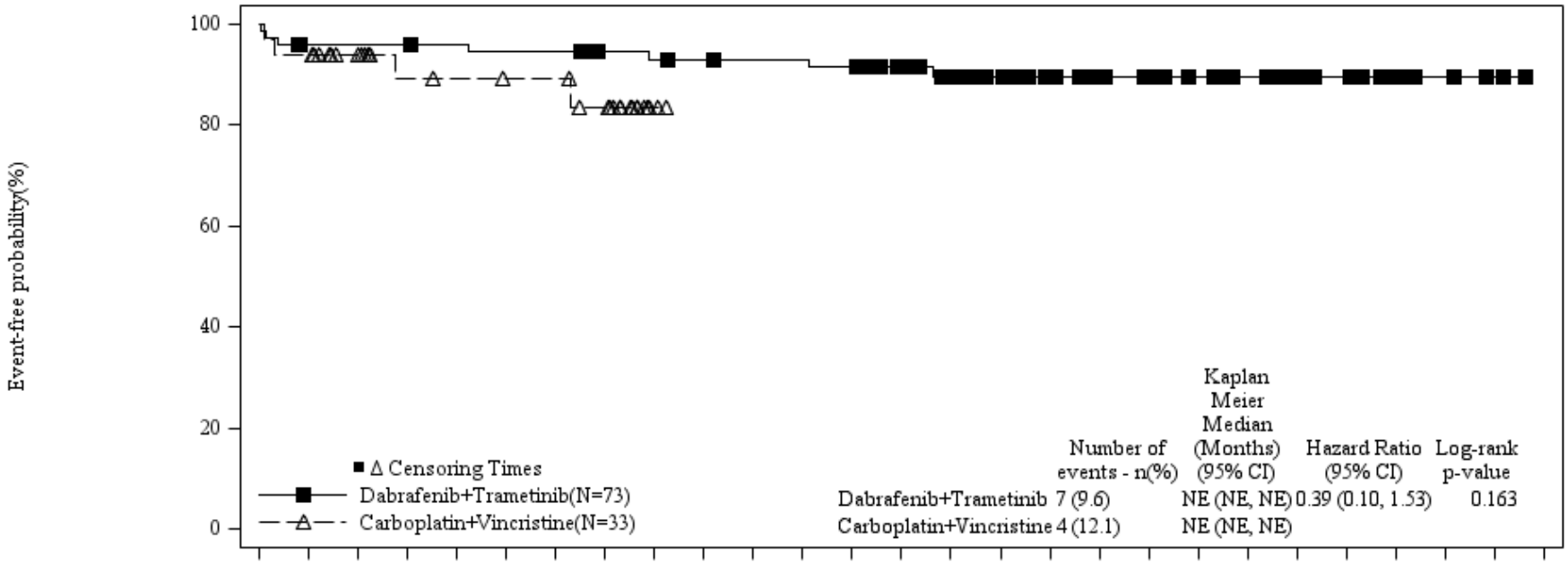
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	67	65	65	64	64	62	60	60	59	57	57	56	51	42	37	30	27	24	22	16	12	10	6	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 45 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Rhinitis



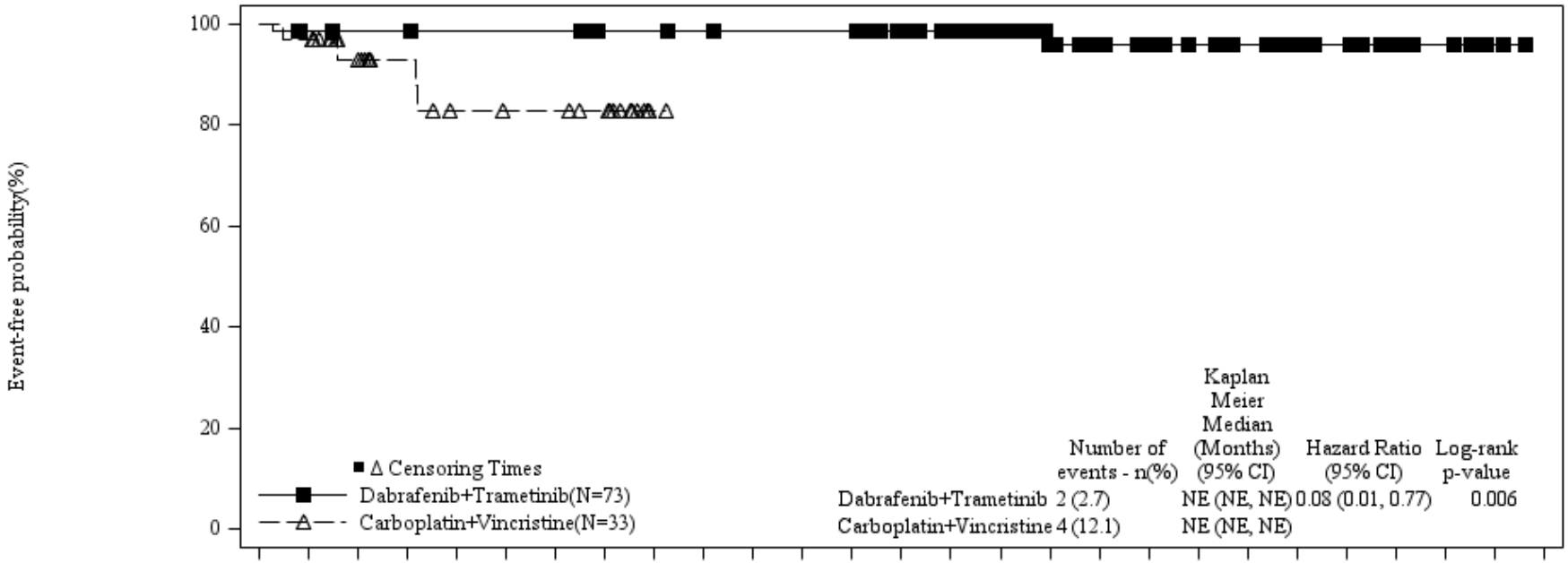
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	68	68	67	66	66	63	62	61	60	60	59	54	46	41	36	31	29	26	18	14	12	7	4	2	0
Carboplatin+Vincristine	33	31	25	19	18	17	17	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 46 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Rhinorrhoea



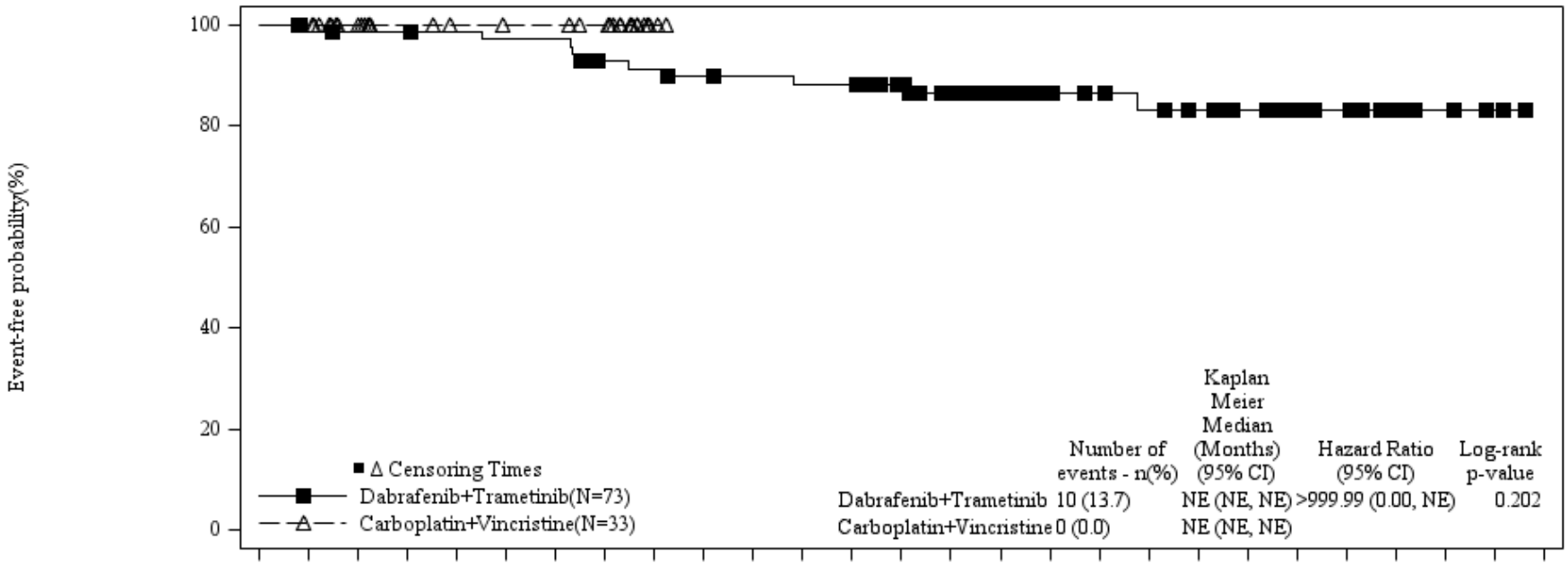
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	69	69	68	68	68	65	65	64	63	63	63	58	51	45	37	31	28	25	18	14	12	7	5	2	0
Carboplatin+Vincristine	33	32	24	18	14	13	13	11	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 47 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Skin papilloma



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	10 (13.7)	NE (NE, NE)	>999.99 (0.00, NE)	0.202
Carboplatin+Vincristine	0 (0.0)	NE (NE, NE)		

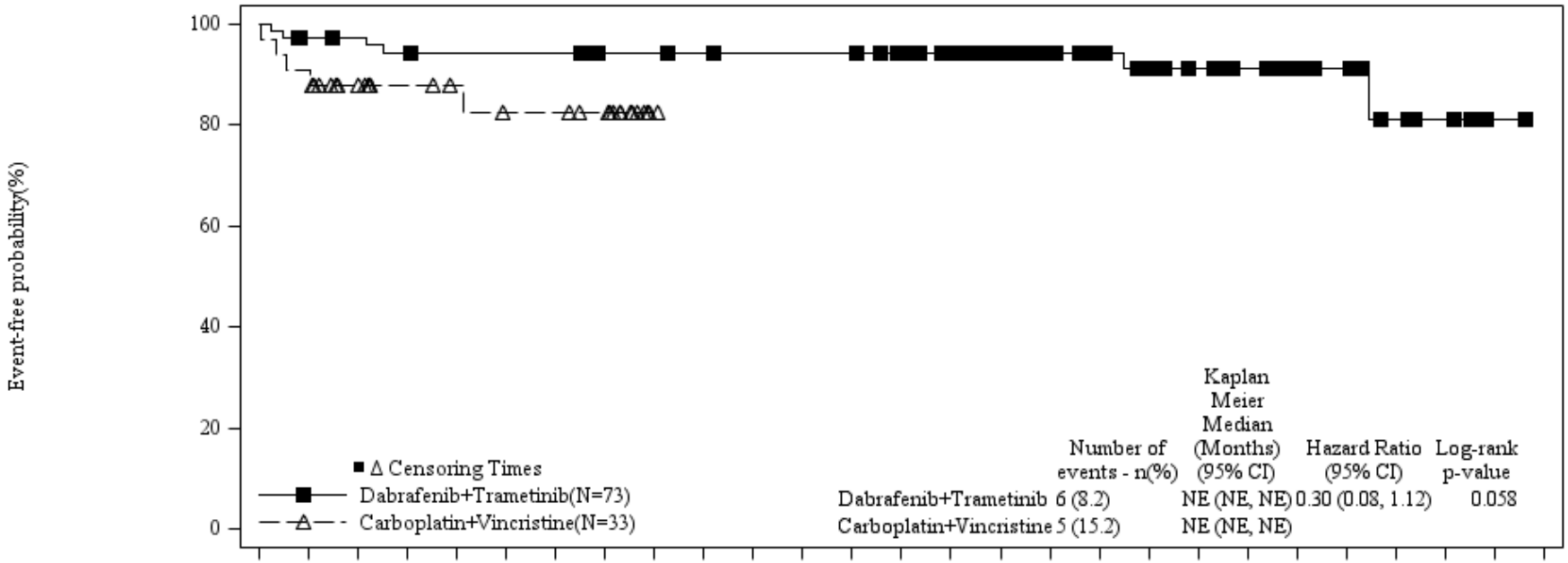
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	69	69	68	67	67	61	60	58	57	56	56	51	43	37	30	28	26	24	18	14	12	7	4	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 48 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Stomatitis



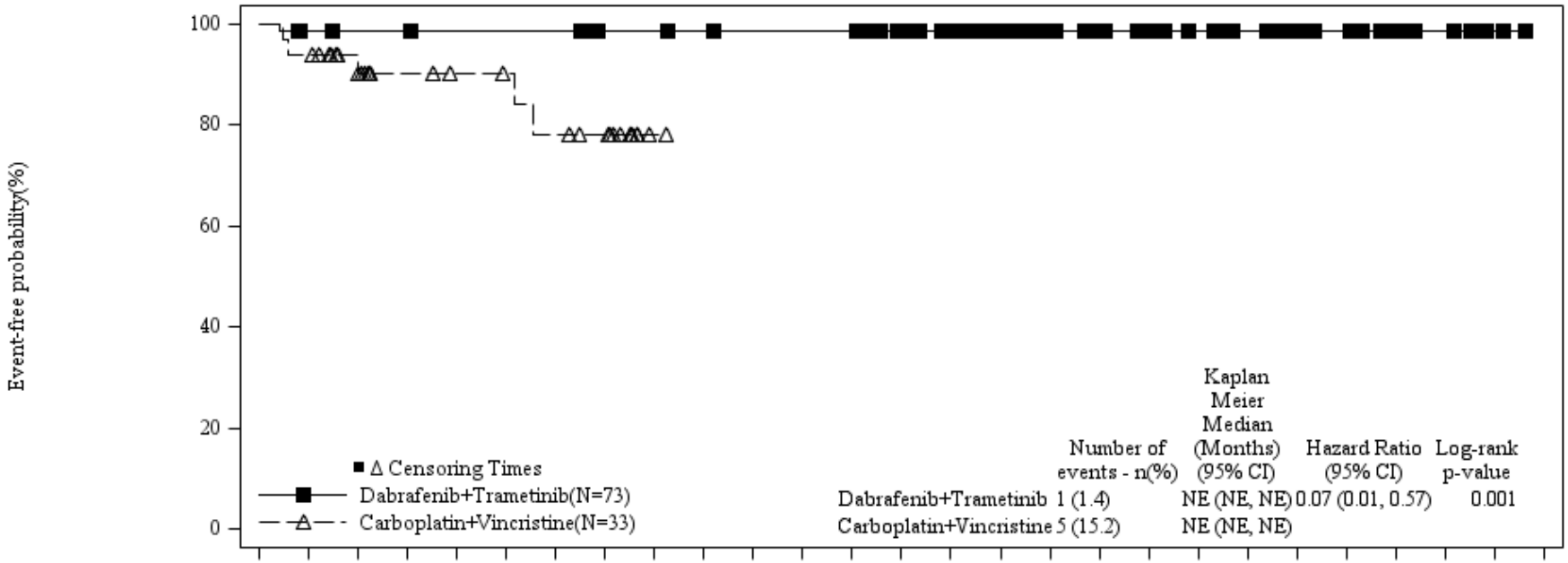
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	68	66	65	65	65	62	62	61	60	60	60	57	50	44	37	31	27	24	18	14	12	7	4	1	0
Carboplatin+Vincristine	33	30	23	18	16	14	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 49 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Thrombocytopenia



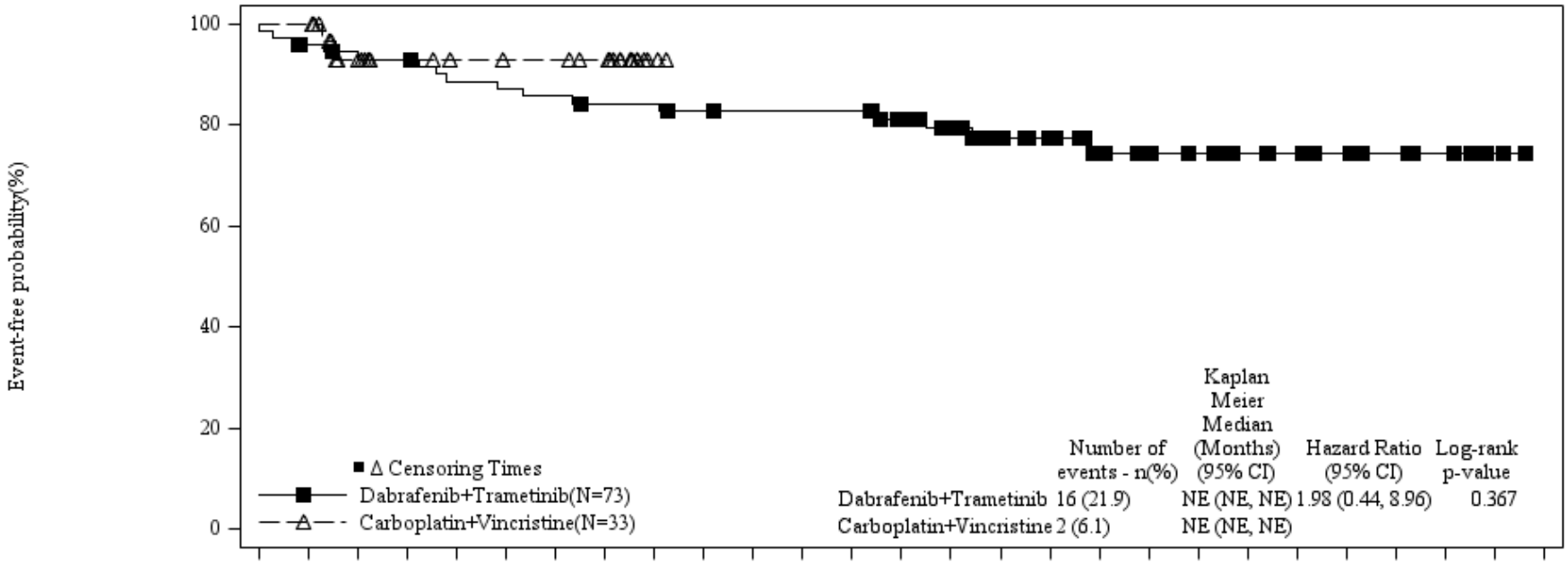
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	69	69	68	68	68	65	65	64	63	63	63	58	51	45	38	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	31	25	18	16	15	13	11	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 50 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Upper respiratory tract infection



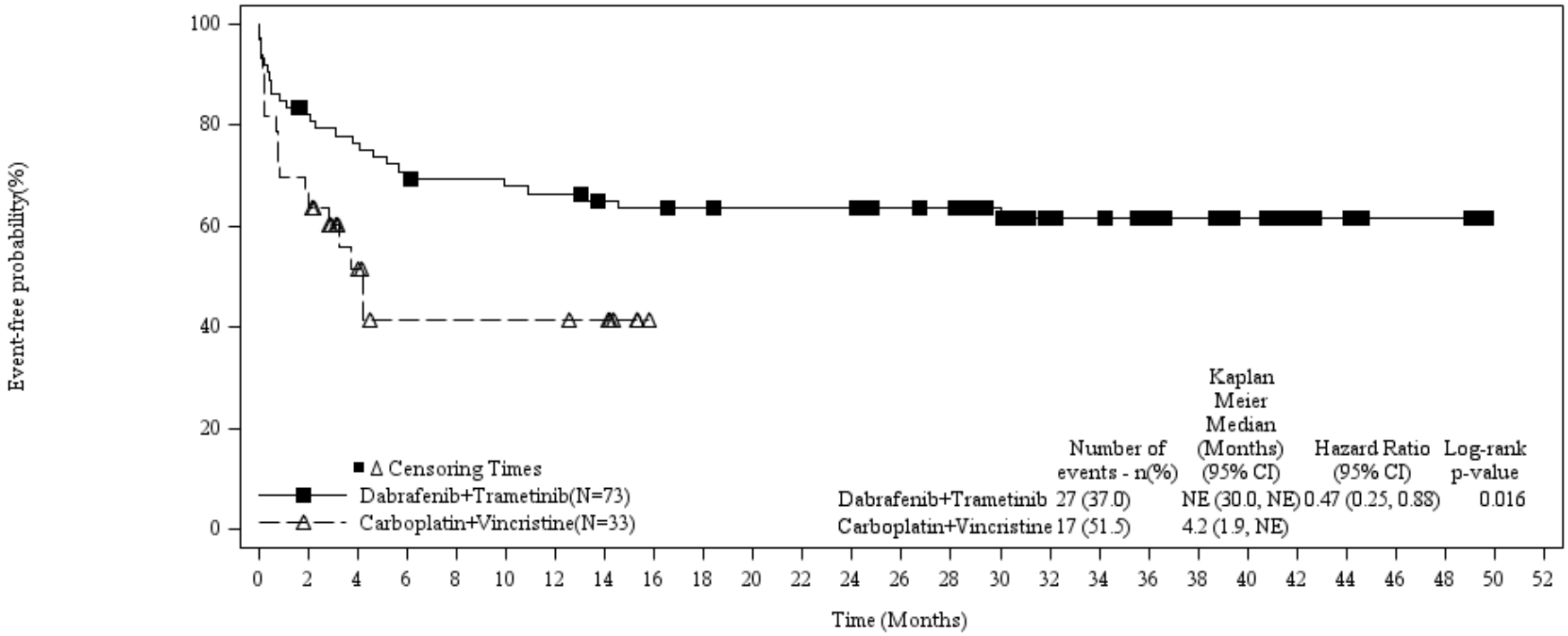
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	65	65	61	60	59	57	57	55	54	54	54	49	41	35	31	24	21	19	13	11	9	7	5	2	0
Carboplatin+Vincristine	33	33	24	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 51 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Vomiting



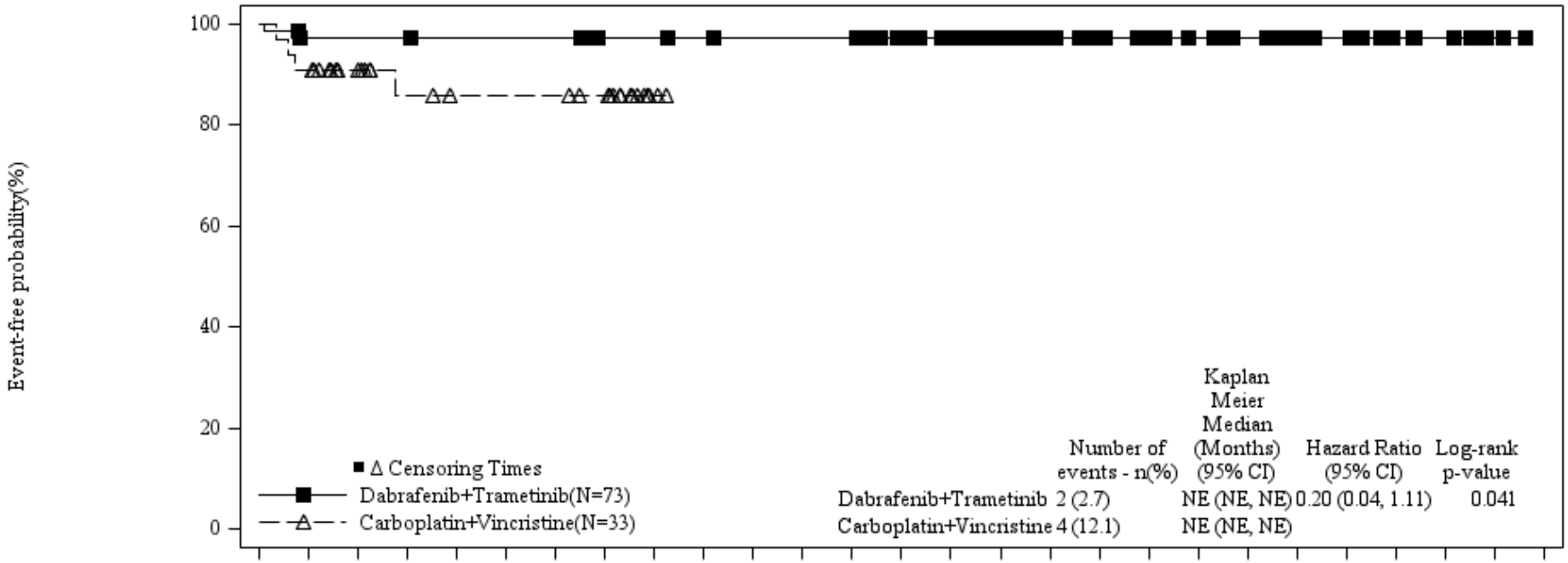
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	58	54	49	48	47	46	43	42	41	40	40	40	37	36	31	24	22	19	17	11	7	5	2	2	0	0
Carboplatin+Vincristine	33	22	12	7	7	7	7	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 52 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Weight decreased



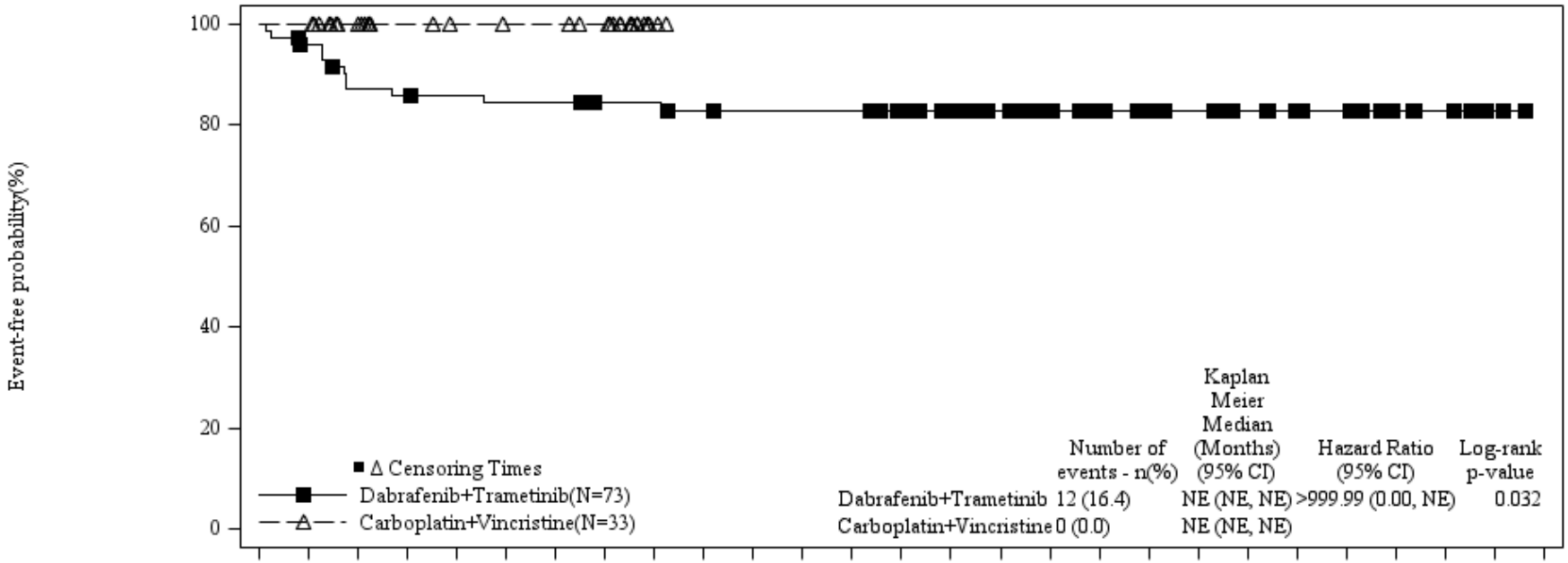
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	69	69	68	68	68	65	65	64	63	63	63	58	51	45	38	32	29	26	18	14	12	7	5	2	0
Carboplatin+Vincristine	33	30	23	17	15	15	15	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 53 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Weight increased



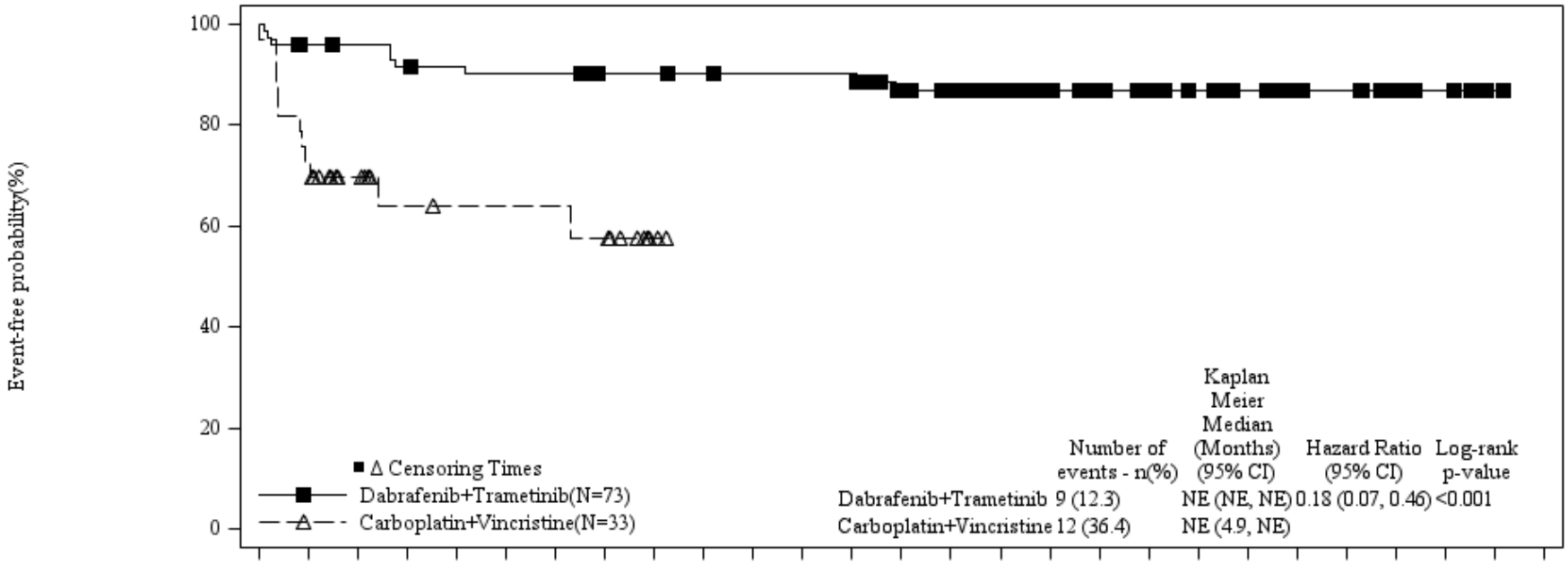
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	61	60	59	58	58	56	56	54	53	53	53	49	44	38	32	27	24	22	15	12	11	7	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-1.3 (Page 54 of 54)
Any AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: White blood cell count decreased



Number of patients still at risk

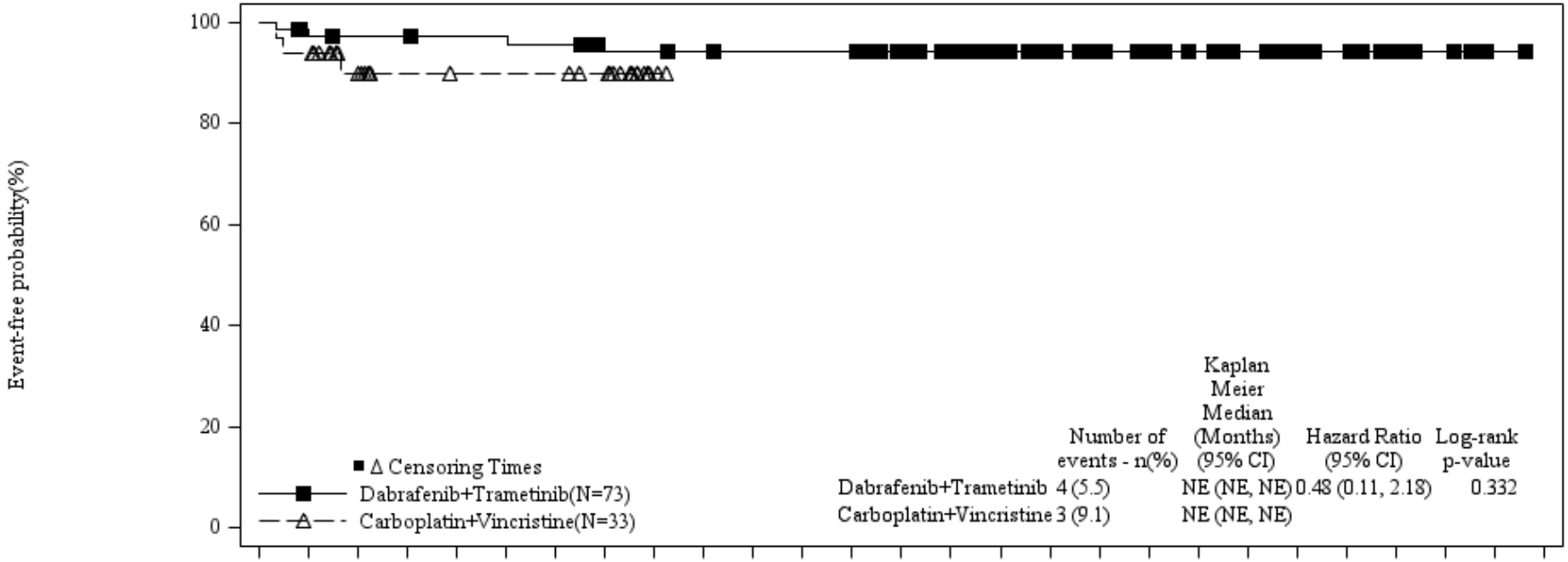
Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	67	64	63	62	62	59	59	58	57	57	57	50	46	40	34	29	26	23	15	11	10	6	4	1	0
Carboplatin+Vincristine	33	24	16	11	10	10	10	9	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 10% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.5. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) nach PT

Figure 4-2.3 (Page 1 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Alanine aminotransferase increased



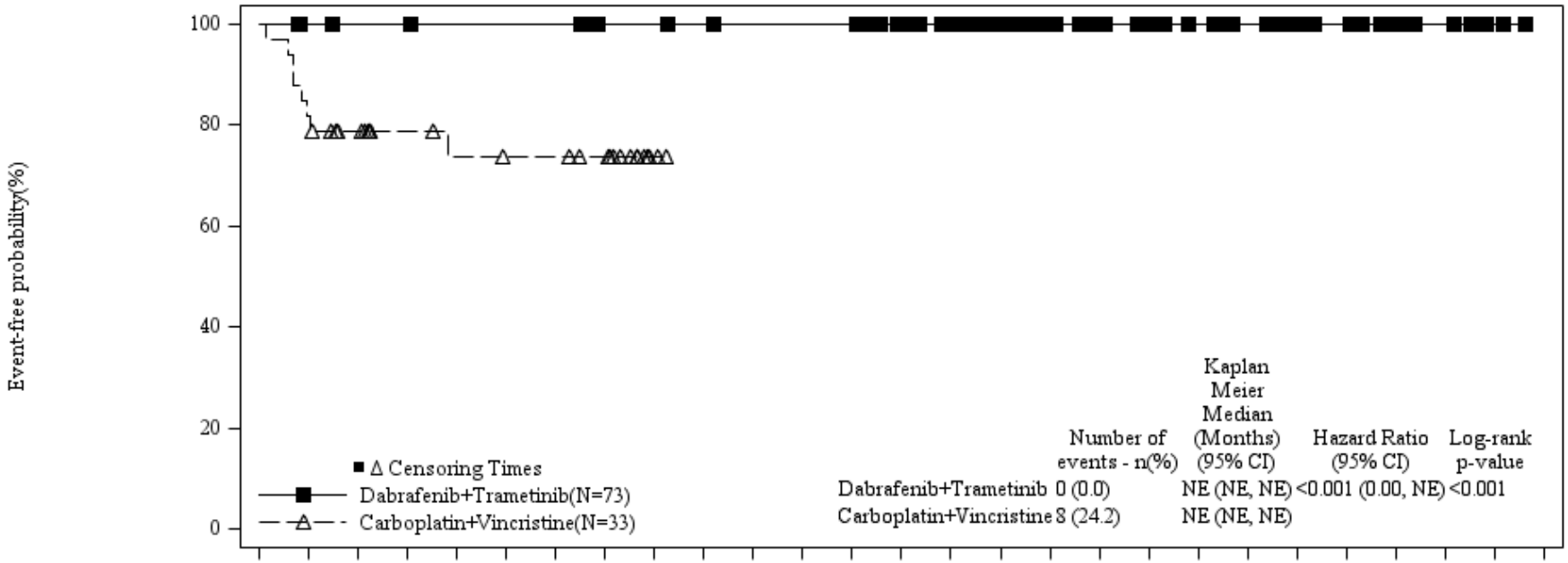
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	68	68	67	67	66	62	62	61	60	60	60	55	49	43	37	31	28	25	18	14	12	7	4	1	0
Carboplatin+Vincristine	33	31	23	17	16	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 2 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Anaemia



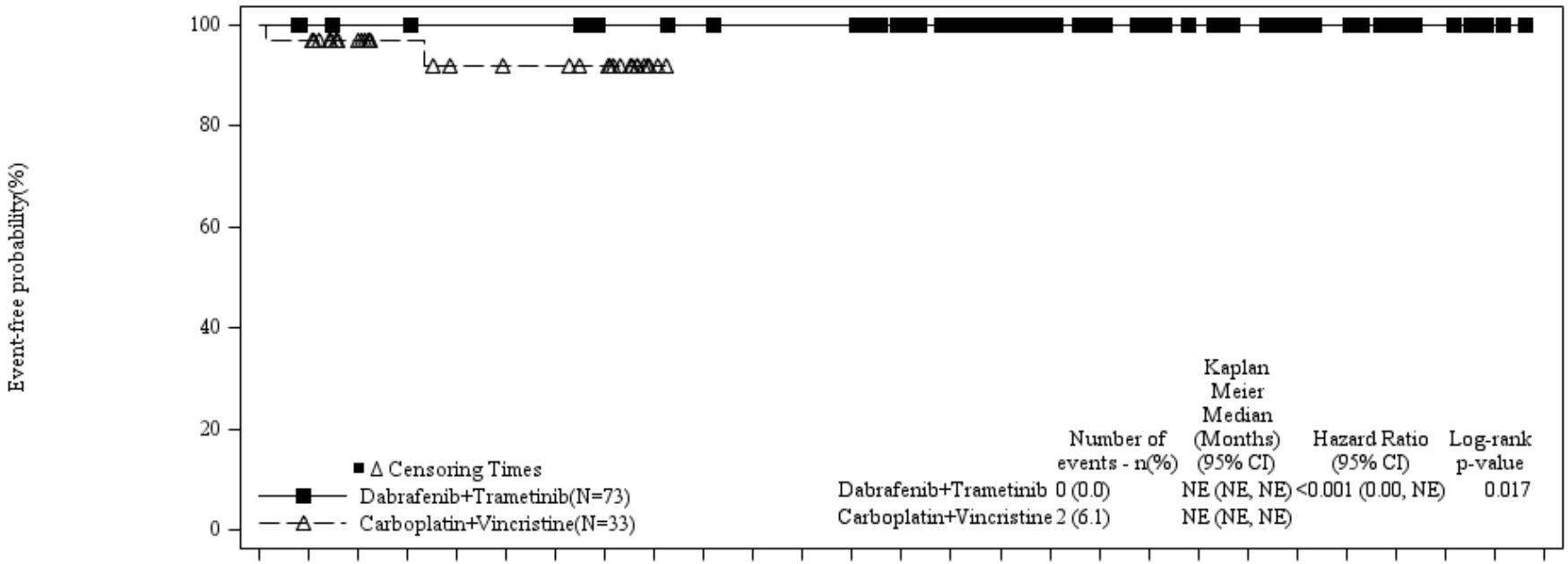
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	27	22	17	15	14	14	12	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 3 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Diarrhoea



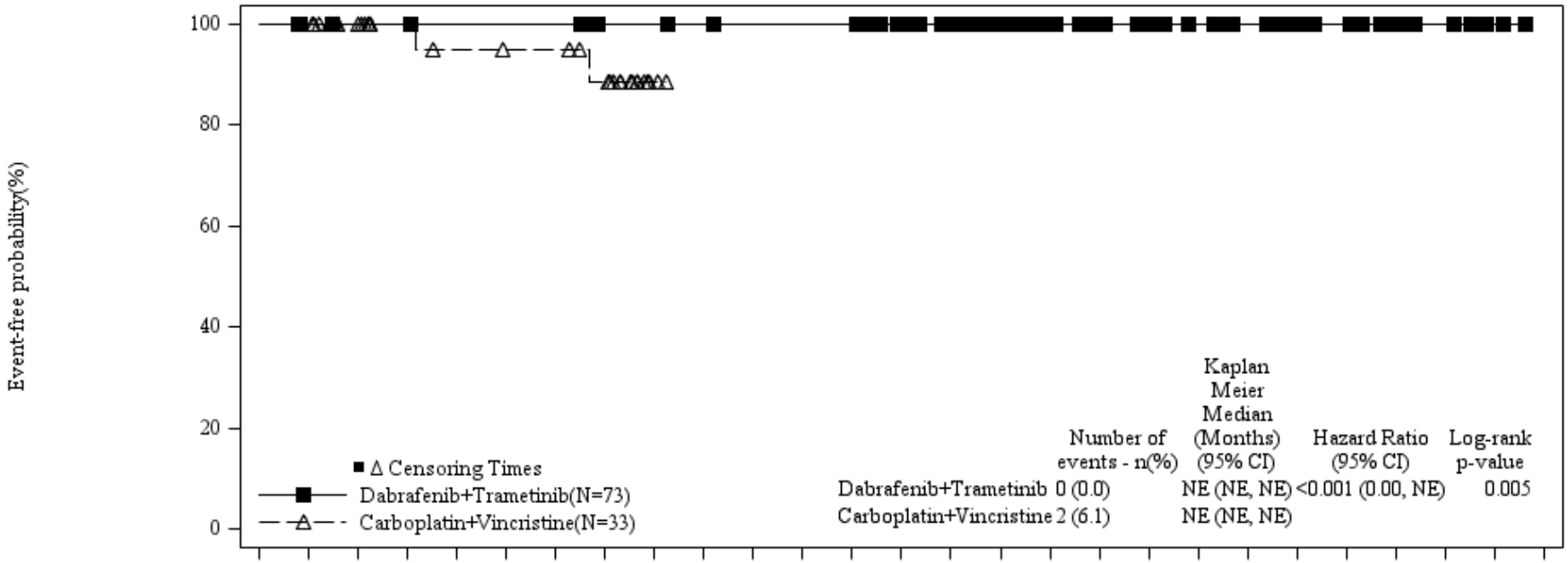
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	25	19	16	15	15	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 4 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Lymphocyte count decreased



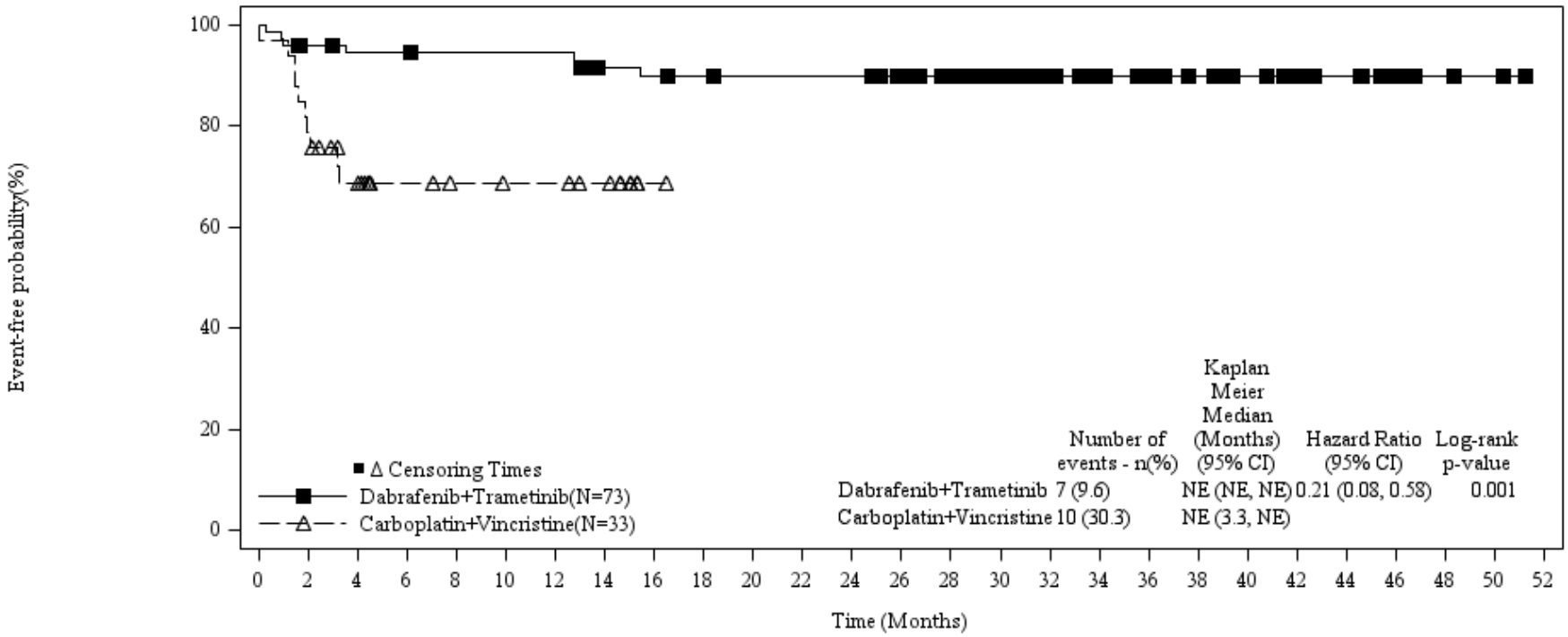
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 5 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Neutropenia



	Number of events - n(%)	Kaplan Meier Median (Months) (95% CI)	Hazard Ratio (95% CI)	Log-rank p-value
Dabrafenib+Trametinib	7 (9.6)	NE (NE, NE)	0.21 (0.08, 0.58)	0.001
Carboplatin+Vincristine	10 (30.3)	NE (3.3, NE)		

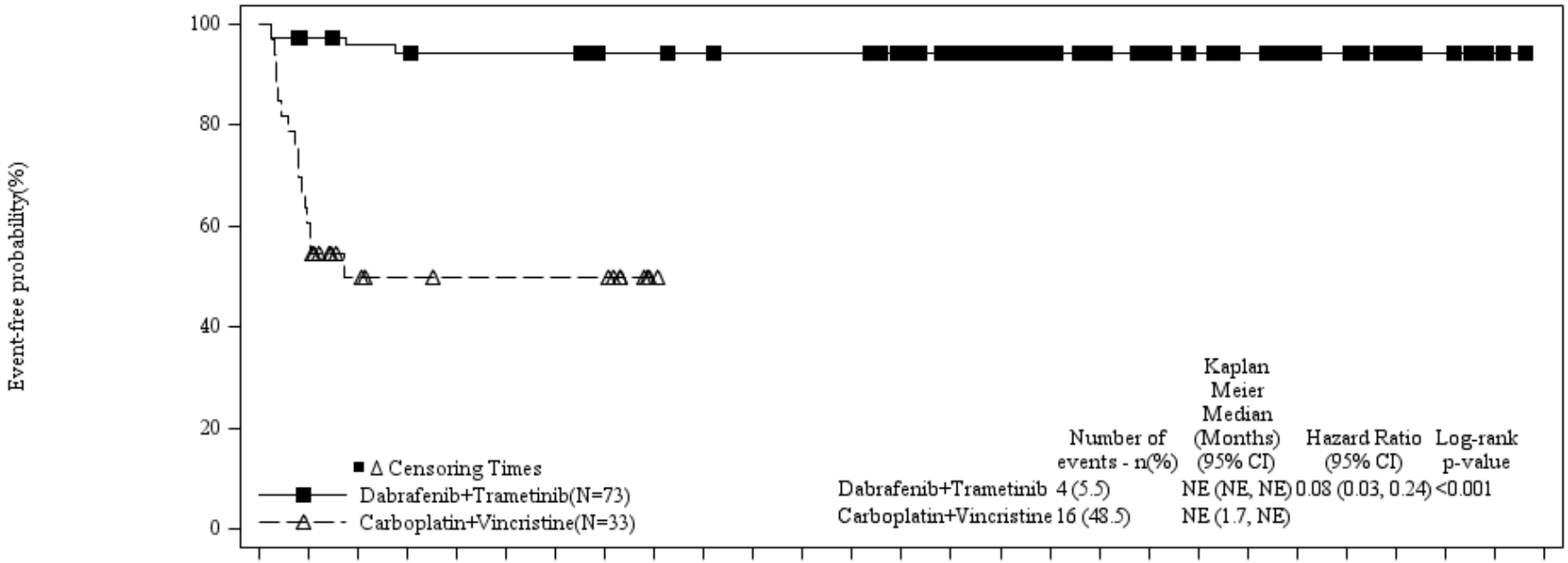
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	68	66	66	65	65	65	60	59	58	57	57	57	54	47	41	34	28	25	22	15	12	10	6	3	2	0
Carboplatin+Vincristine	33	26	19	13	11	10	10	8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 6 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Neutrophil count decreased



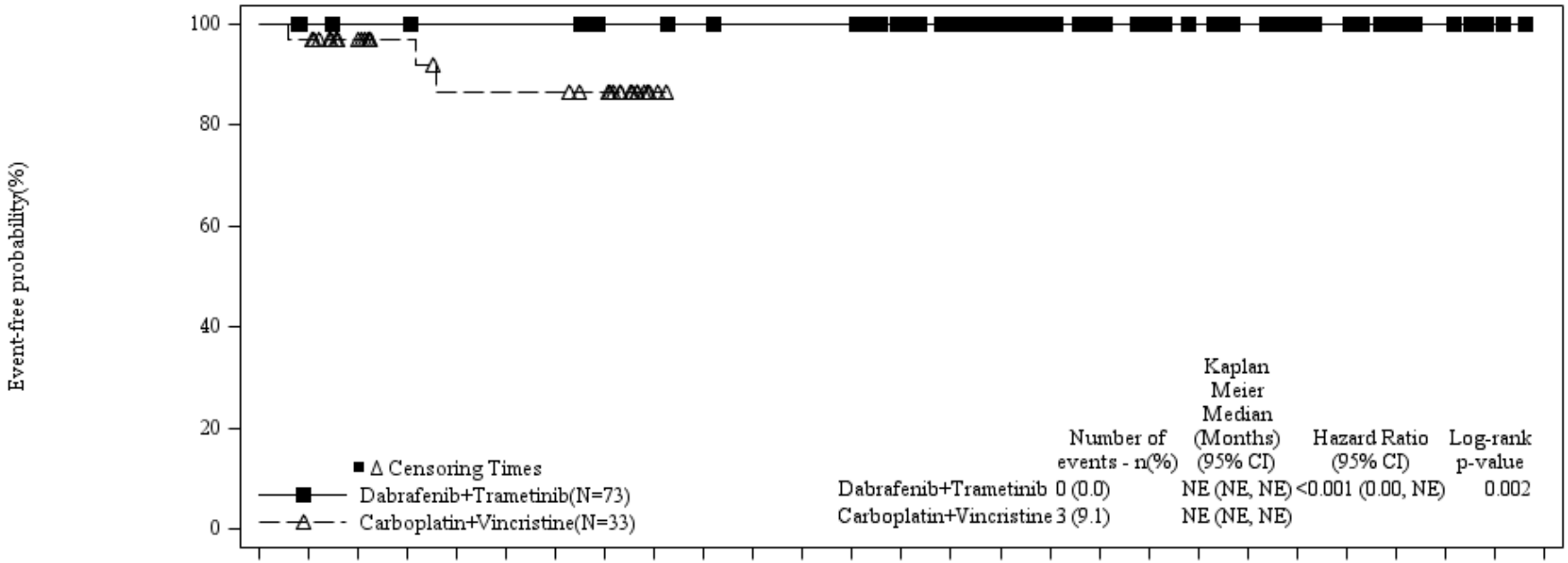
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	66	65	65	65	62	62	61	60	60	60	56	50	44	38	32	29	26	18	14	12	7	5	2	0
Carboplatin+Vincristine	33	20	11	9	8	8	8	8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 7 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Platelet count decreased



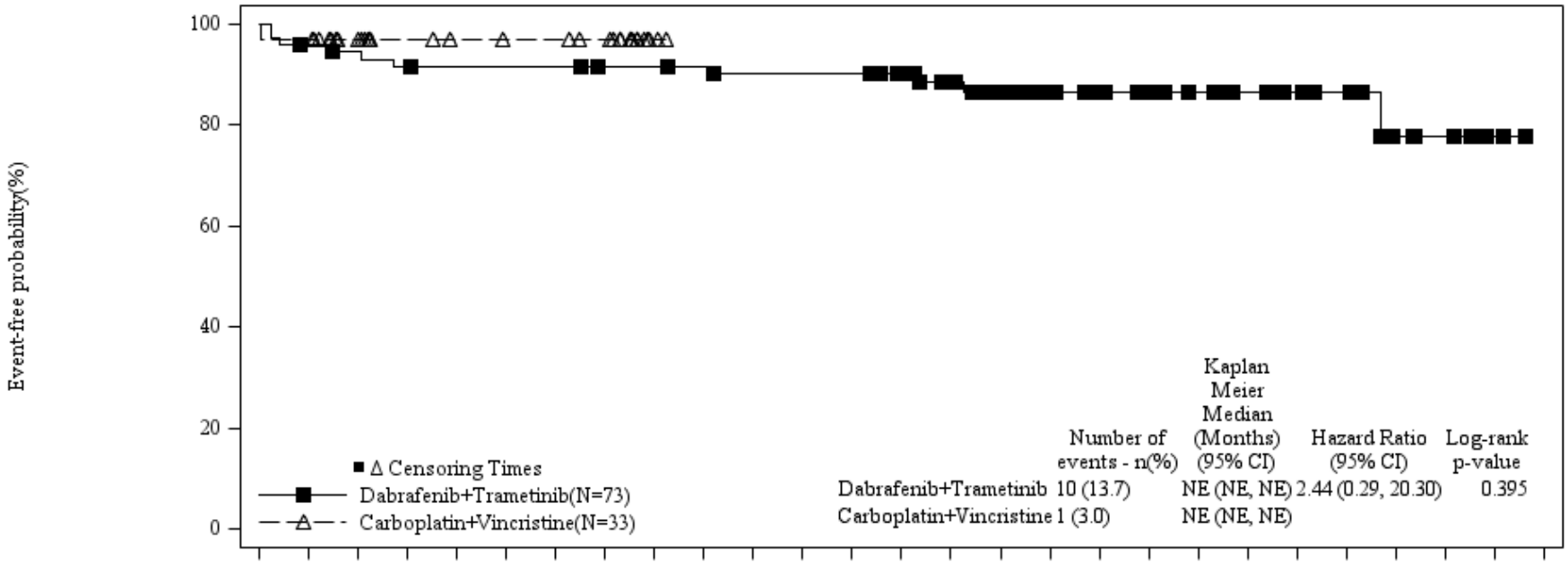
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	25	19	16	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 8 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pyrexia



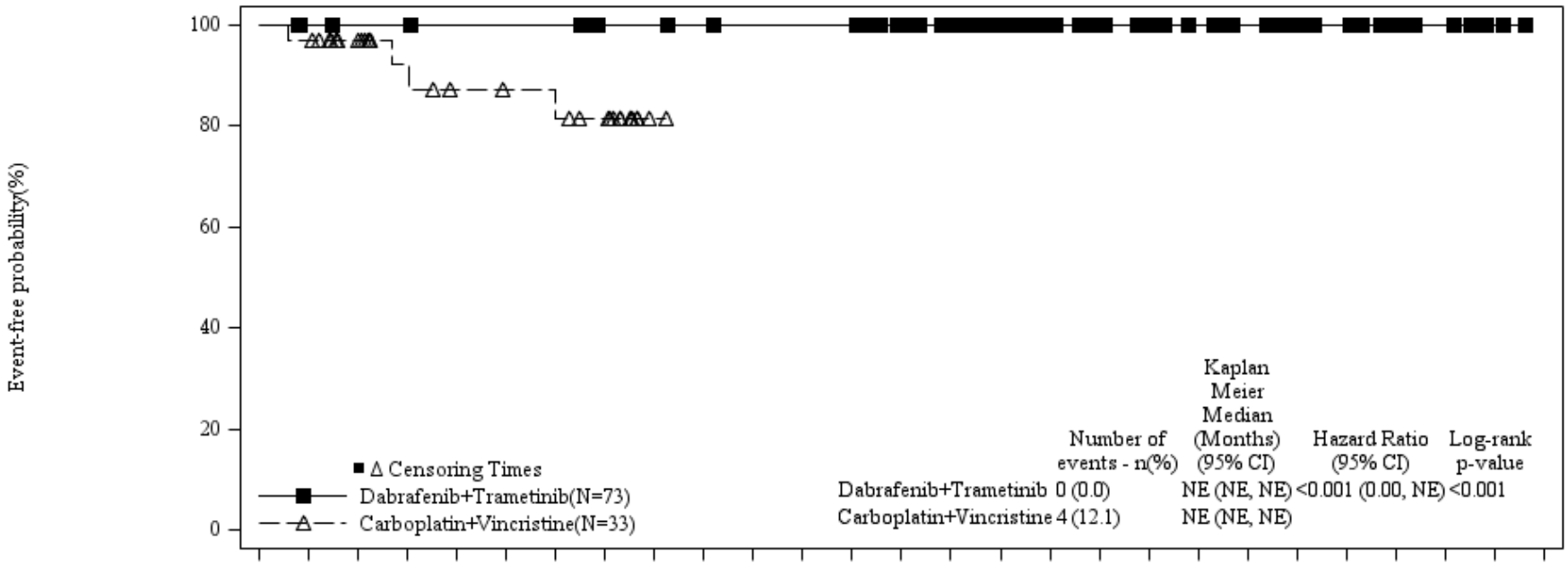
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	69	67	65	64	64	64	62	62	61	59	59	59	55	47	41	34	30	27	24	18	15	13	7	5	2	0
Carboplatin+Vincristine	33	32	25	19	17	16	16	14	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 9 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Thrombocytopenia



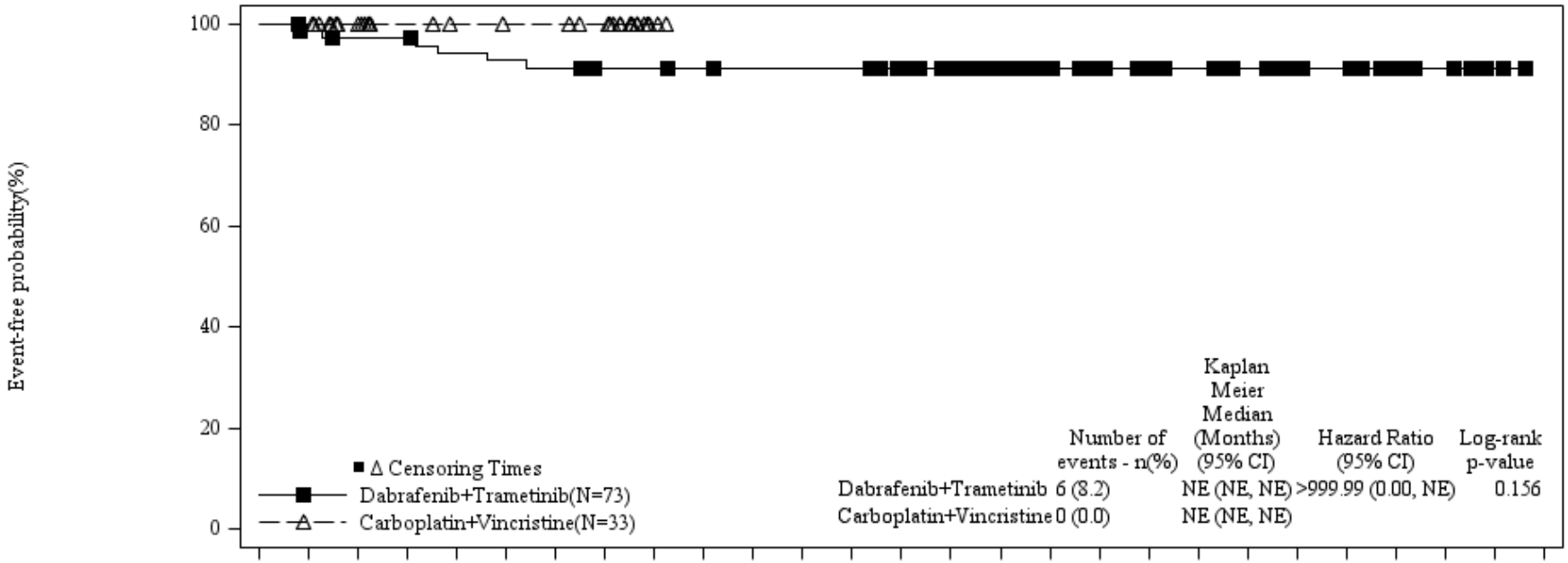
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	32	26	19	16	15	14	12	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 10 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Weight increased



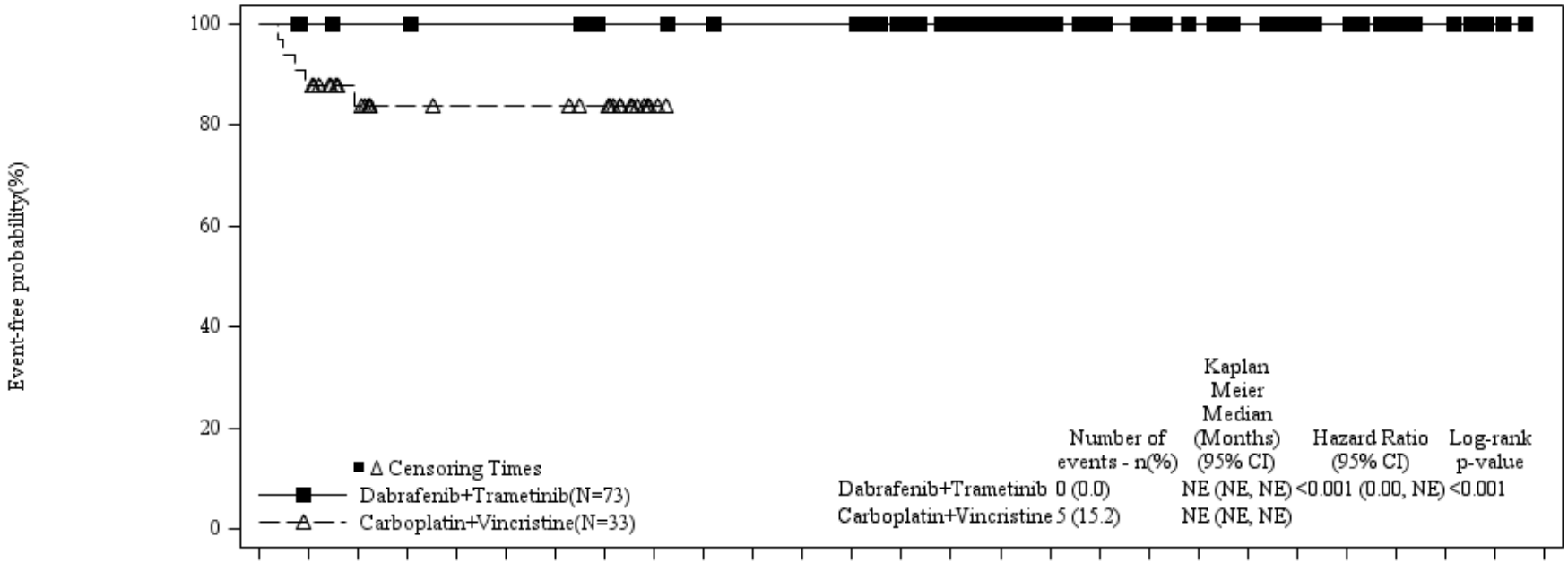
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	70	68	68	65	64	63	61	61	60	59	59	59	55	48	42	35	30	27	25	18	14	13	8	5	2	0
Carboplatin+Vincristine	33	33	26	20	18	17	17	15	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

Figure 4-2.3 (Page 11 of 11)
Grade >= 3 AE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: White blood cell count decreased



Number of patients still at risk

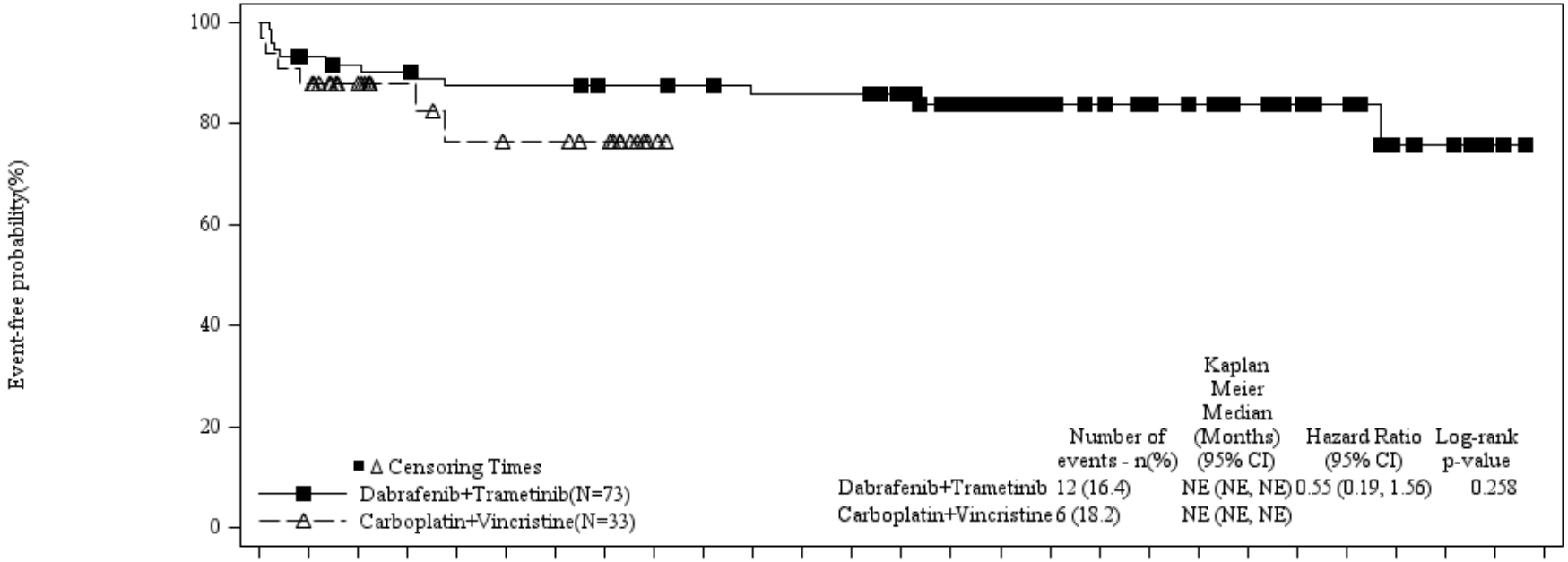
Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	71	70	70	69	69	69	66	66	65	64	64	64	59	52	46	39	33	30	27	19	15	13	8	5	2	0
Carboplatin+Vincristine	33	29	21	16	15	15	15	13	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.6. Schwerwiegende unerwünschte Ereignisse nach PT

Figure 4-3.3 (Page 1 of 1)
SAE by PT: Kaplan Meier plot of time to first event
Safety Set - L

Time to first PT: Pyrexia



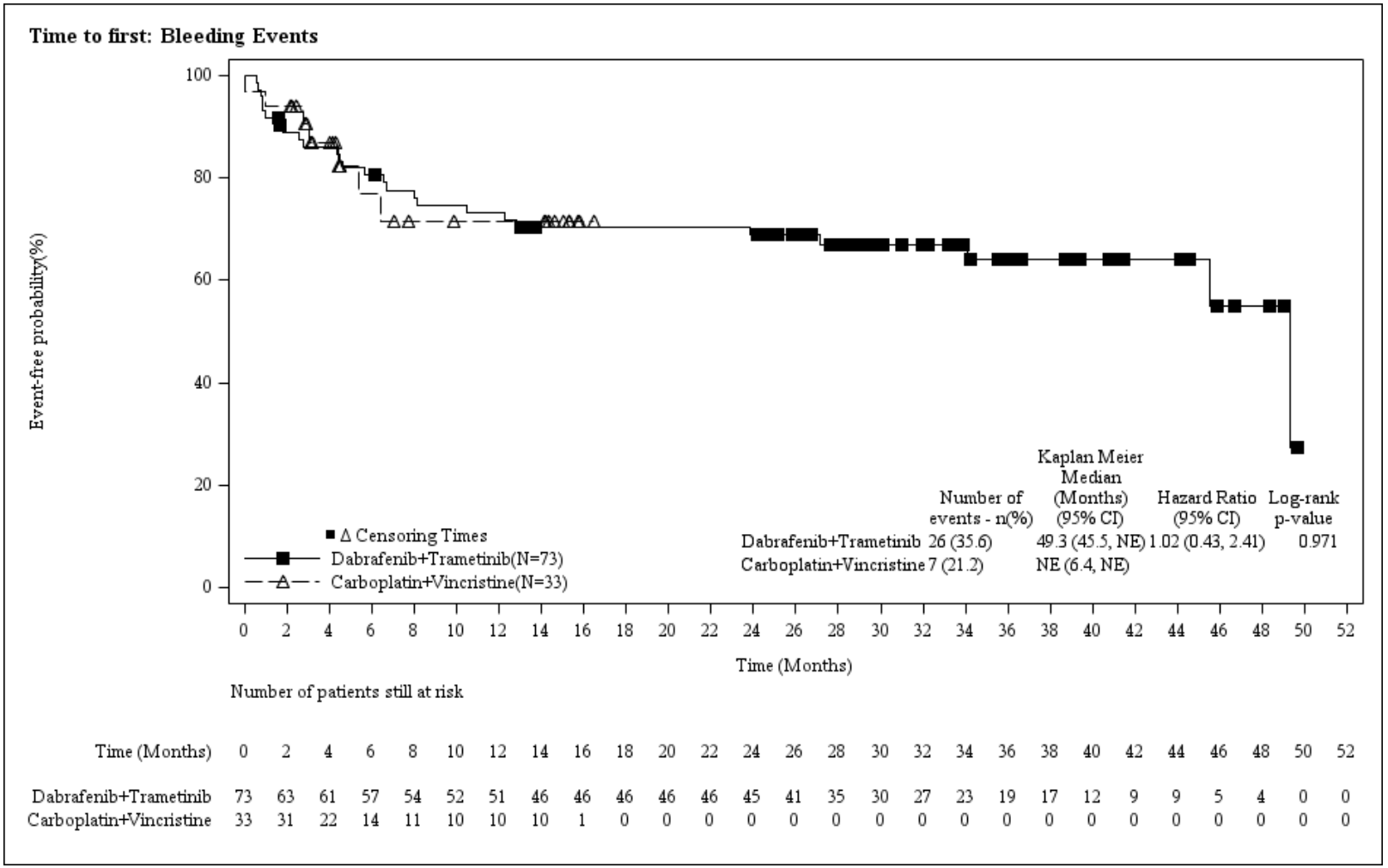
Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
Dabrafenib+Trametinib	73	66	64	63	60	60	60	58	58	57	55	55	55	51	43	37	30	27	24	22	16	14	12	7	5	2	0
Carboplatin+Vincristine	33	29	22	16	13	12	12	10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

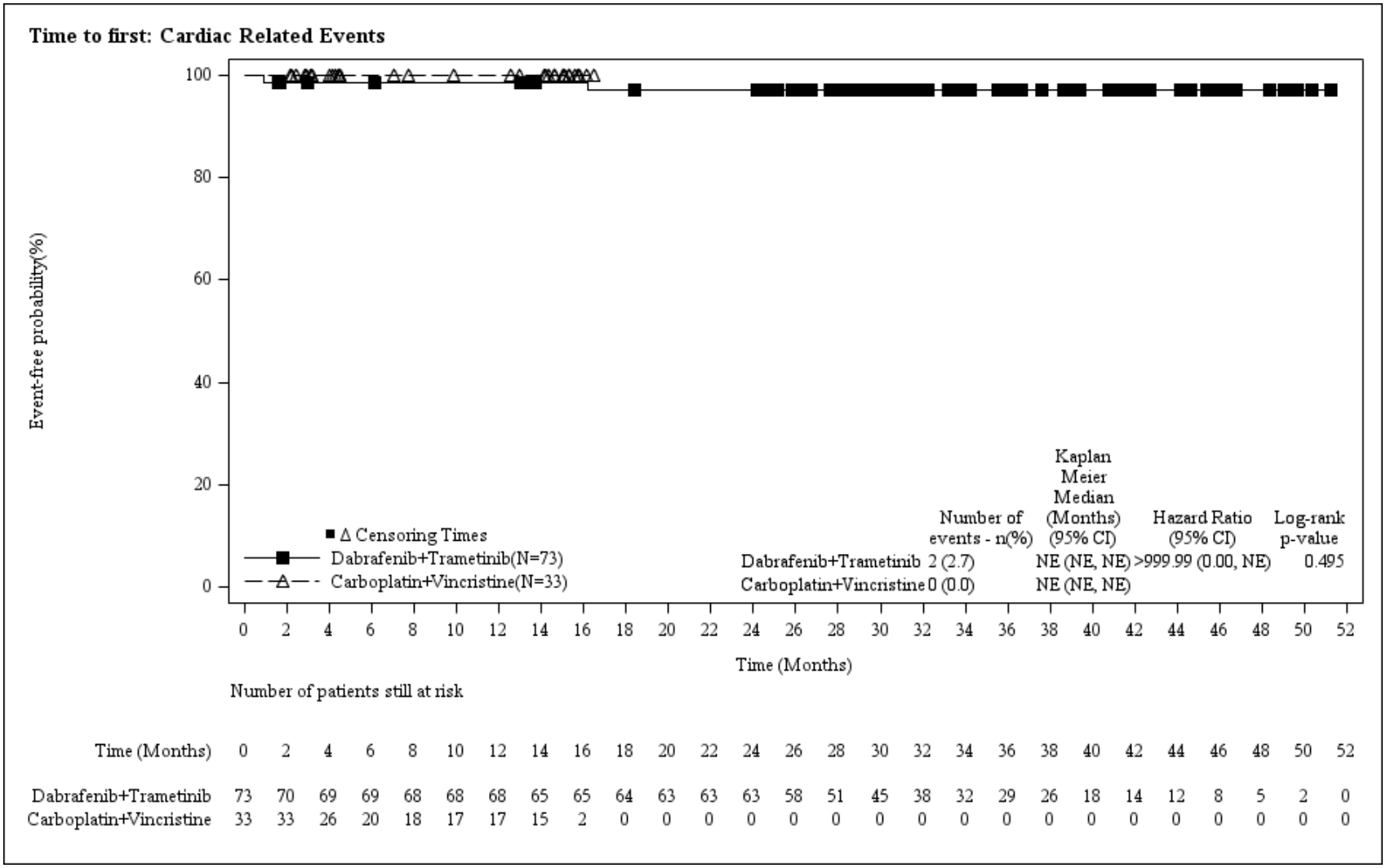
Only events are displayed that occurred in at least 5% of patients in at least one of the treatment arms OR in at least 10 patients and in at least 1% of patients in one treatment arm.

2.3.7. Unerwünschte Ereignisse von besonderem Interesse (AESI)

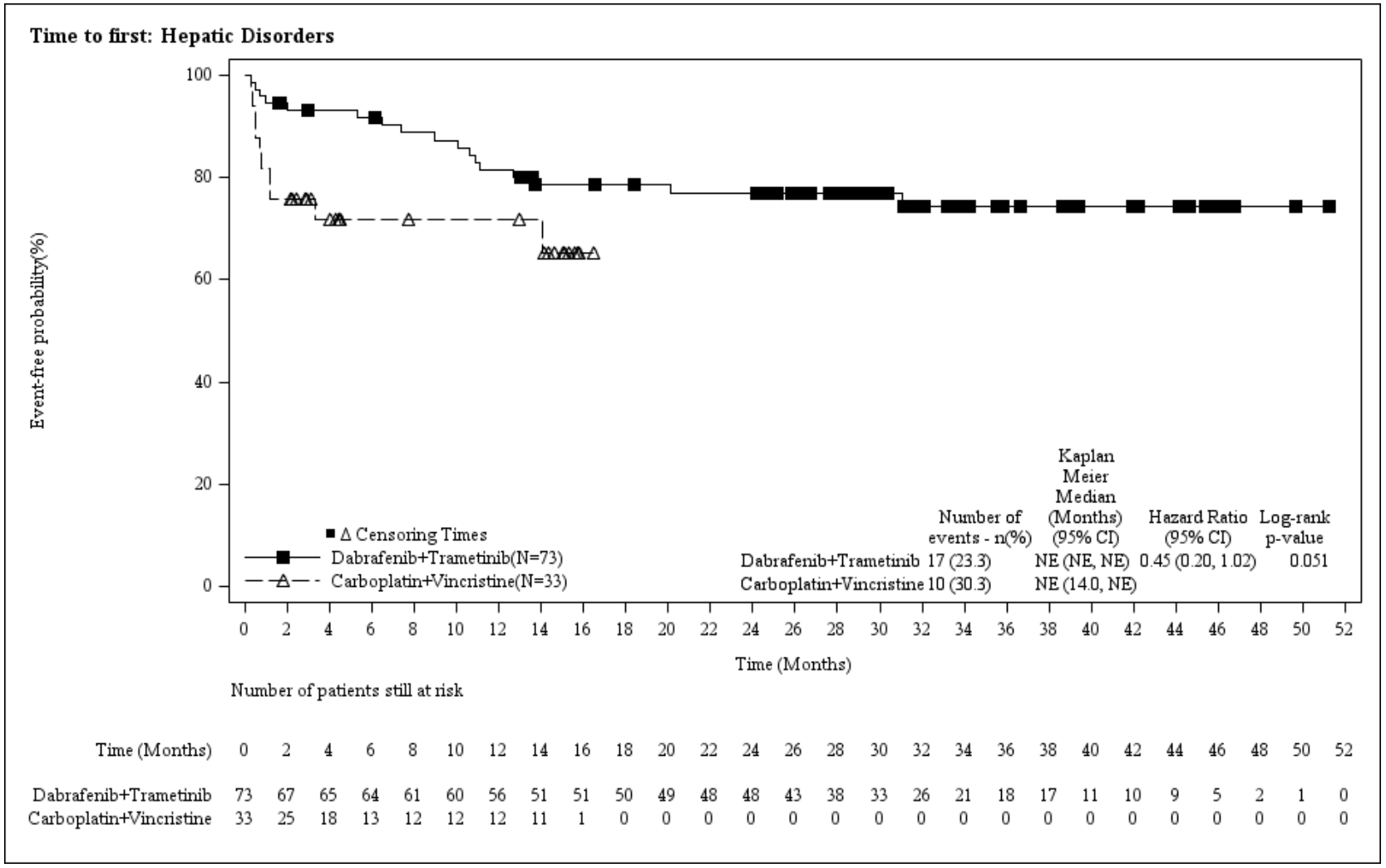
AESI: Kaplan Meier plot of time to first event
Safety Set – L



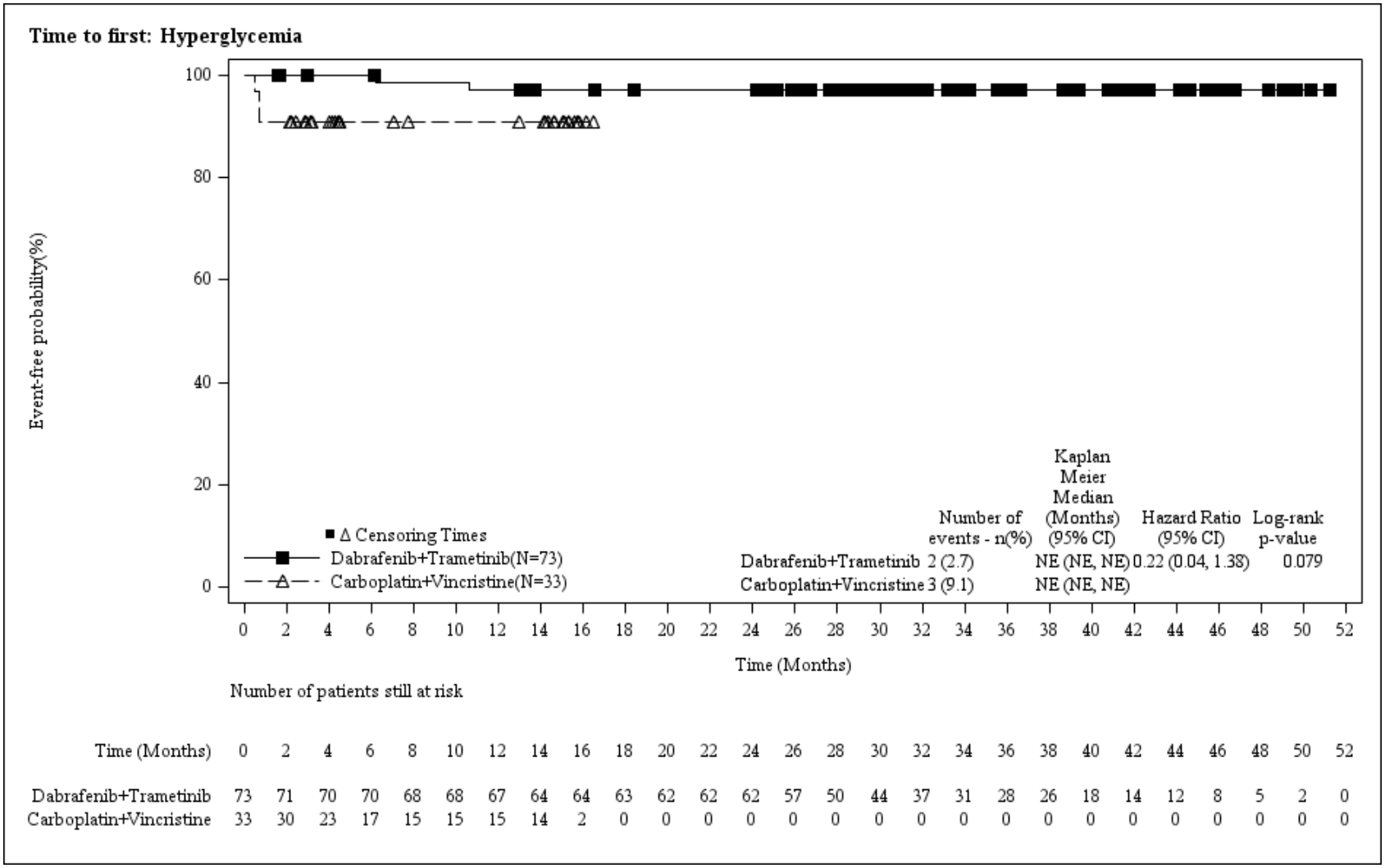
AESI: Kaplan Meier plot of time to first event
Safety Set – L



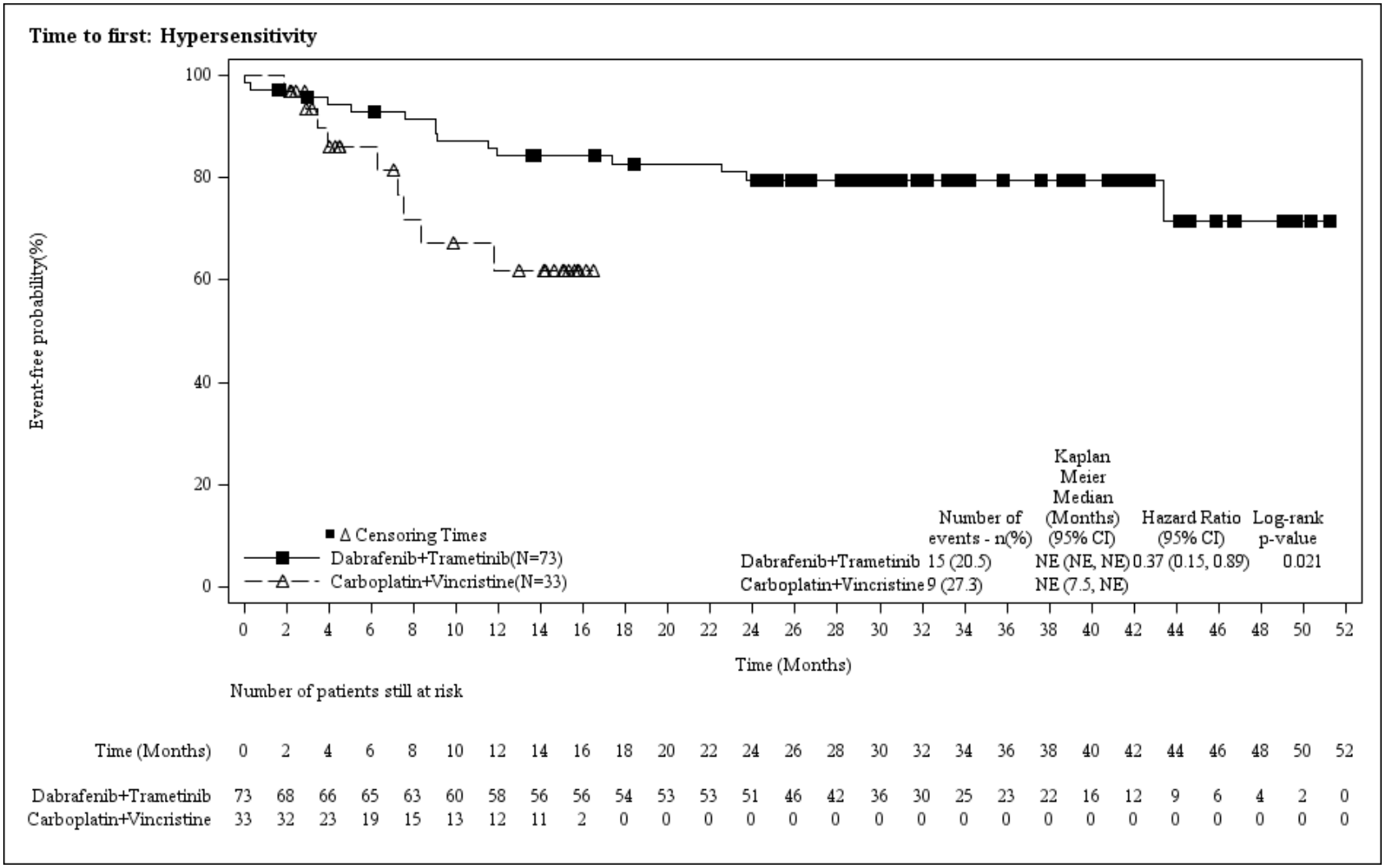
AESI: Kaplan Meier plot of time to first event
Safety Set – L



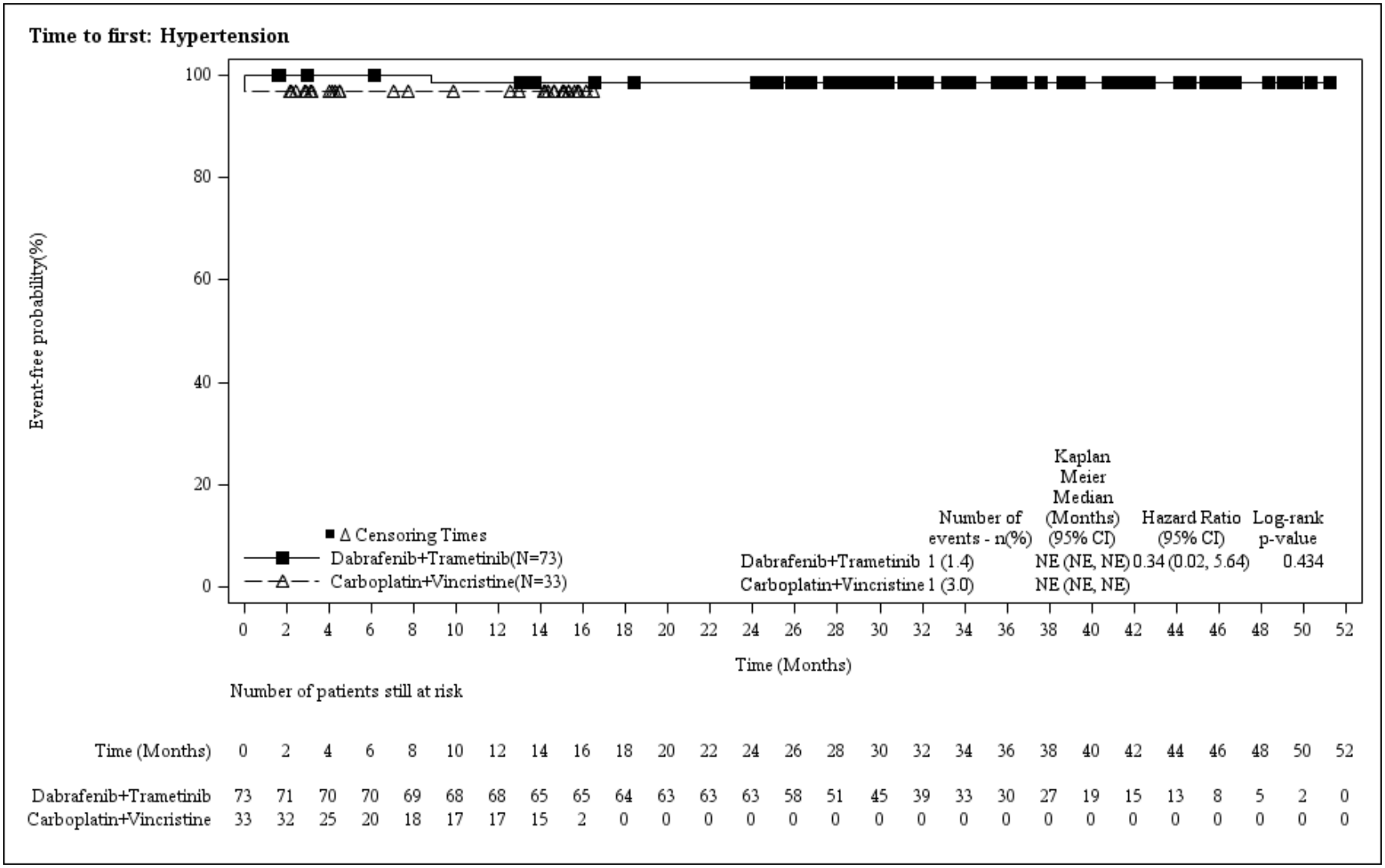
AESI: Kaplan Meier plot of time to first event
Safety Set – L



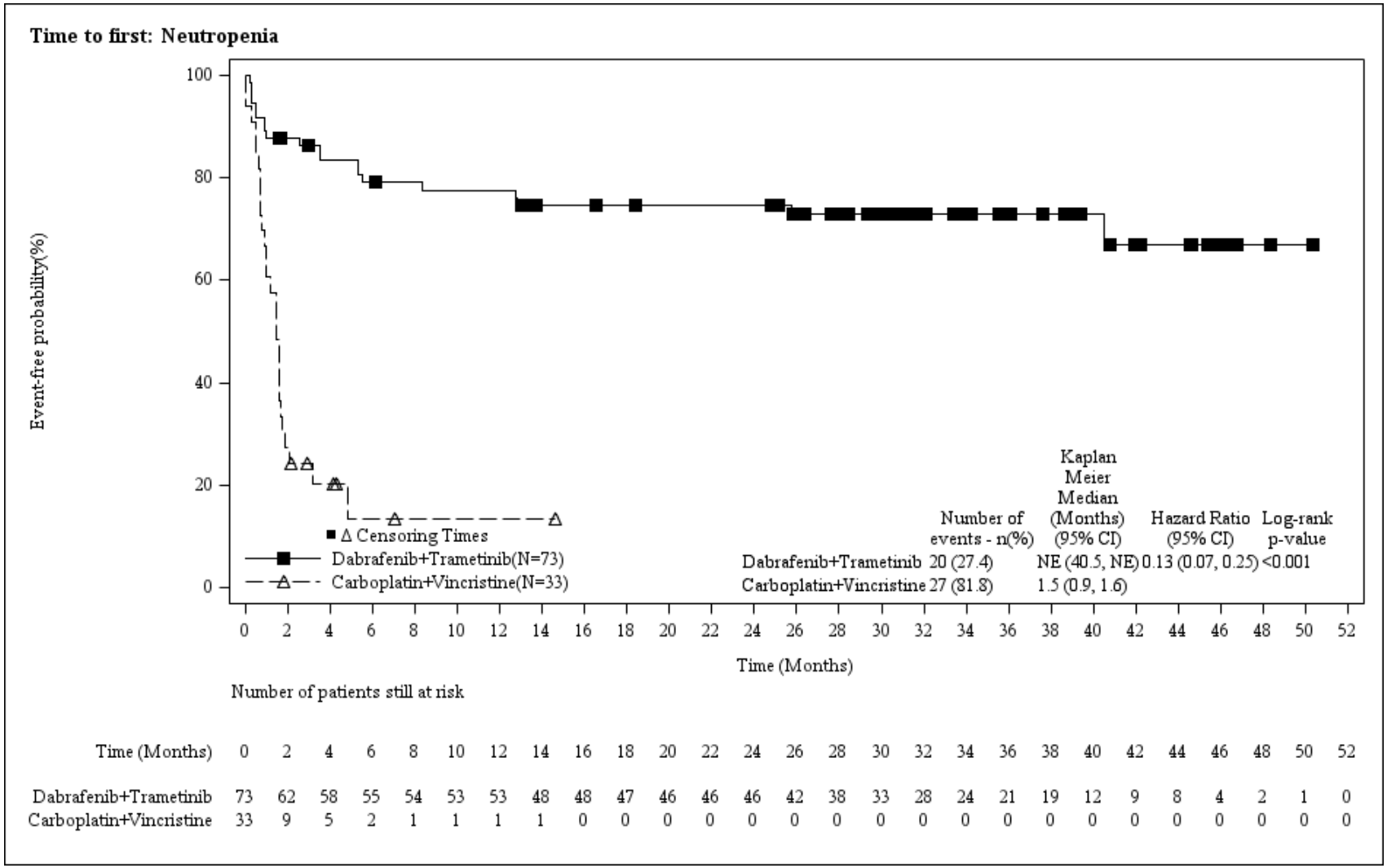
AESI: Kaplan Meier plot of time to first event
Safety Set – L



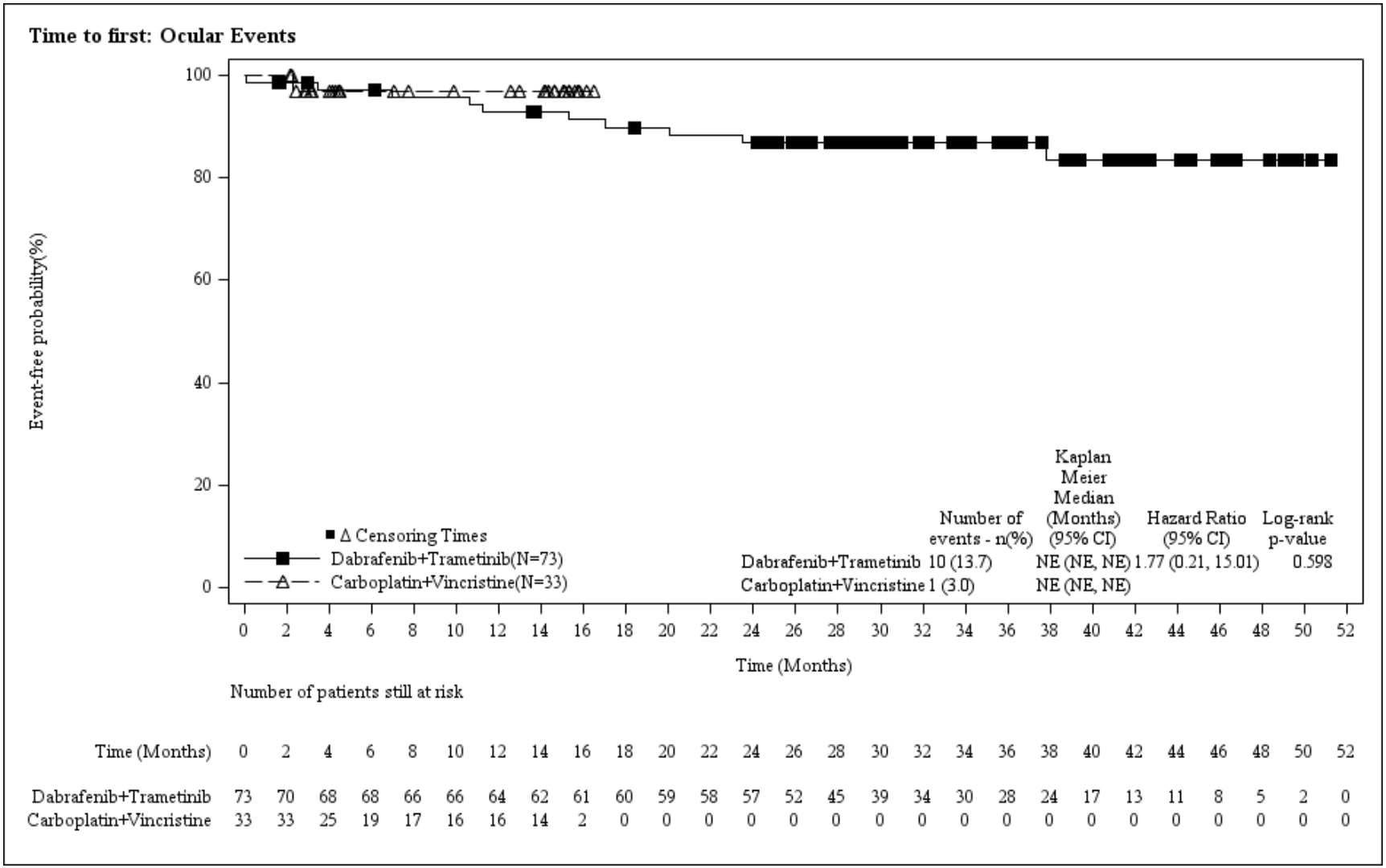
AESI: Kaplan Meier plot of time to first event
Safety Set – L



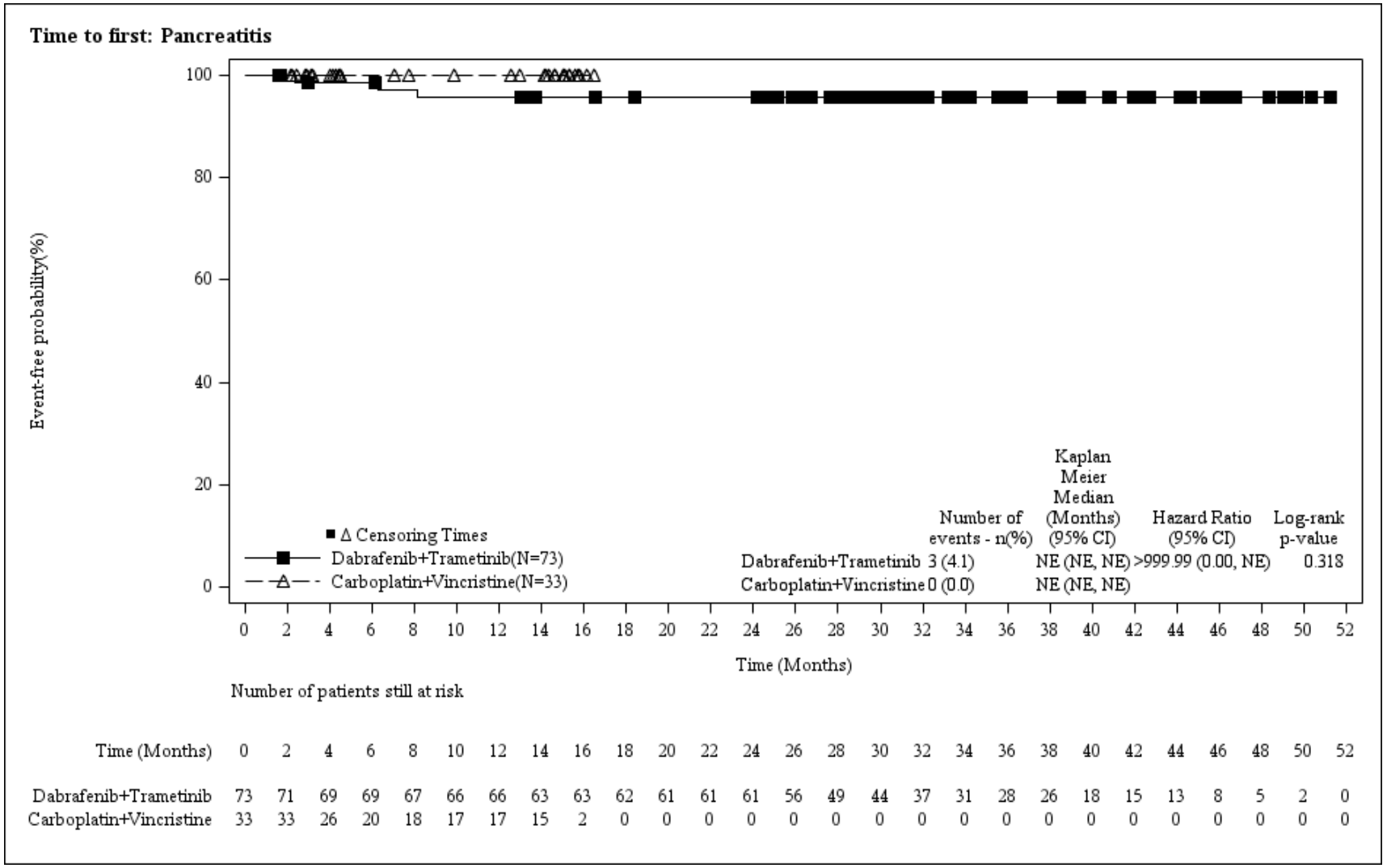
AESI: Kaplan Meier plot of time to first event
Safety Set – L



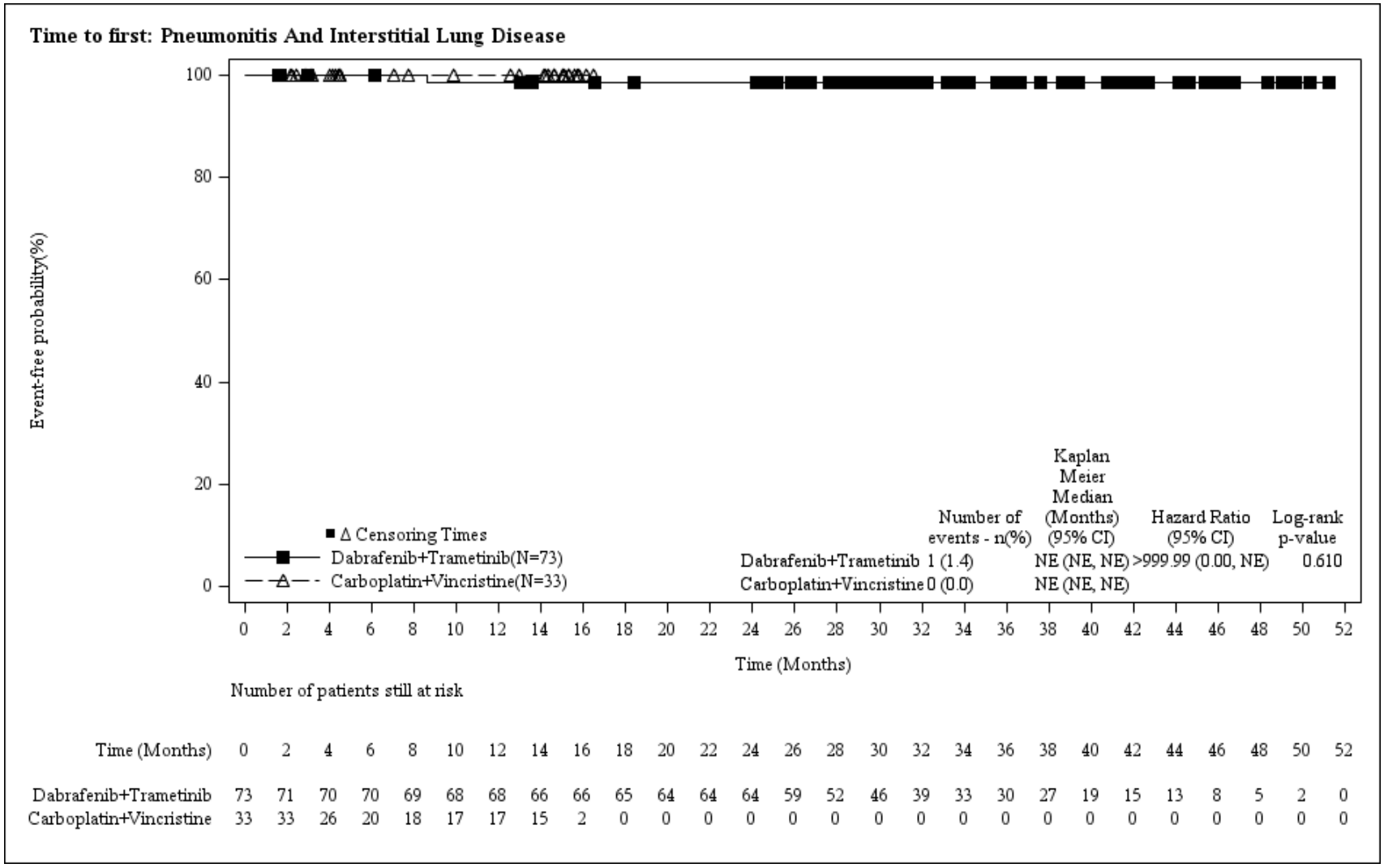
AESI: Kaplan Meier plot of time to first event
Safety Set – L



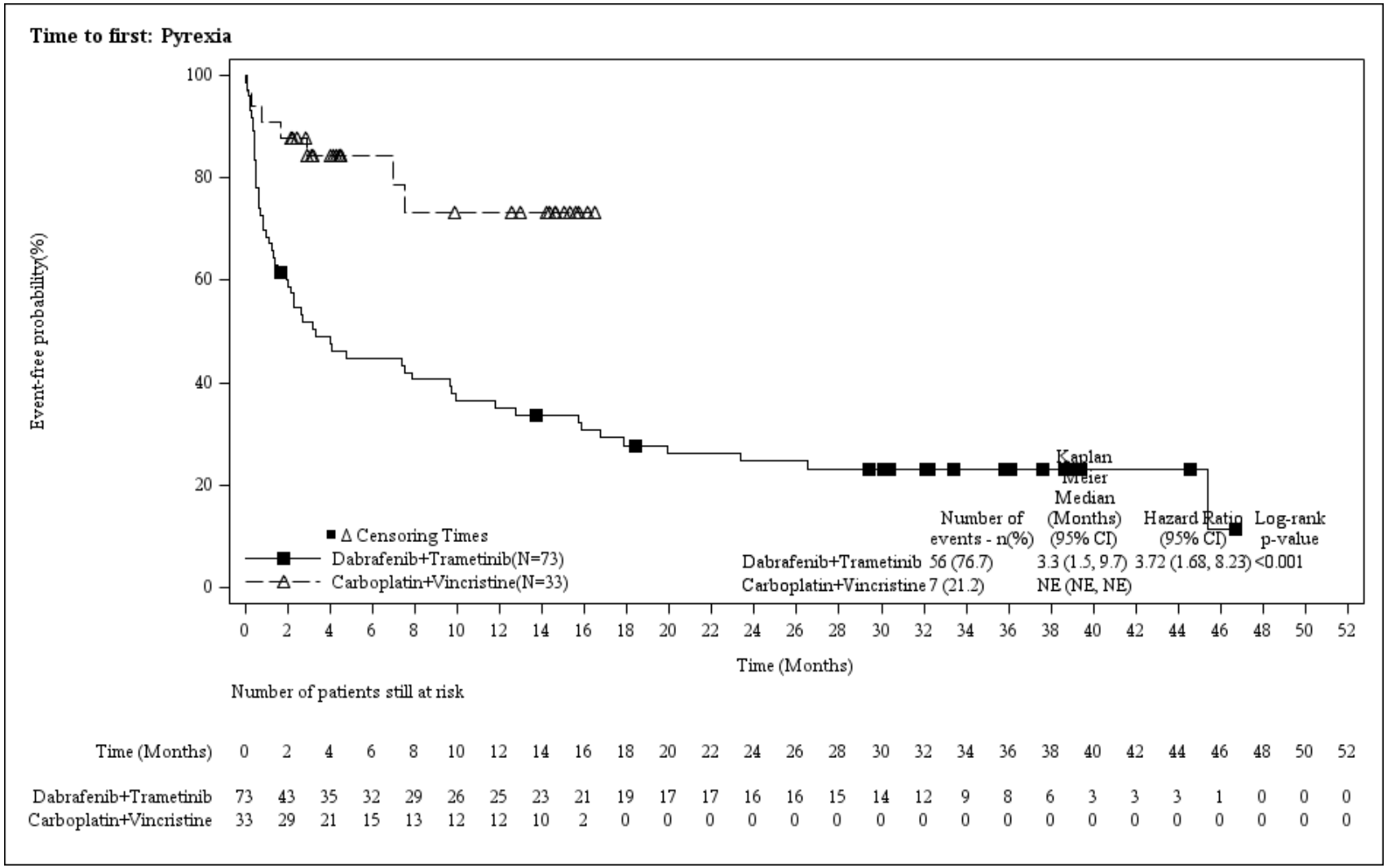
AESI: Kaplan Meier plot of time to first event
Safety Set – L



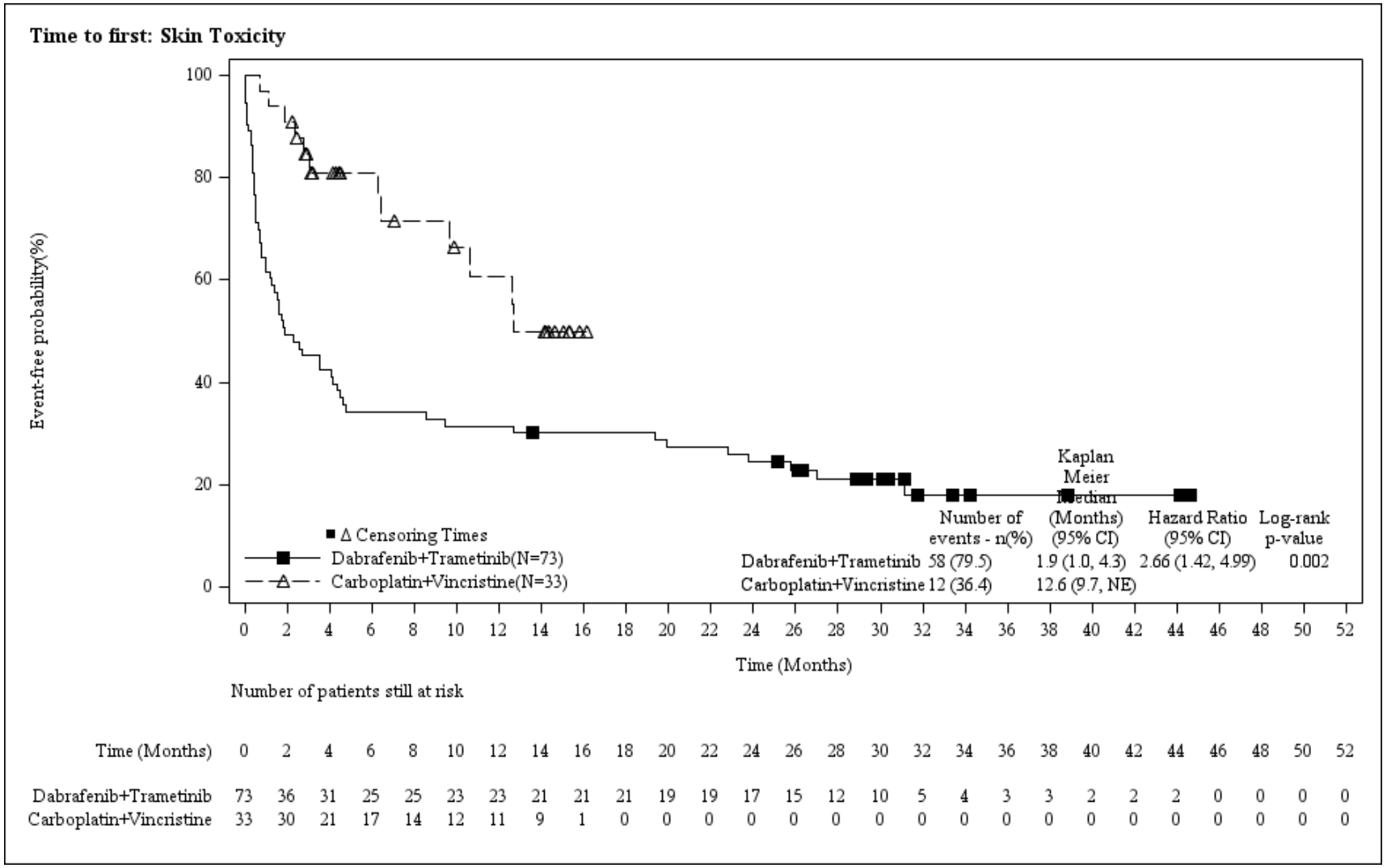
AESI: Kaplan Meier plot of time to first event
Safety Set – L



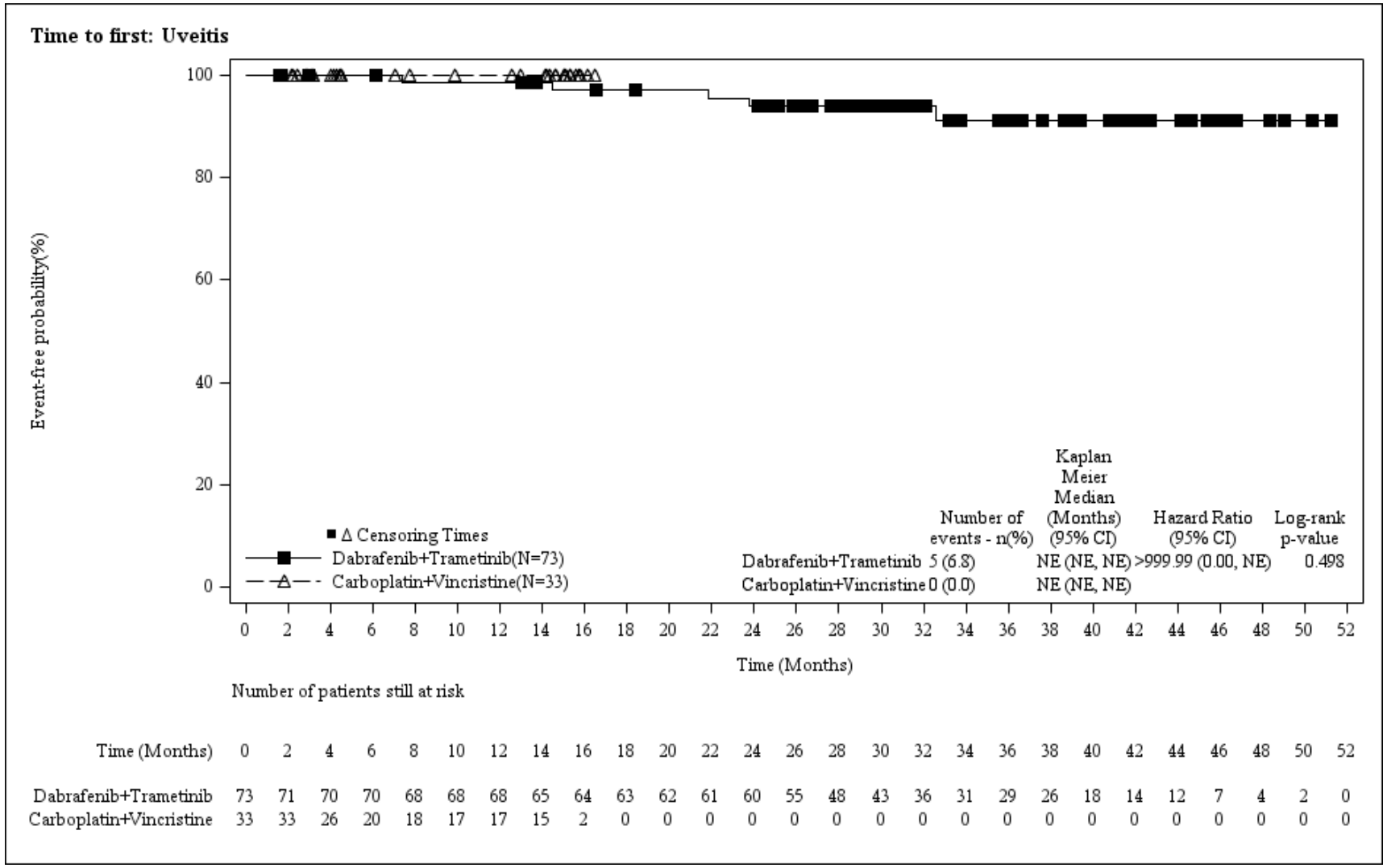
AESI: Kaplan Meier plot of time to first event
Safety Set – L



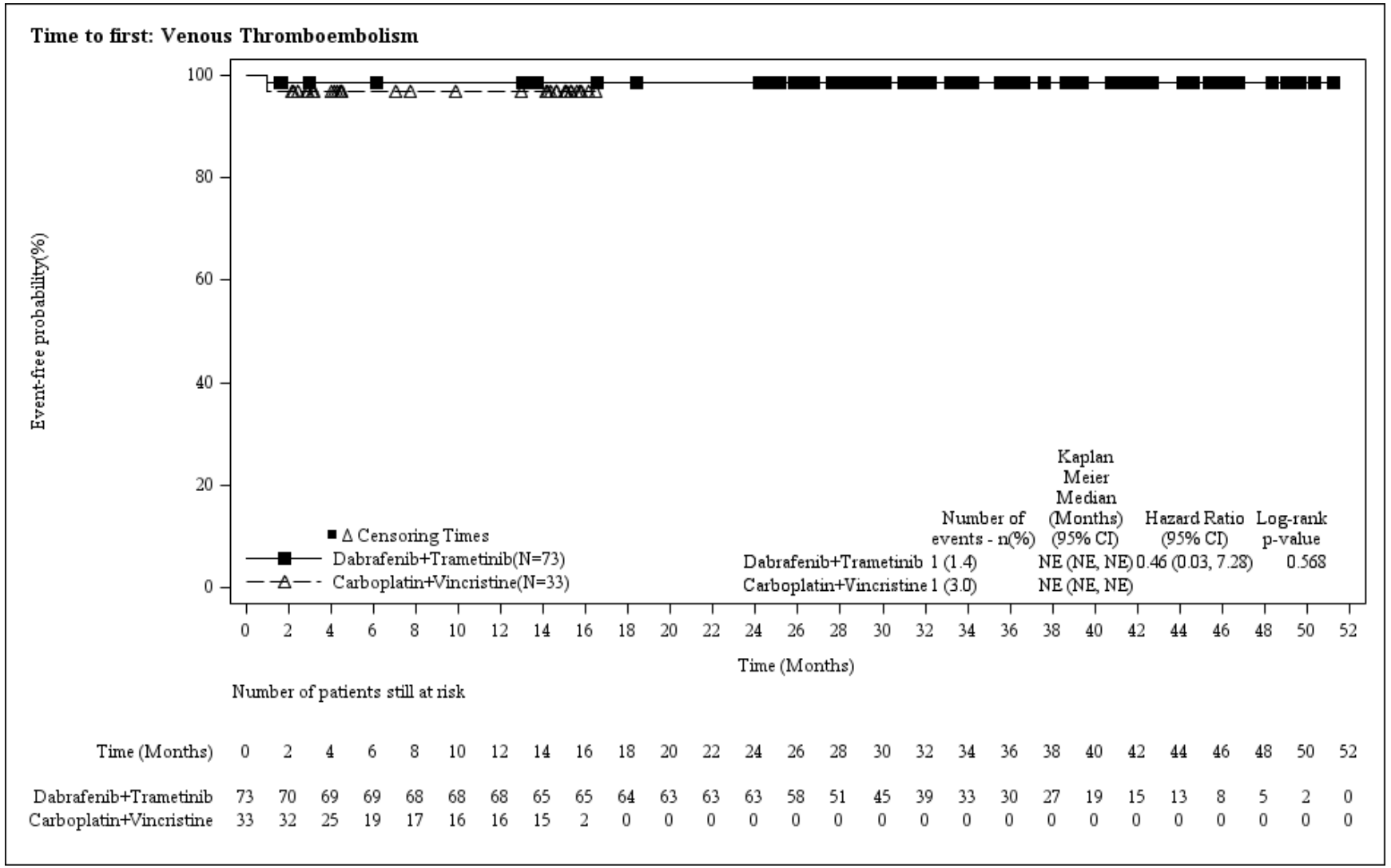
AESI: Kaplan Meier plot of time to first event
Safety Set – L



AESI: Kaplan Meier plot of time to first event
Safety Set – L

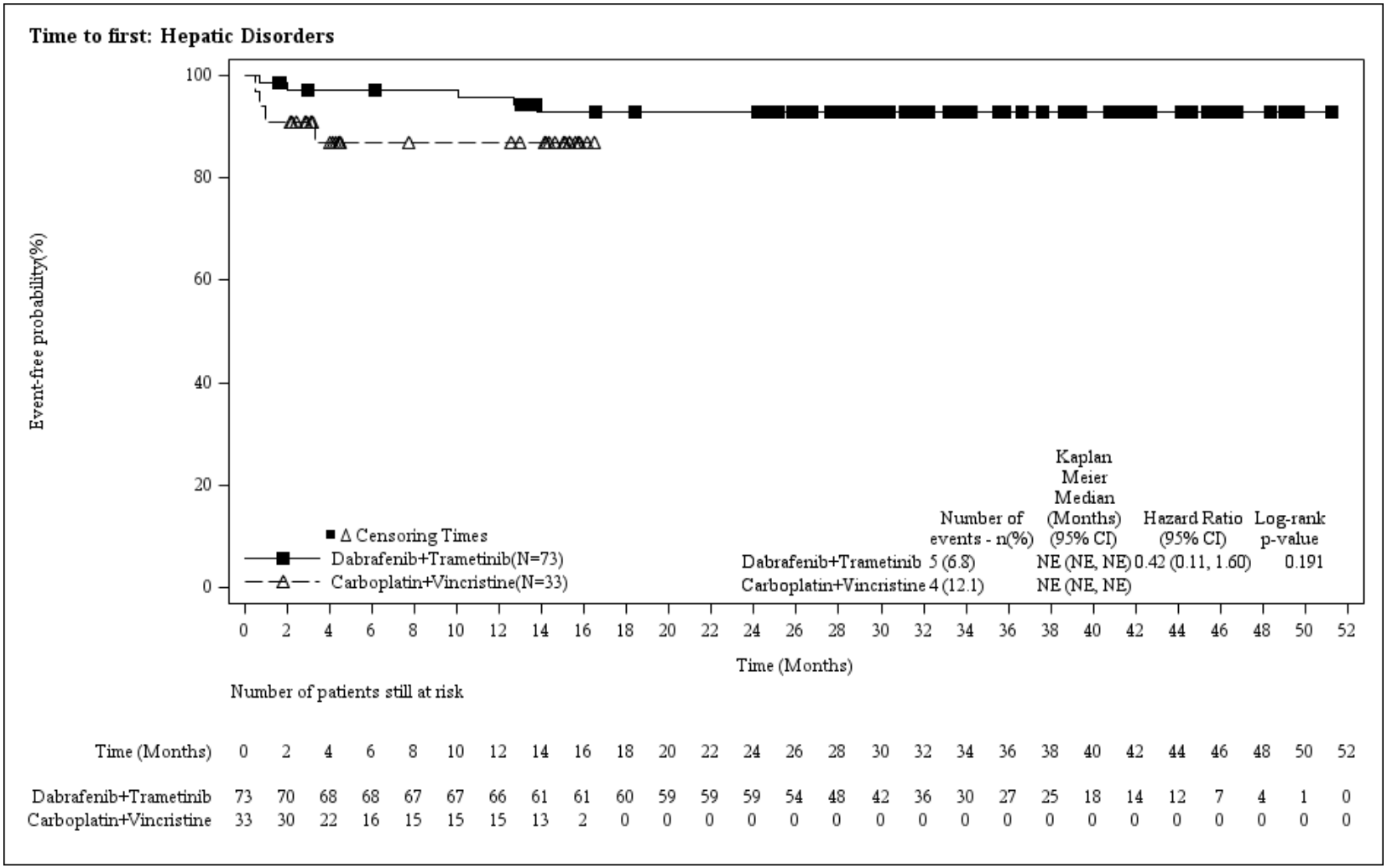


AESI: Kaplan Meier plot of time to first event
Safety Set – L

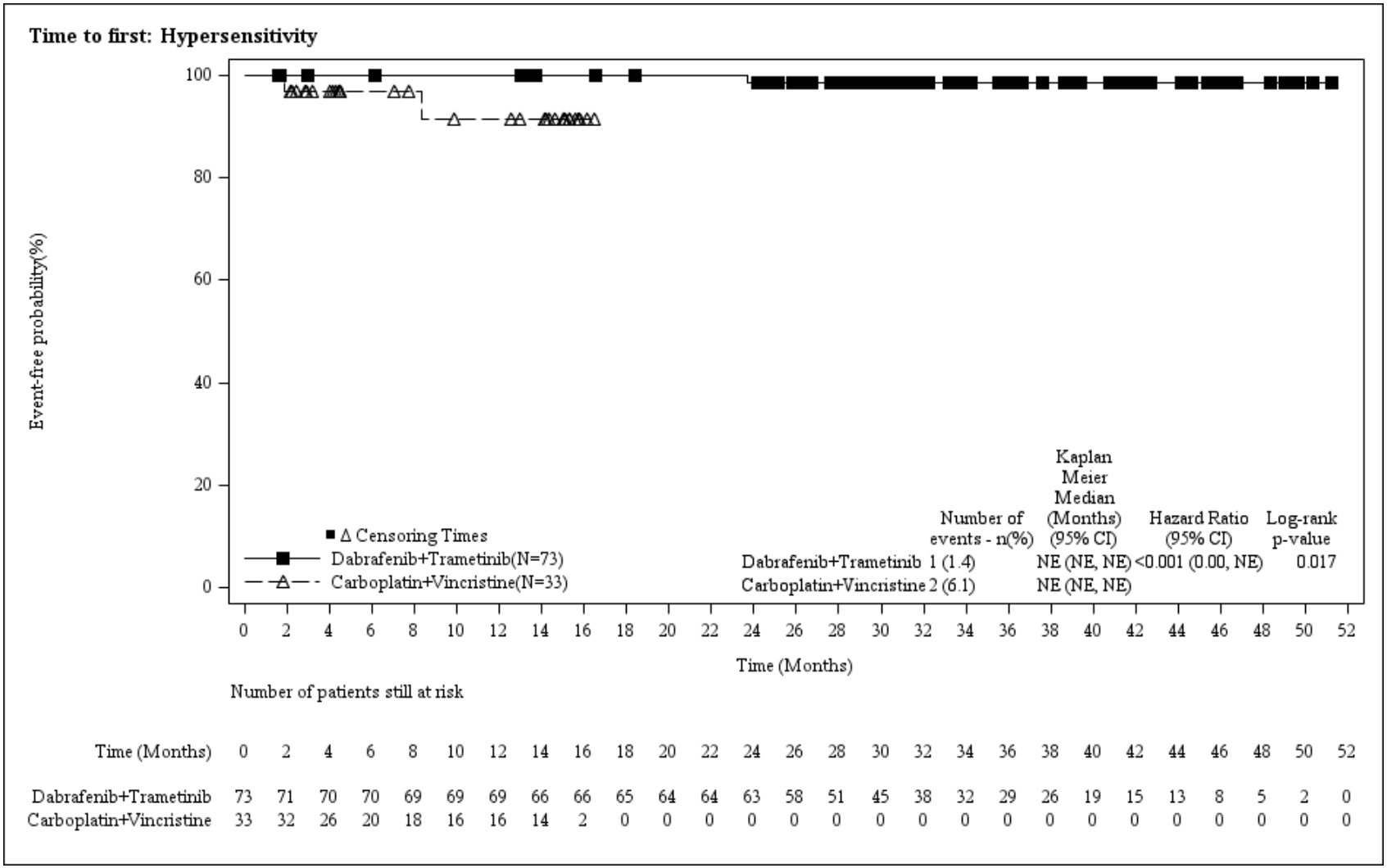


2.3.8. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) von besonderem Interesse (AESI)

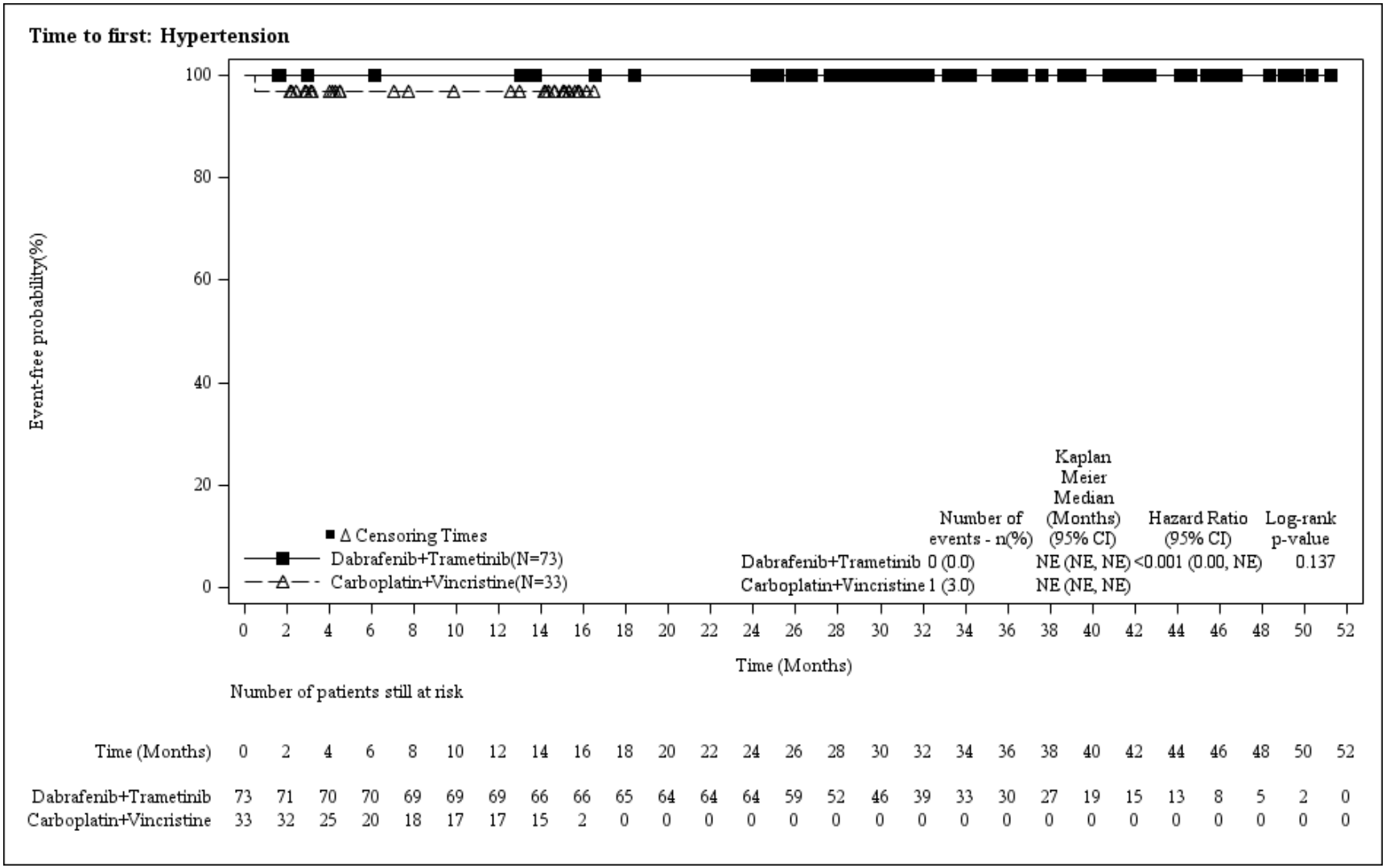
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



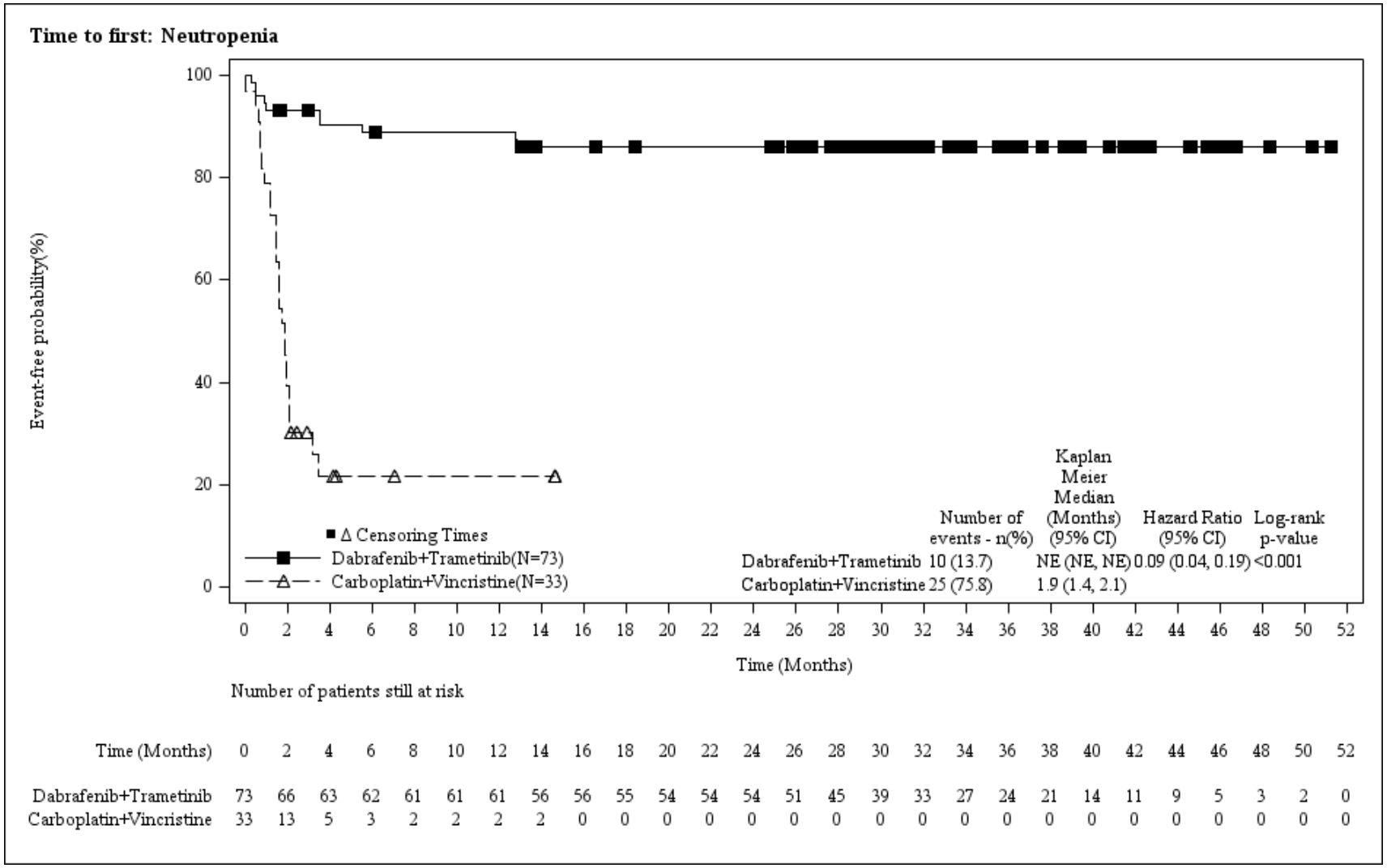
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



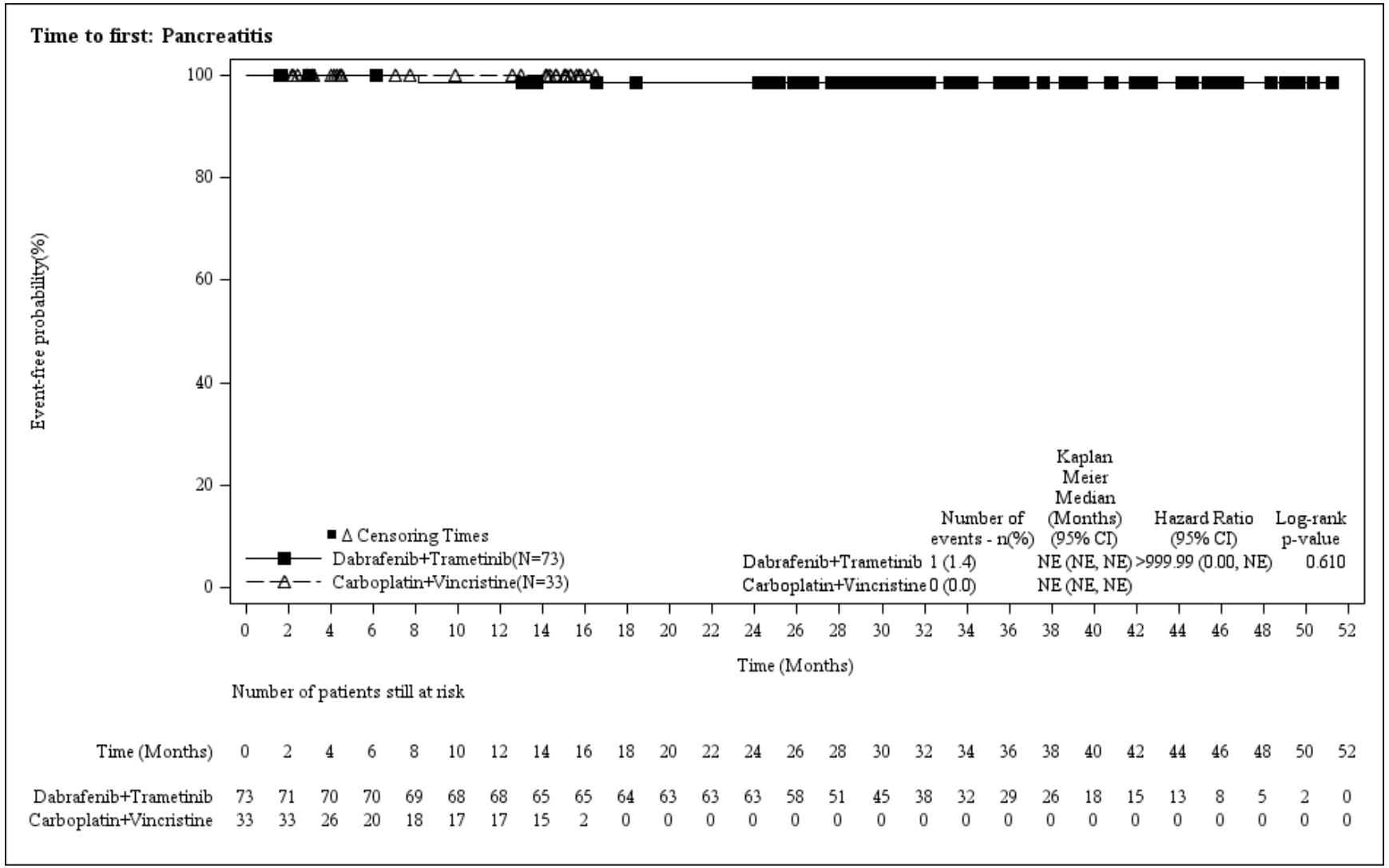
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



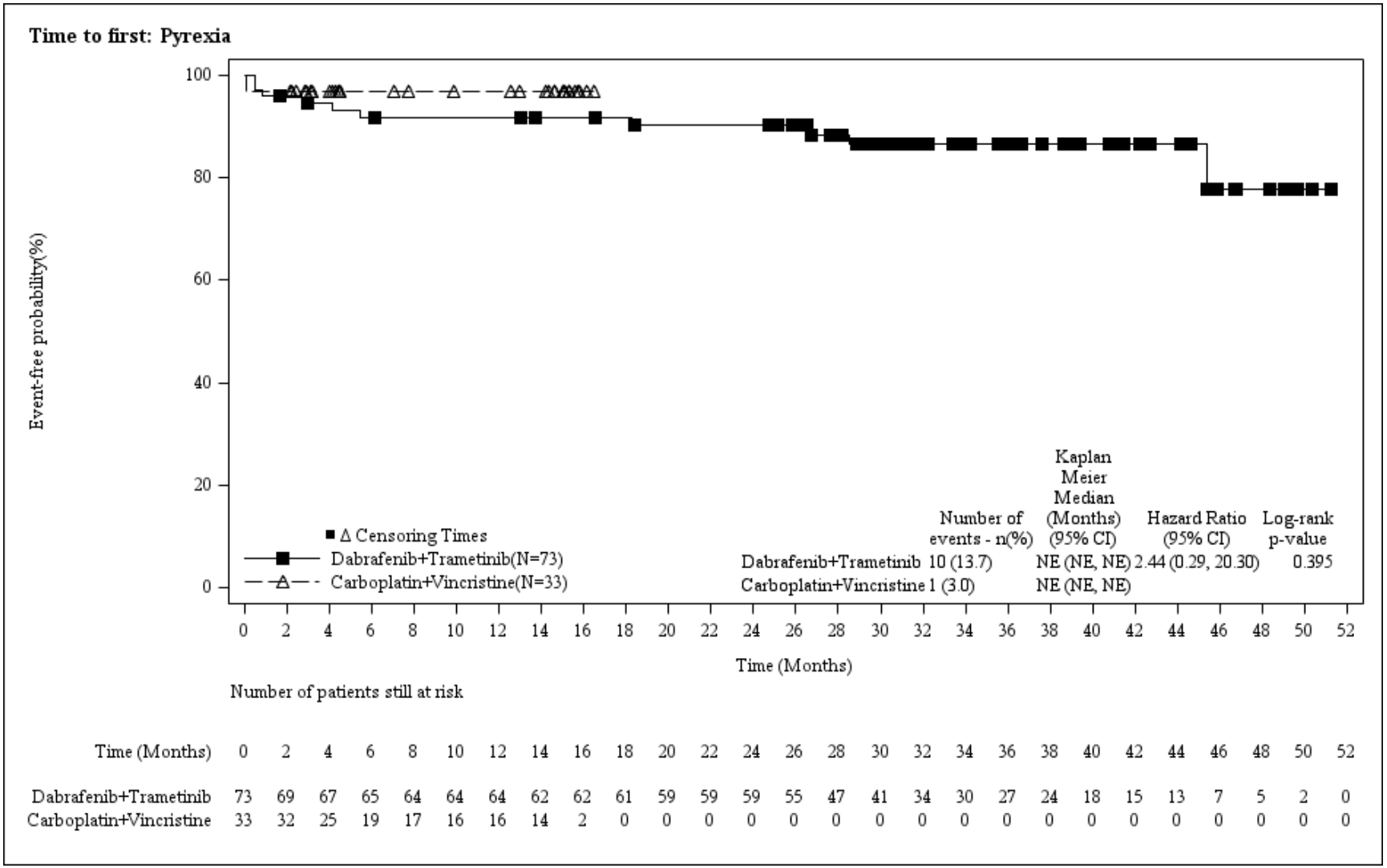
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



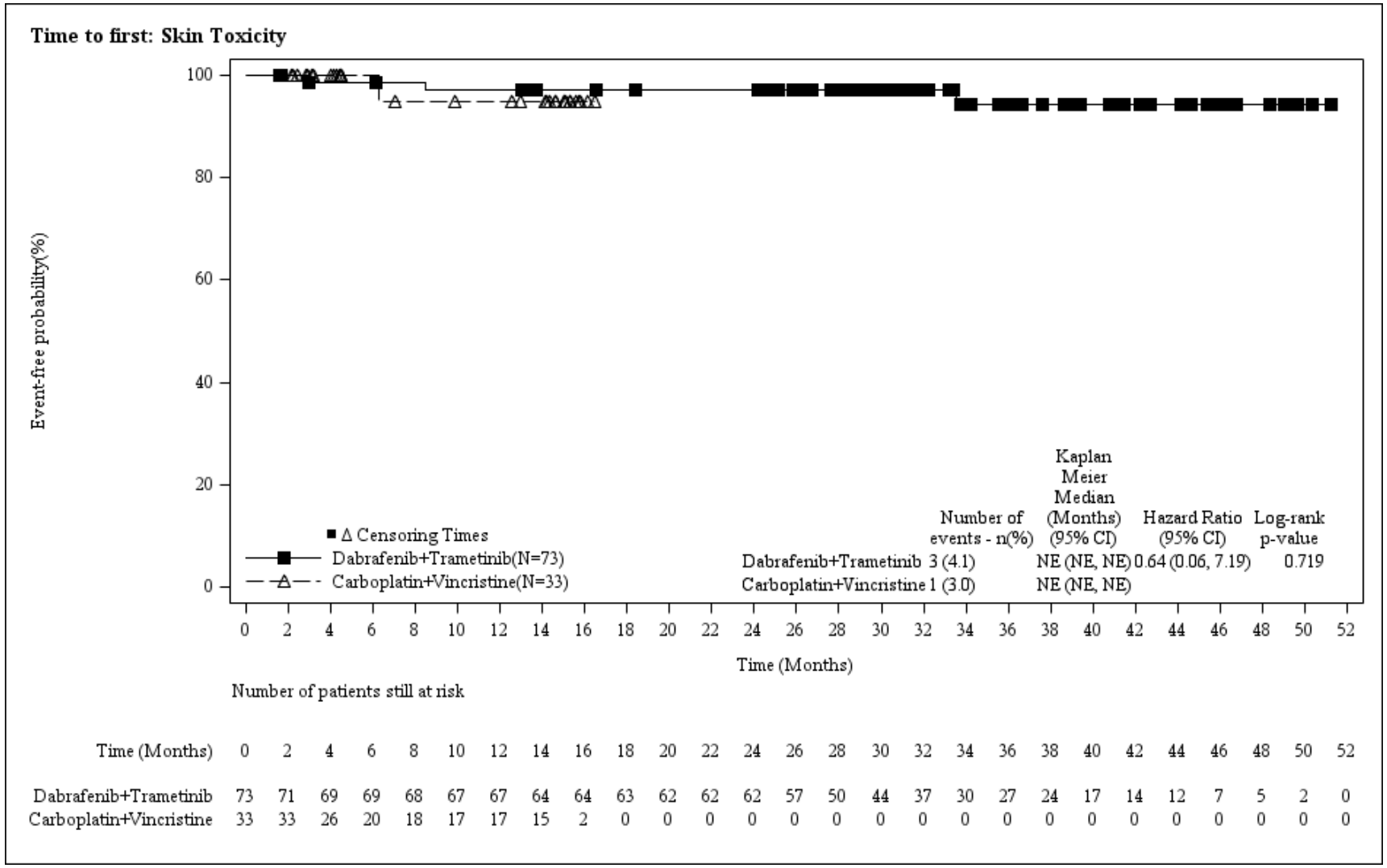
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



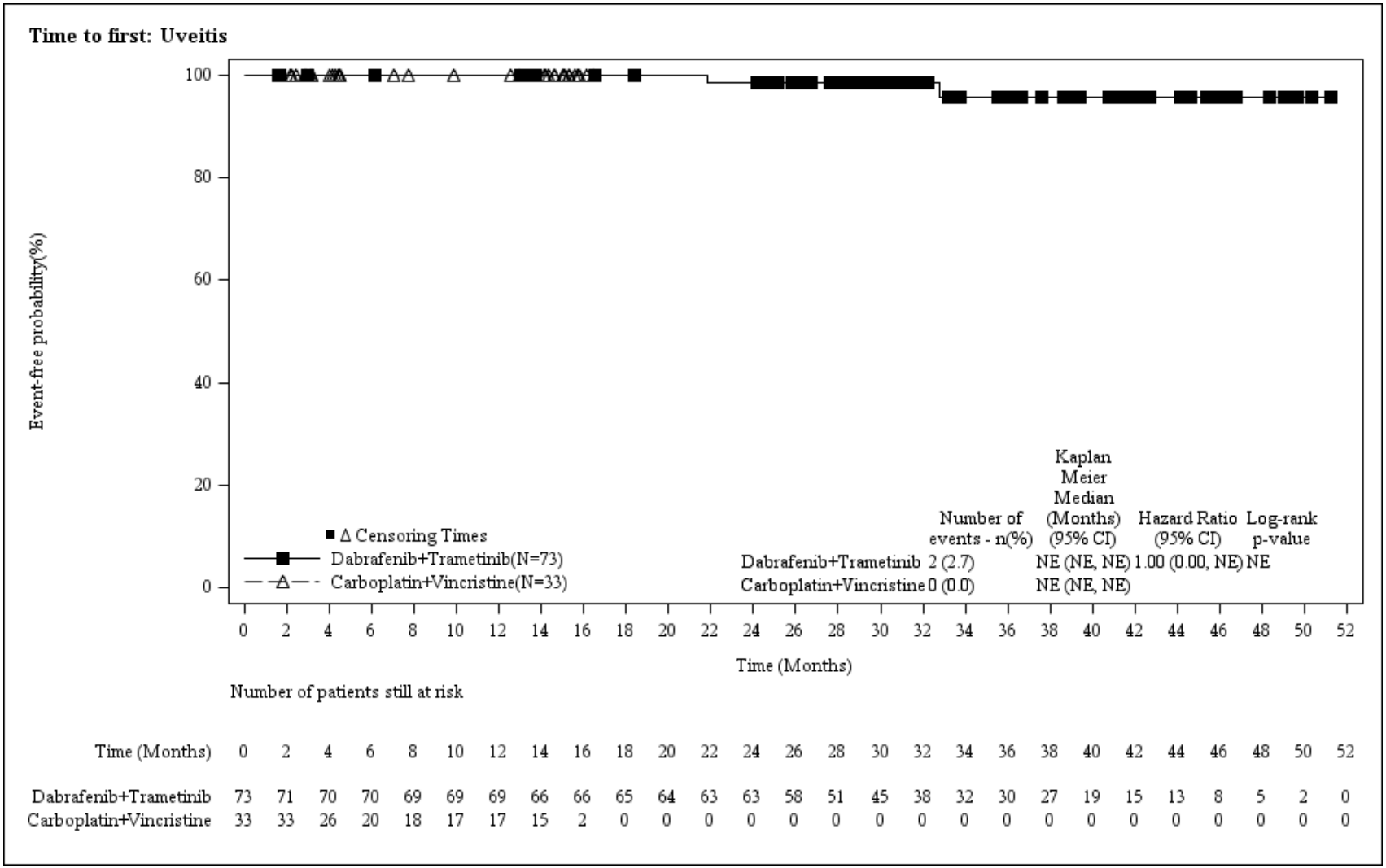
Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L



Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L

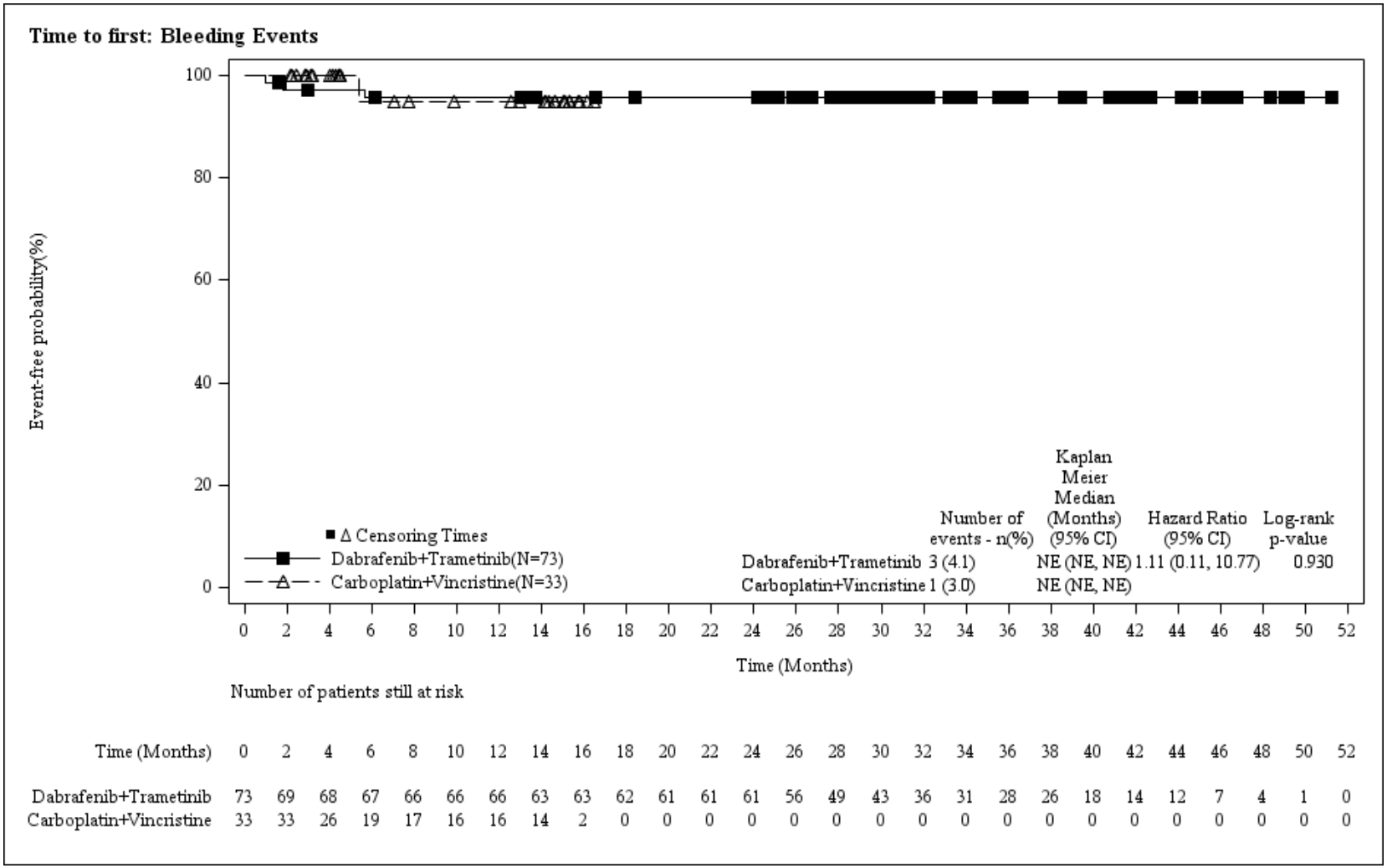


Grade >= 3 AESI: Kaplan Meier plot of time to first event
Safety Set – L

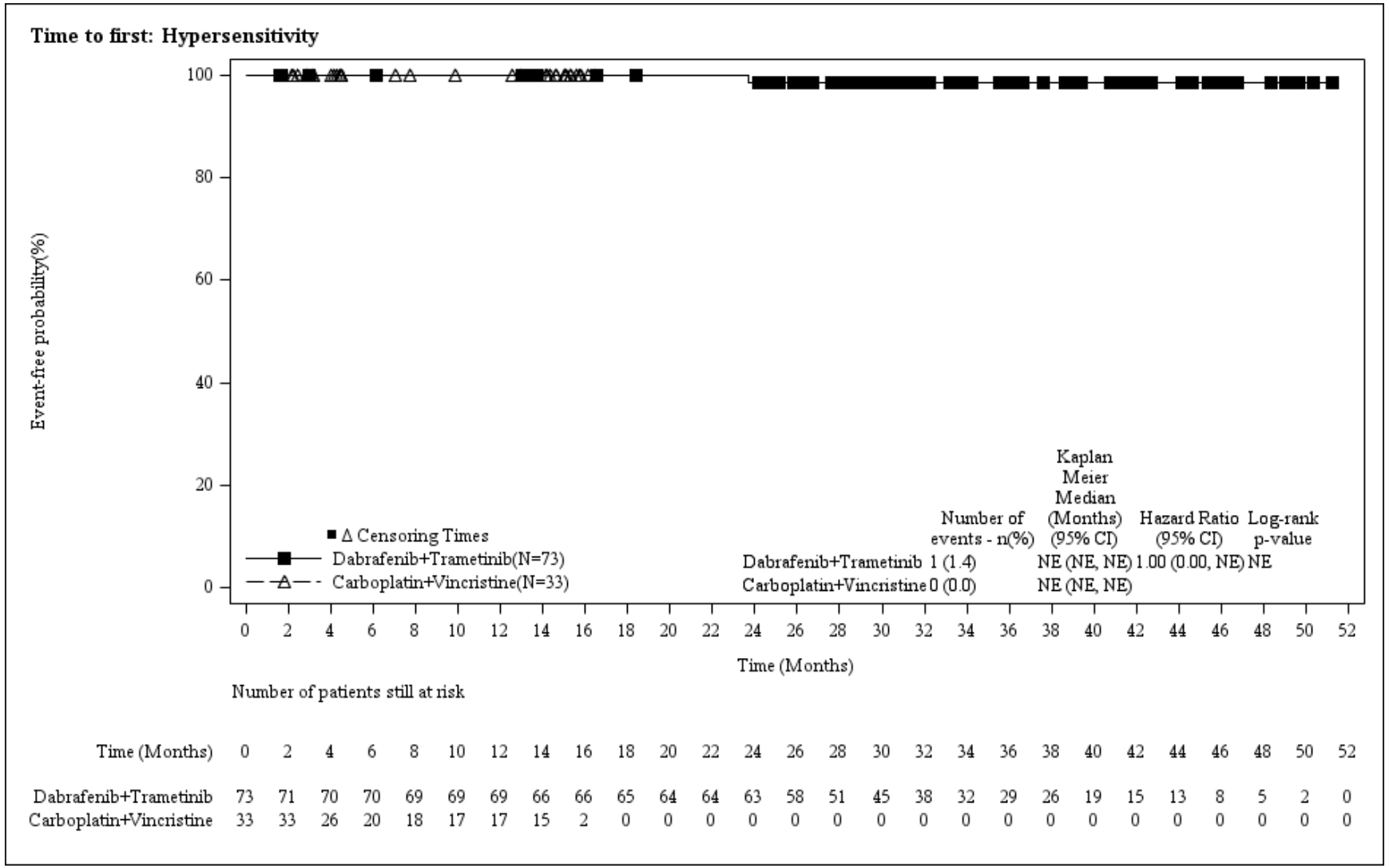


2.3.9. Schwerwiegende unerwünschte Ereignisse von besonderem Interesse (AESI)

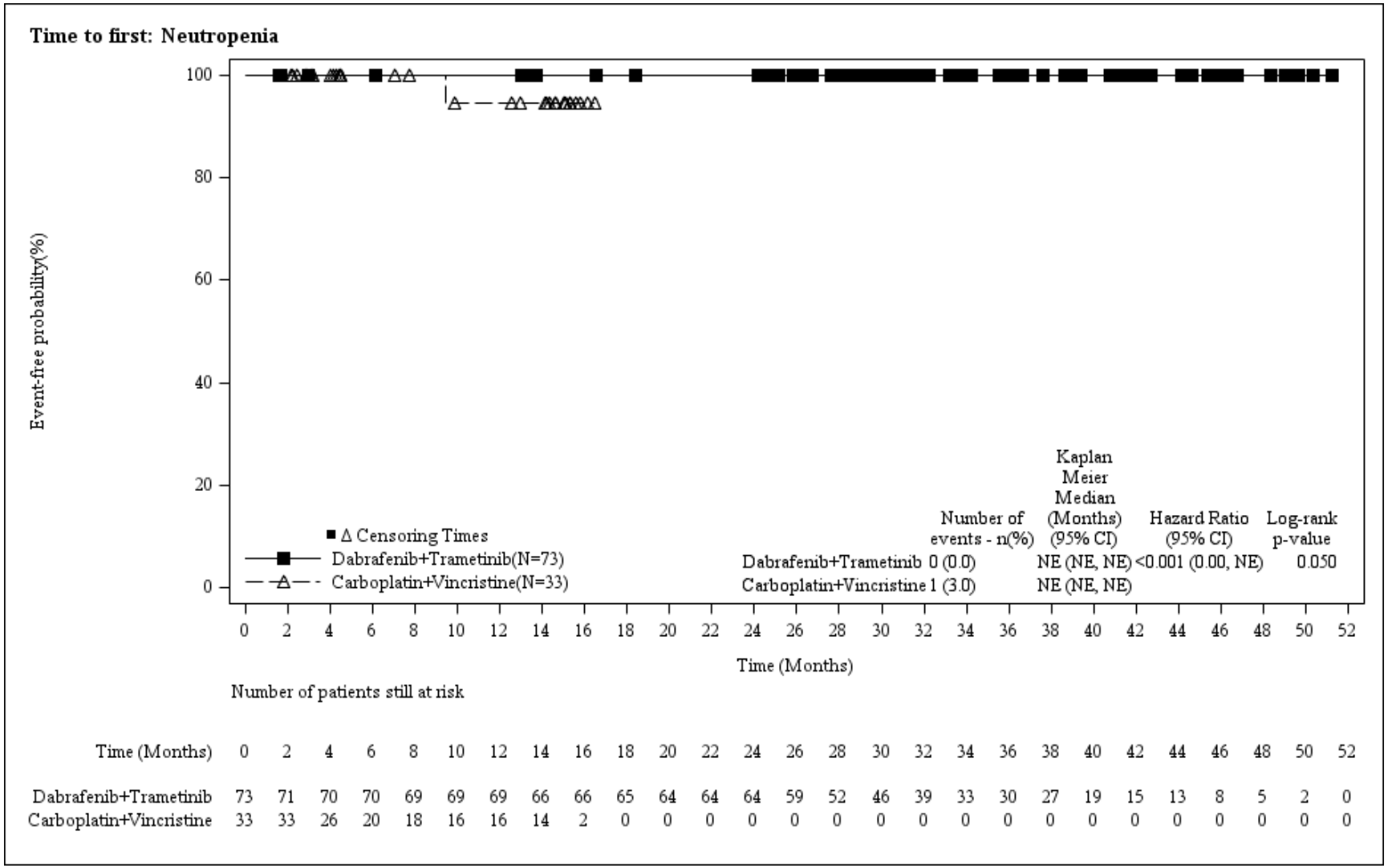
Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



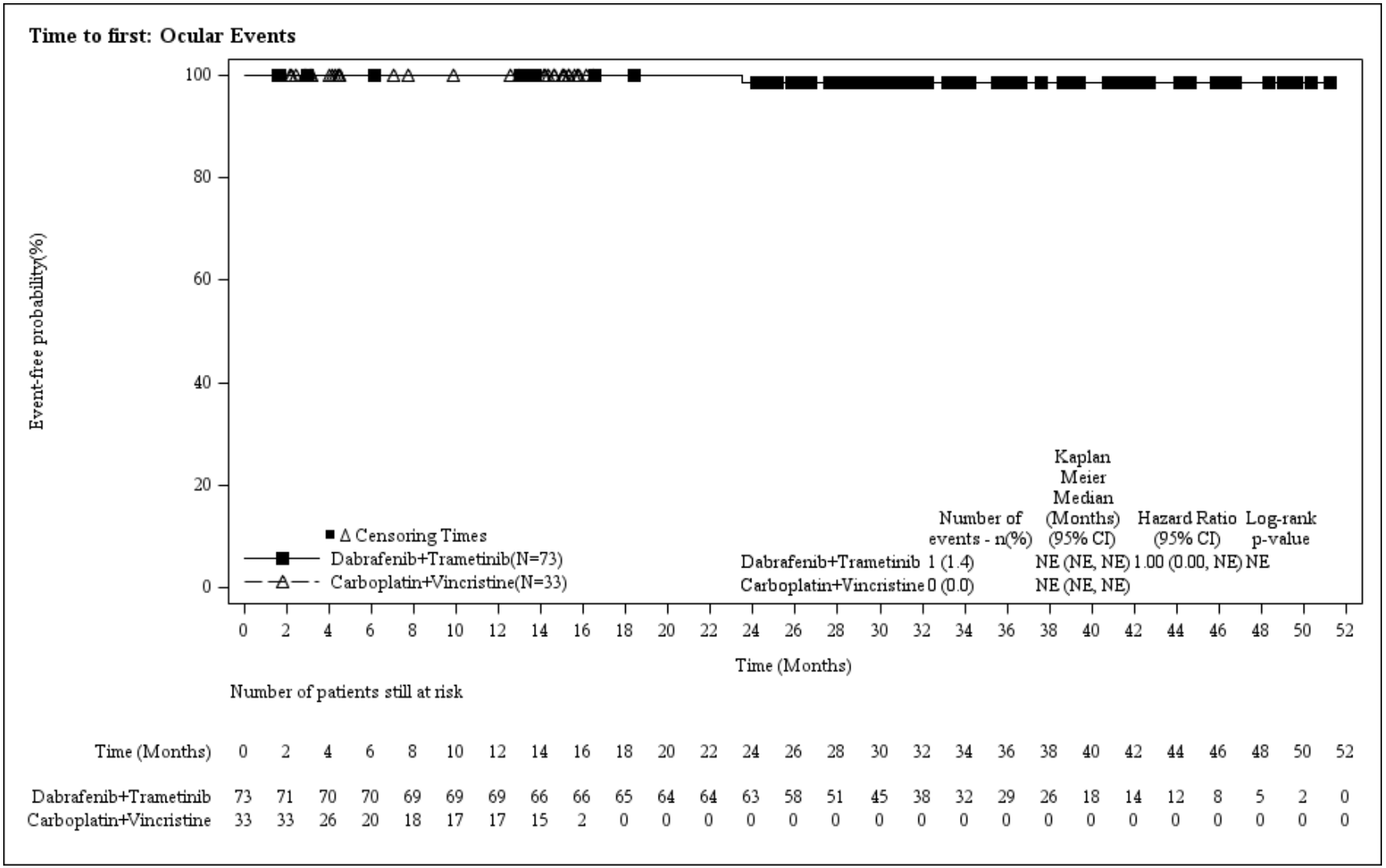
Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



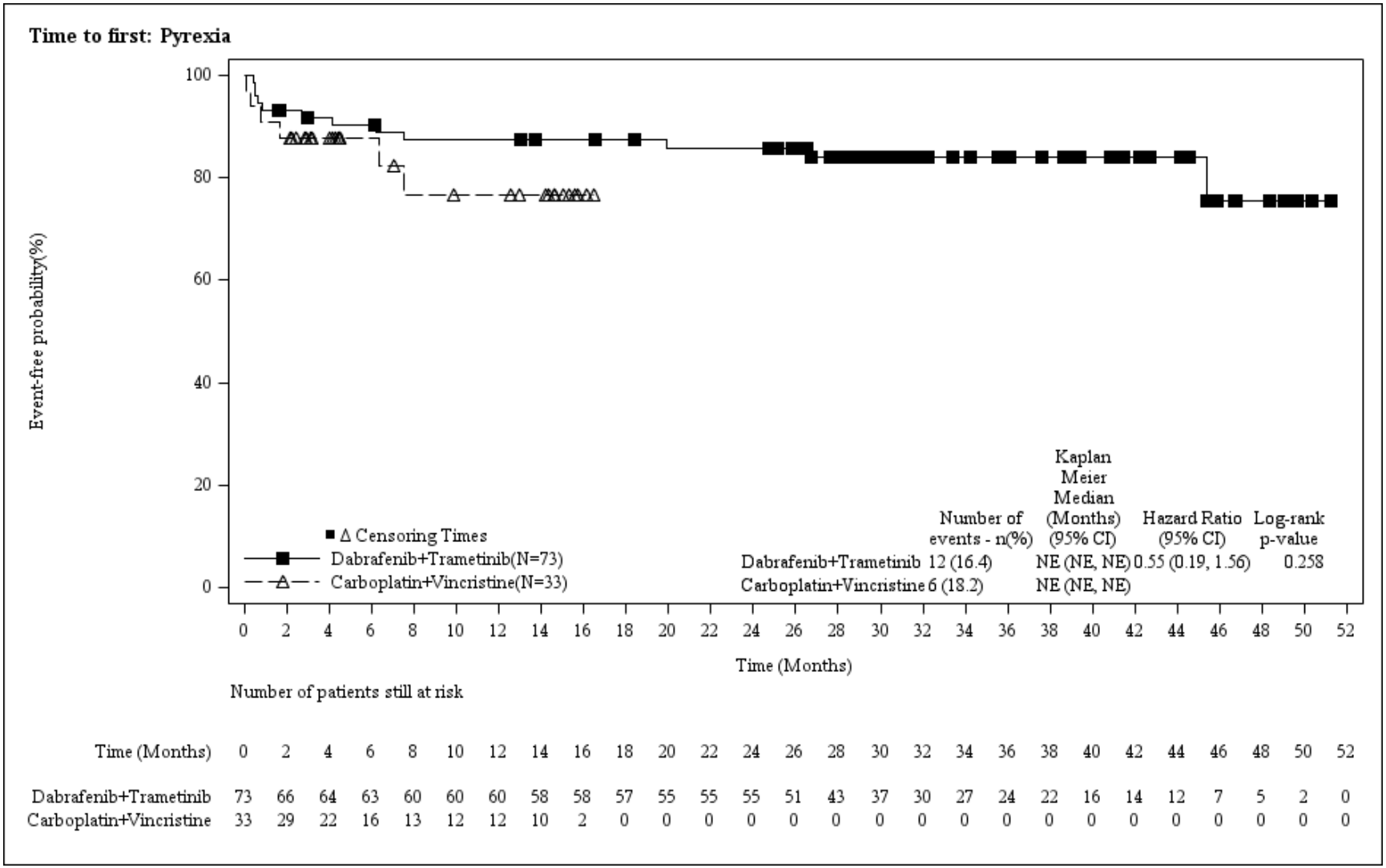
Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



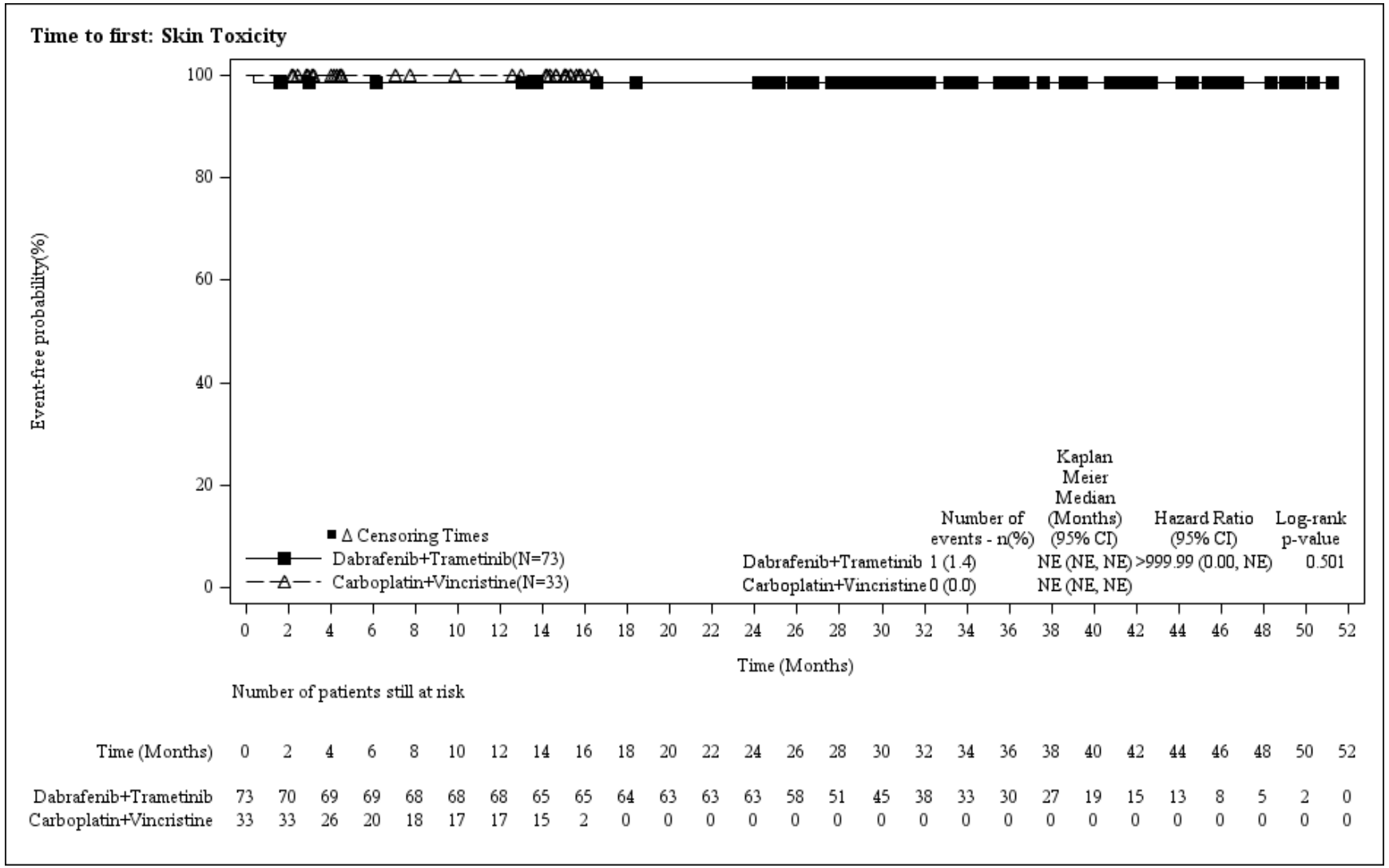
Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



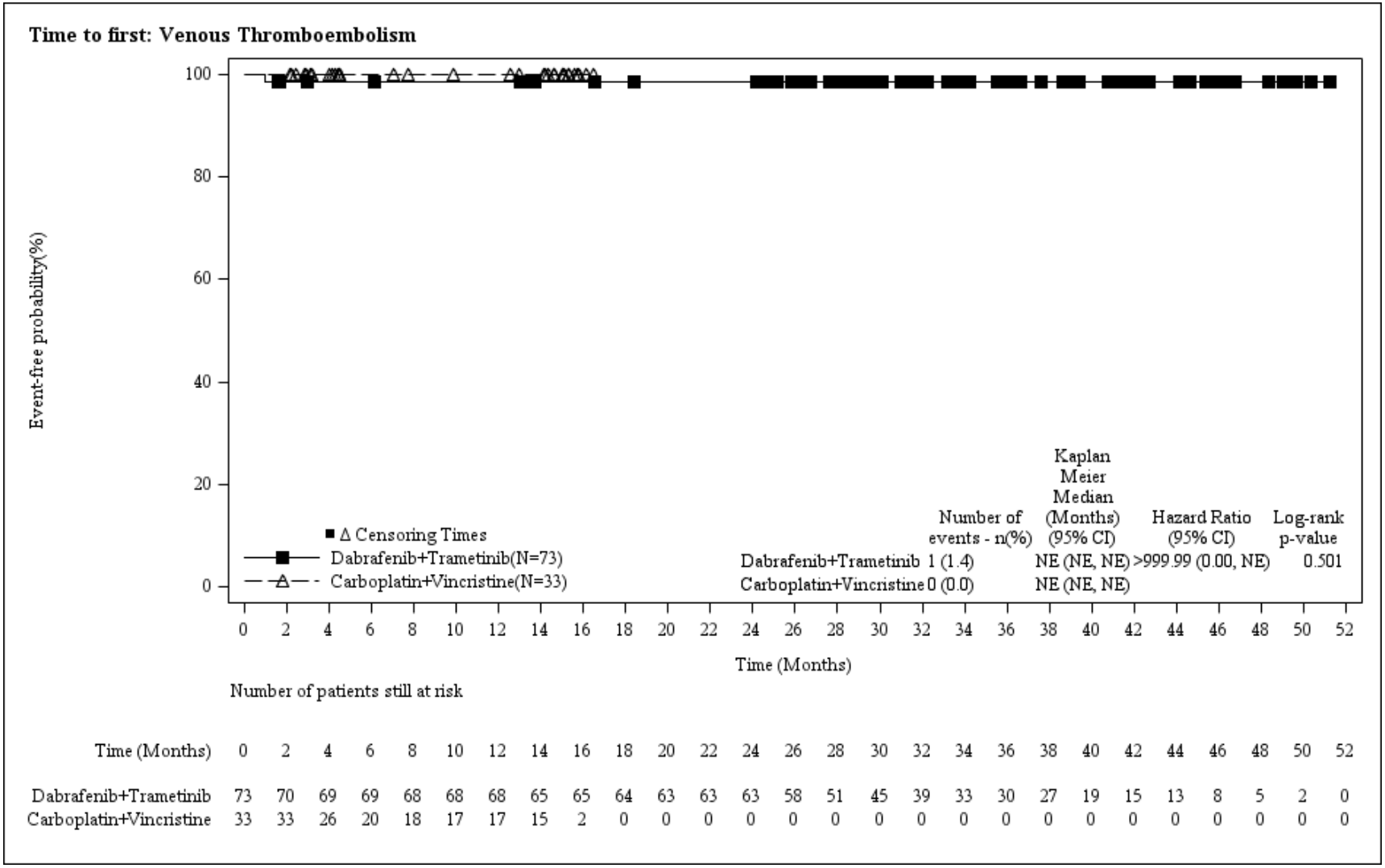
Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



Serious AESI: Kaplan Meier plot of time to first event
Safety Set – L



2.4. Abbrüche wegen unerwünschter Ereignisse nach SOC und PT

AE leading to discontinuation by SOC and PT: Number and percentage of patients with event
Safety Set – L

	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33	
Primary system organ class Preferred term	**All grades n (%)**	**Grade >=3 n (%)**	**All grades n (%)**	**Grade >=3 n (%)**
Number of subjects with at least one event n(%)	4 (5.5)	3 (4.1)	8 (24.2)	3 (9.1)
Blood and lymphatic system disorders	0	0	1 (3.0)	1 (3.0)
Neutropenia	0	0	1 (3.0)	1 (3.0)
Eye disorders	0	0	1 (3.0)	0
Eyelid ptosis	0	0	1 (3.0)	0
Gastrointestinal disorders	0	0	1 (3.0)	0
Nausea	0	0	1 (3.0)	0
General disorders and administration site conditions	3 (4.1)	2 (2.7)	0	0
Pyrexia	2 (2.7)	2 (2.7)	0	0
Chills	1 (1.4)	0	0	0
Fatigue	1 (1.4)	0	0	0
Immune system disorders	0	0	2 (6.1)	0
Hypersensitivity	0	0	2 (6.1)	0
Injury, poisoning and procedural complications	0	0	2 (6.1)	0

Numbers (n) represent counts of subjects.
A subject with multiple severity grades for an AE is only counted under the maximum grade.
MedDRA version 26.0, CTCAE version 4.03.

AE leading to discontinuation by SOC and PT: Number and percentage of patients with event
Safety Set - L

Primary system organ class Preferred term	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33	
	All grades n (%)	Grade >=3 n (%)	All grades n (%)	Grade >=3 n (%)
Infusion related reaction	0	0	2 (6.1)	0
Investigations	1 (1.4)	1 (1.4)	0	0
Weight increased	1 (1.4)	1 (1.4)	0	0
Nervous system disorders	1 (1.4)	0	2 (6.1)	1 (3.0)
Headache	1 (1.4)	0	1 (3.0)	1 (3.0)
Dizziness	0	0	1 (3.0)	1 (3.0)
Neuropathy peripheral	0	0	1 (3.0)	0
Peripheral motor neuropathy	0	0	1 (3.0)	1 (3.0)
Skin and subcutaneous tissue disorders	0	0	1 (3.0)	1 (3.0)
Urticaria	0	0	1 (3.0)	1 (3.0)

Numbers (n) represent counts of subjects.
A subject with multiple severity grades for an AE is only counted under the maximum grade.
MedDRA version 26.0, CTCAE version 4.03.

Ergänzende Analysen zur Studie CDRB436G2201 – Subgruppenanalysen

3. Subgruppenanalysen zum Tumoransprechen

3.1. Gesamtansprechrate

ORR based on Independent Reviewer assessment per RANO criteria - subgroup analysis
Full Analysis Set - L

	Treatment groups				
	Dabrafenib+ Trametinib N=73	Carboplatin+ Vincristine N=37	Comparison		
	n/N* (%)	n/N* (%)	RR	[95% CI]	p-value
Radiographic progression as indication to treatment					
Yes	23/44 (52.3)	3/15 (20.0)	2.61	[0.91, 7.47]	0.031
No	17/29 (58.6)	3/22 (13.6)	4.30	[1.44, 12.85]	<0.001

Risk Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) with corresponding 95% CI and two-sided p-value were estimated using the Cochran-Mantel-Haenszel method.
RR: Risk Ratio; CI: Conifdence Interval; n: Number of patients with event; N*: Number of patients included in the analysis.

4. Subgruppenanalysen zur Verträglichkeit

4.1. Gesamtraten unerwünschter Ereignisse

Any AE: Time to first event - subgroup analysis
Safety Set - L

Parameter: Any AE

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	20 / 20 (100)	0.3 (0.1, 0.8)	13 / 13 (100)	0.1 (0.0, 0.3)	0.59 (0.28, 1.21)	0.144
6 - <12 Years	25 / 25 (100)	0.2 (0.1, 0.5)	9 / 9 (100)	0.1 (0.0, 0.8)	0.78 (0.35, 1.72)	0.544
12 - <18 Years	28 / 28 (100)	0.3 (0.1, 0.5)	11 / 11 (100)	0.1 (0.0, 0.5)	0.91 (0.44, 1.88)	0.821

Subgroups which contain at least 10 events in one subgroup are displayed, regardless of whether they are significant for interactions or not.
Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Grade >= 3 AE: Time to first event - subgroup analysis
Safety Set - L

Parameter: Grade >=3 AE

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	12 / 20 (60.0)	11.9 (3.5, NE)	12 / 13 (92.3)	0.9 (0.3, 1.7)	0.15 (0.06, 0.39)	<0.001
6 - <12 Years	12 / 25 (48.0)	NE (1.6, NE)	8 / 9 (88.9)	1.6 (0.5, 2.1)	0.31 (0.11, 0.84)	0.014
12 - <18 Years	15 / 28 (53.6)	33.5 (8.1, NE)	11 / 11 (100)	0.8 (0.3, 1.9)	0.12 (0.04, 0.33)	<0.001

Subgroups which contain at least 10 events in one subgroup are displayed, regardless of whether they are significant for interactions or not.
Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

SAE: Time to first event - subgroup analysis
Safety Set - L

Parameter: Any SAE

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (95% CI)	n/N* (%)	Median (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	13 / 20 (65.0)	10.6 (1.1, NE)	5 / 13 (38.5)	6.3 (3.0, NE)	1.12 (0.39, 3.23)	0.839
6 - <12 Years	10 / 25 (40.0)	44.6 (13.9, NE)	2 / 9 (22.2)	NE (2.1, NE)	1.09 (0.22, 5.41)	0.912
12 - <18 Years	11 / 28 (39.3)	43.5 (7.5, NE)	7 / 11 (63.6)	5.4 (0.6, NE)	0.35 (0.13, 0.98)	0.035

Subgroups which contain at least 10 events in one subgroup are displayed, regardless of whether they are significant for interactions or not.
Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

4.2. Unerwünschte Ereignisse nach SOC und PT

4.2.1. Unerwünschte Ereignisse nach SOC

Any AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC - Blood and lymphatic system disorders

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	9 / 20 (45.0)	NE (3.5, NE)	11 / 13 (84.6)	0.5 (0.3, 3.2)	0.17 (0.06, 0.46)	<0.001
6 - <12 Years	6 / 25 (24.0)	NE (NE, NE)	7 / 9 (77.8)	1.2 (0.8, NE)	0.19 (0.06, 0.61)	0.002
12 - <18 Years	9 / 28 (32.1)	NE (15.4, NE)	7 / 11 (63.6)	1.9 (0.3, NE)	0.26 (0.09, 0.75)	0.007

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC - Gastrointestinal disorders

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	18 / 20 (90.0)	4.0 (0.4, 12.0)	11 / 13 (84.6)	0.5 (0.1, 4.2)	0.60 (0.28, 1.31)	0.200
6 - <12 Years	20 / 25 (80.0)	1.6 (0.3, 2.5)	6 / 9 (66.7)	0.3 (0.0, NE)	0.84 (0.33, 2.13)	0.726
12 - <18 Years	21 / 28 (75.0)	2.9 (0.7, 13.3)	10 / 11 (90.9)	0.1 (0.0, 2.8)	0.36 (0.16, 0.79)	0.008

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC – Investigations

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	14 / 20 (70.0)	13.1 (5.6, 25.8)	8 / 13 (61.5)	1.6 (0.5, NE)	0.43 (0.17, 1.09)	0.068
6 - <12 Years	13 / 25 (52.0)	20.0 (5.3, NE)	6 / 9 (66.7)	1.6 (0.3, NE)	0.21 (0.06, 0.75)	0.008
12 - <18 Years	17 / 28 (60.7)	3.2 (1.0, NE)	8 / 11 (72.7)	0.7 (0.0, NE)	0.59 (0.25, 1.37)	0.226

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC - Metabolism and nutrition disorders

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	4 / 20 (20.0)	NE (NE, NE)	5 / 13 (38.5)	NE (0.2, NE)	0.37 (0.10, 1.41)	0.132
6 - <12 Years	5 / 25 (20.0)	NE (NE, NE)	5 / 9 (55.6)	1.2 (0.3, NE)	0.15 (0.04, 0.61)	0.003
12 - <18 Years	8 / 28 (28.6)	NE (23.7, NE)	5 / 11 (45.5)	NE (0.2, NE)	0.35 (0.11, 1.17)	0.075

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC - Skin and subcutaneous tissue disorders

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	17 / 20 (85.0)	2.2 (0.7, 4.5)	5 / 13 (38.5)	NE (1.0, NE)	2.48 (0.92, 6.74)	0.063
6 - <12 Years	22 / 25 (88.0)	2.3 (1.3, 22.8)	4 / 9 (44.4)	9.0 (1.0, NE)	1.61 (0.54, 4.85)	0.391
12 - <18 Years	25 / 28 (89.3)	0.9 (0.5, 4.0)	8 / 11 (72.7)	9.7 (1.1, NE)	1.60 (0.71, 3.61)	0.262

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

4.2.2. Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) nach SOC

Grade >= 3 AE by SOC: Time to first event - subgroup analysis
Safety Set - L

Parameter: SOC – Investigations

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	7 / 20 (35.0)	NE (12.6, NE)	7 / 13 (53.8)	1.9 (0.7, NE)	0.26 (0.08, 0.81)	0.014
6 - <12 Years	4 / 25 (16.0)	NE (NE, NE)	3 / 9 (33.3)	NE (0.6, NE)	0.30 (0.06, 1.42)	0.110
12 - <18 Years	6 / 28 (21.4)	NE (NE, NE)	8 / 11 (72.7)	1.9 (0.7, NE)	0.15 (0.05, 0.44)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 5% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for SOCs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

4.2.3. Unerwünschte Ereignisse nach PT

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT - Alanine aminotransferase increased

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	3 / 20 (15.0)	NE (NE, NE)	1 / 13 (7.7)	NE (NE, NE)	1.03 (0.10, 10.27)	0.982
6 - <12 Years	2 / 25 (8.0)	NE (NE, NE)	3 / 9 (33.3)	NE (0.3, NE)	0.07 (0.01, 0.75)	0.005
12 - <18 Years	5 / 28 (17.9)	NE (NE, NE)	5 / 11 (45.5)	NE (0.5, NE)	0.30 (0.09, 1.06)	0.046

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT – Anaemia

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	7 / 20 (35.0)	NE (3.5, NE)	9 / 13 (69.2)	0.5 (0.3, NE)	0.21 (0.07, 0.64)	0.003
6 - <12 Years	3 / 25 (12.0)	NE (NE, NE)	6 / 9 (66.7)	1.6 (0.8, NE)	0.10 (0.02, 0.48)	<0.001
12 - <18 Years	4 / 28 (14.3)	NE (44.0, NE)	5 / 11 (45.5)	NE (0.3, NE)	0.18 (0.04, 0.76)	0.009

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT - Dry skin

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	3 / 20 (15.0)	NE (NE, NE)	1 / 13 (7.7)	NE (NE, NE)	1.54 (0.16, 15.03)	0.707
6 - <12 Years	6 / 25 (24.0)	NE (NE, NE)	0 / 9 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.290
12 - <18 Years	11 / 28 (39.3)	NE (10.0, NE)	0 / 11 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.047

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT – Nausea

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	3 / 20 (15.0)	NE (28.9, NE)	5 / 13 (38.5)	NE (1.4, NE)	0.22 (0.04, 1.15)	0.050
6 - <12 Years	8 / 25 (32.0)	NE (7.6, NE)	4 / 9 (44.4)	NE (0.0, NE)	0.34 (0.10, 1.23)	0.087
12 - <18 Years	10 / 28 (35.7)	NE (8.0, NE)	8 / 11 (72.7)	0.1 (0.0, NE)	0.23 (0.09, 0.60)	0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT - Neutrophil count decreased

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	1 / 20 (5.0)	NE (NE, NE)	7 / 13 (53.8)	1.7 (0.7, NE)	0.06 (0.01, 0.47)	<0.001
6 - <12 Years	5 / 25 (20.0)	NE (NE, NE)	3 / 9 (33.3)	NE (0.6, NE)	0.39 (0.09, 1.73)	0.199
12 - <18 Years	5 / 28 (17.9)	NE (40.5, NE)	6 / 11 (54.5)	1.9 (1.2, NE)	0.22 (0.06, 0.80)	0.012

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT – Pyrexia

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	14 / 20 (70.0)	5.4 (1.0, 16.8)	4 / 13 (30.8)	NE (2.9, NE)	2.05 (0.66, 6.33)	0.203
6 - <12 Years	20 / 25 (80.0)	4.1 (0.7, 15.7)	0 / 9 (0.0)	NE (NE, NE)	>999.99 (0.00, NE)	0.008
12 - <18 Years	21 / 28 (75.0)	2.5 (0.7, 11.8)	2 / 11 (18.2)	NE (0.8, NE)	4.79 (1.12, 20.58)	0.020

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.

Any AE by PT: Time to first event - subgroup analysis
Safety Set - L

Parameter: PT – Vomiting

	Treatment groups					
	Dabrafenib+Trametinib N=73		Carboplatin+Vincristine N=33		Comparison	
	n/N* (%)	Median (months) (95% CI)	n/N* (%)	Median (months) (95% CI)	HR (95% CI)	p-value
Age						
< 6 Years	10 / 20 (50.0)	30.0 (1.9, NE)	5 / 13 (38.5)	NE (0.8, NE)	0.96 (0.32, 2.88)	0.943
6 - <12 Years	8 / 25 (32.0)	NE (5.2, NE)	3 / 9 (33.3)	NE (0.7, NE)	0.67 (0.17, 2.68)	0.565
12 - <18 Years	9 / 28 (32.1)	NE (14.6, NE)	9 / 11 (81.8)	2.0 (0.2, 4.2)	0.20 (0.08, 0.53)	<0.001

Median (time to event) and its 95% CI are generated by KM estimation.
Hazard Ratio (Dabrafenib + Trametinib vs. Carboplatin + Vincristine) estimated by Cox proportional hazards model.
Two-sided p-value based on a Log-rank test.
Events in at least 10% of patients in at least one of the treatment arms OR events in at least 10 patients and in at least 1% of patients in one treatment arm.
Results are only given for PTs that are significant in the main analysis.
AE: Adverse Event; CI: Confidence Interval; HR: Hazard Ratio; n: Number of patients with event; N*: Number of patients included in the analysis.