Dossier zur Nutzenbewertung gemäß § 35a SGB V

Tremelimumab (Tremelimumab AstraZeneca)

AstraZeneca GmbH

Anhang 4-G: Ergänzende Unterlagen

Tremelimumab in Kombination mit Durvalumab und einer platinbasierten Chemotherapie zur Erstlinienbehandlung des metastasierten nicht-kleinzelligen Lungenkarzinoms (NSCLC) ohne sensibilisierende EGFR-Mutationen oder ALK-positive Mutationen

Stand: 30.03.2023

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Anhang 4-G 1: Population mit einer PD-L1-Expression <50%

Anhang 4-G 1.1: Sensitivitätsanalyse: mittlere Änderung der Symptome

Anhang 4-G 1.1.1: EORTC QLQ-C30 - Symptomskalen

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Table 9.7.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	32,3 (24,17)	-0,4 (1,32)	209	32,2 (24,45)	2,2 (1,30)	-2,5 (1,85) [-6,2; 1,1]	0,1715
Woche 6	170	30,7 (24,93)	-0,2 (1,54)	183	31,9 (23,91)	3,6 (1,50)	-3,9 (2,15) [-8,1; 0,4]	0,0728
Woche 9	167	30,3 (24,10)	-0,4 (1,51)	159	28,9 (22,36)	4,4 (1,52)	-4,8 (2,15) [-9,0; -0,5]	0,0275
Woche 12	158	30,4 (23,34)	-0,2 (1,53)	147	30,6 (23,21)	3,6 (1,56)	-3,7 (2,18) [-8,0; 0,6]	0,0881
Woche 16	148	30,8 (23,80)	1,3 (1,76)	137	29,9 (21,75)	4,0 (1,81)	-2,7 (2,53) [-7,7; 2,3]	0,2830
Woche 20	139	29,0 (23,98)	-1,1 (1,65)	113	30,0 (23,14)	2,5 (1,76)	-3,6 (2,40) [-8,3; 1,1]	0,1357
Woche 24	118	30,0 (24,41)	0,6 (1,60)	94	29,8 (22,88)	1,5 (1,74)	-0,8 (2,37) [-5,5; 3,8]	0,7286

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 9.7.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	30,0 (25,06)	0,9 (1,72)	88	27,0 (22,46)	1,0 (1,85)	-0,1 (2,52) [-5,1; 4,9]	0,9677
Woche 32	95	27,8 (23,20)	-1,3 (1,96)	64	25,9 (20,19)	3,7 (2,31)	-5,1 (3,02) [-11,0; 0,9]	0,0955
Durchschnitt über alle Visiten	212	32,4 (24,60)	-0,1 (1,14)	217	32,3 (24,18)	2,9 (1,17)	-3,0 (1,63) [-6,2; 0,2]	0,0651
Hedges' g SMD							-0,2 (0,10) [-0,4; 0,0]	0,0655

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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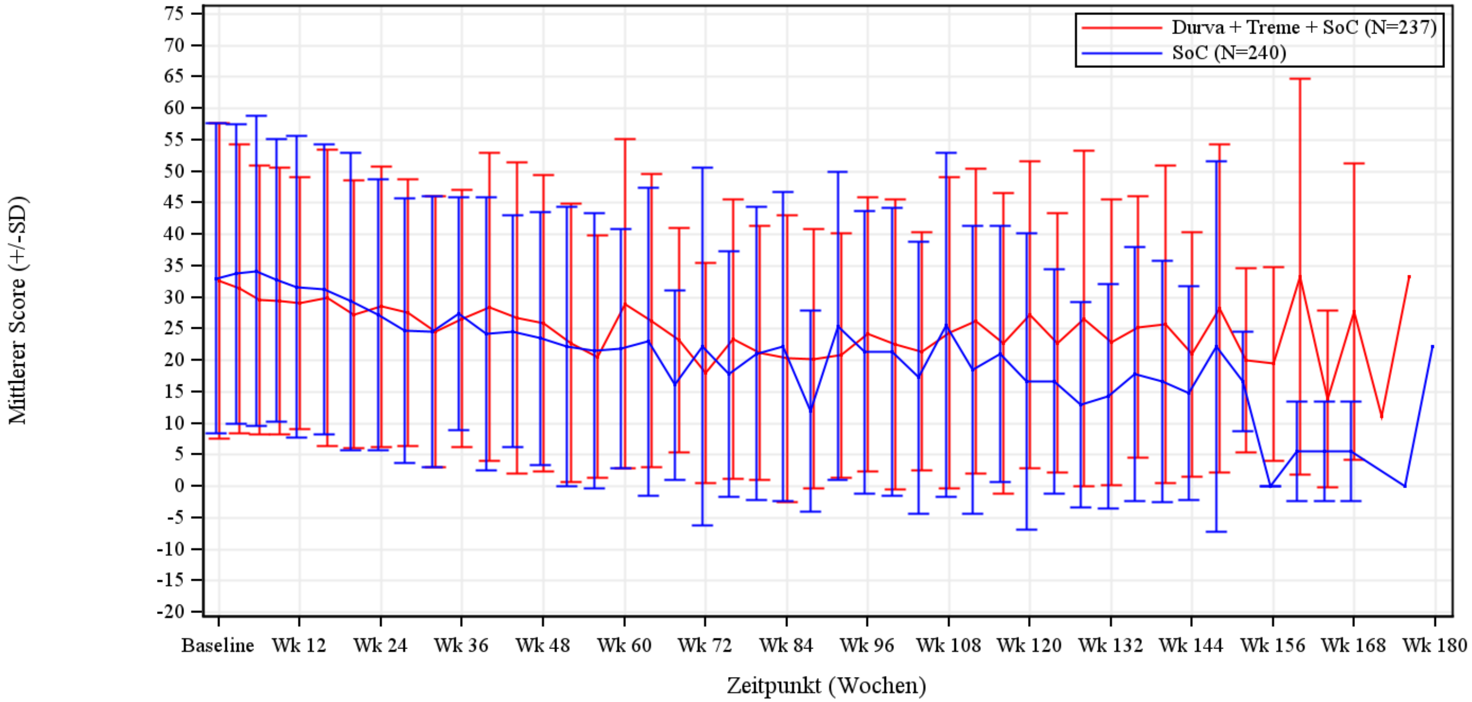
Figure 9.7.3.2 Mean change from baseline of EORTC QLQ-C30 fatigue (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Anzahl Patienten

Durva + Treme + SoC	226	212	173	170	160	151	143	121	108	98	91	80	73	64	62	55	51	46	43	43	39	43	35	34	31	34	34	28	26	25	23	22	20	20	18	18	16	18	11	10	8	4	4	2	1	1	0
SoC	229	213	188	163	152	140	116	97	91	66	62	49	46	35	35	31	28	29	20	23	18	20	17	14	17	12	13	9	13	9	9	10	8	6	7	5	4	3	3	2	2	2	2	2	0	1	1

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

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Table 9.8.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	8,7 (18,31)	3,7 (1,20)	209	7,4 (15,31)	3,1 (1,18)	0,6 (1,68) [-2,7; 3,9]	0,7259
Woche 6	170	8,4 (17,79)	3,0 (1,35)	183	7,7 (16,18)	4,1 (1,31)	-1,2 (1,88) [-4,9; 2,5]	0,5351
Woche 9	167	9,1 (19,16)	1,2 (1,22)	159	7,2 (16,51)	1,2 (1,24)	-0,1 (1,74) [-3,5; 3,3]	0,9590
Woche 12	158	7,7 (17,10)	1,9 (1,36)	147	6,2 (13,12)	3,1 (1,39)	-1,2 (1,95) [-5,0; 2,6]	0,5446
Woche 16	148	8,7 (18,39)	0,9 (1,08)	137	6,6 (15,31)	-0,1 (1,12)	1,0 (1,56) [-2,1; 4,1]	0,5215
Woche 20	139	7,8 (17,06)	-0,2 (1,13)	113	7,4 (16,05)	-0,4 (1,23)	0,3 (1,67) [-3,0; 3,6]	0,8626
Woche 24	118	8,1 (17,80)	2,1 (1,50)	94	7,4 (14,59)	1,9 (1,62)	0,2 (2,21) [-4,2; 4,5]	0,9327

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 9.8.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	6,9 (16,68)	0,1 (1,35)	88	6,6 (13,73)	1,6 (1,46)	-1,6 (1,99) [-5,5; 2,3]	0,4292
Woche 32	95	6,7 (17,09)	-0,6 (1,09)	64	7,3 (13,24)	-1,5 (1,28)	0,9 (1,68) [-2,4; 4,2]	0,5950
Durchschnitt über alle Visiten	212	8,6 (18,32)	1,3 (0,79)	217	7,8 (16,20)	1,4 (0,81)	-0,1 (1,13) [-2,3; 2,1]	0,9179
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9180

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs265g.sas Executed : 2022-10-17T211424

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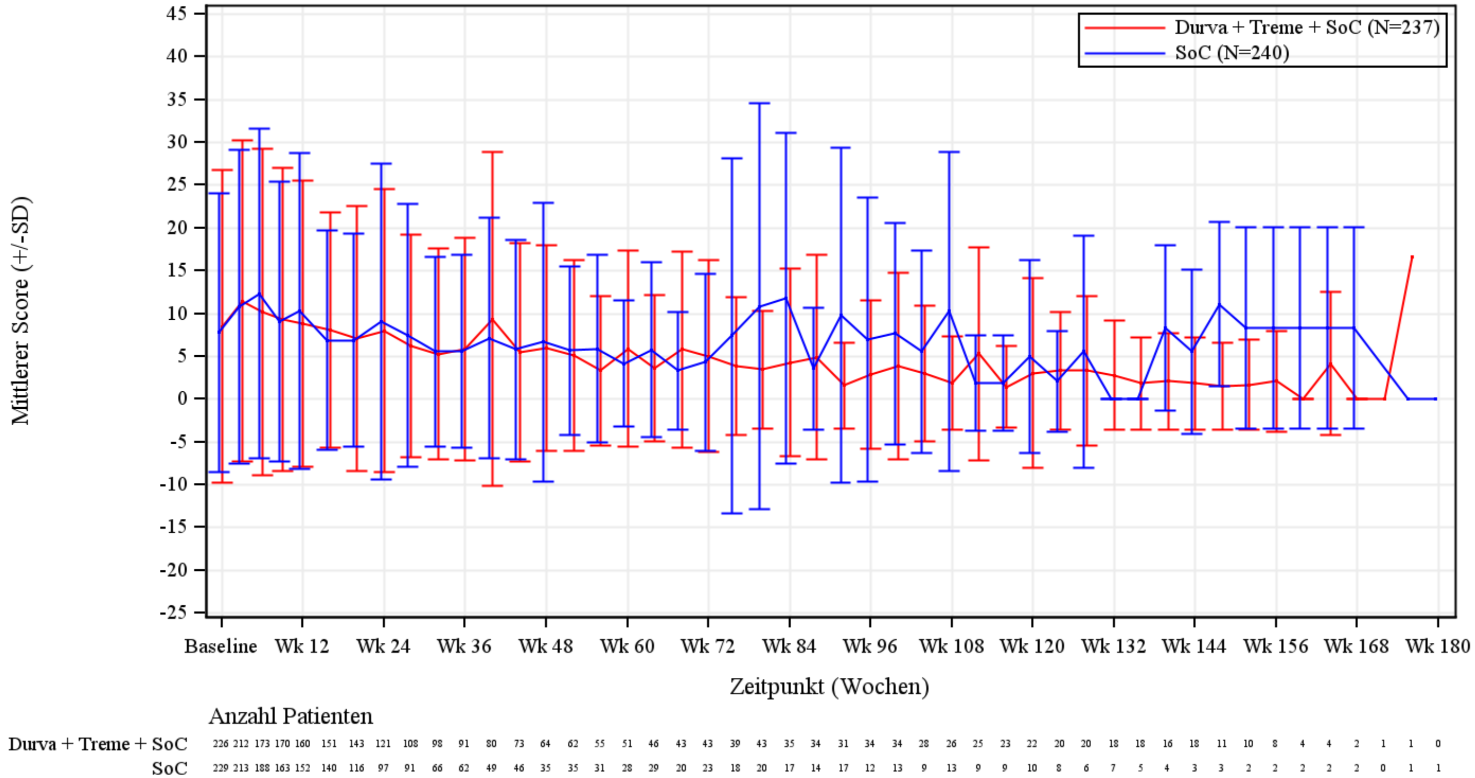
Figure 9.8.3.2 Mean change from baseline of EORTC QLQ-C30 nausea and vomiting (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs365g.sas Executed : 2022-10-17T222122

Table 9.9.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	27,7 (26,19)	-5,5 (1,47)	209	26,8 (28,11)	-1,7 (1,46)	-3,8 (2,07) [-7,9; 0,3]	0,0673
Woche 6	170	25,4 (25,40)	-7,1 (1,59)	183	27,2 (28,93)	-5,1 (1,55)	-2,0 (2,22) [-6,3; 2,4]	0,3810
Woche 9	167	25,7 (25,06)	-8,4 (1,61)	159	24,7 (27,80)	-4,5 (1,62)	-3,9 (2,28) [-8,3; 0,6]	0,0916
Woche 12	158	26,7 (25,93)	-8,0 (1,62)	147	23,2 (26,14)	-3,2 (1,65)	-4,9 (2,32) [-9,4; -0,3]	0,0365
Woche 16	148	26,1 (25,95)	-5,0 (1,78)	137	23,8 (27,48)	-2,6 (1,85)	-2,4 (2,57) [-7,5; 2,6]	0,3430
Woche 20	139	25,8 (25,63)	-2,9 (1,83)	113	22,6 (26,34)	-1,6 (1,97)	-1,3 (2,69) [-6,6; 4,0]	0,6340
Woche 24	118	25,8 (26,74)	-2,2 (1,96)	94	23,8 (25,92)	-1,1 (2,13)	-1,1 (2,89) [-6,8; 4,6]	0,7136

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs275g.sas Executed : 2022-10-17T211843

Table 9.9.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	27,2 (26,59)	-2,8 (2,09)	88	22,2 (27,99)	0,0 (2,26)	-2,8 (3,08) [-8,9; 3,2]	0,3568
Woche 32	95	23,9 (25,92)	-2,5 (2,22)	64	24,2 (28,78)	3,7 (2,58)	-6,2 (3,40) [-12,9; 0,5]	0,0697
Durchschnitt über alle Visiten	212	27,4 (26,33)	-4,9 (1,25)	217	27,2 (28,66)	-1,8 (1,28)	-3,1 (1,79) [-6,7; 0,4]	0,0794
Hedges' g SMD							-0,2 (0,10) [-0,4; 0,0]	0,0797

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs275g.sas Executed : 2022-10-17T211843

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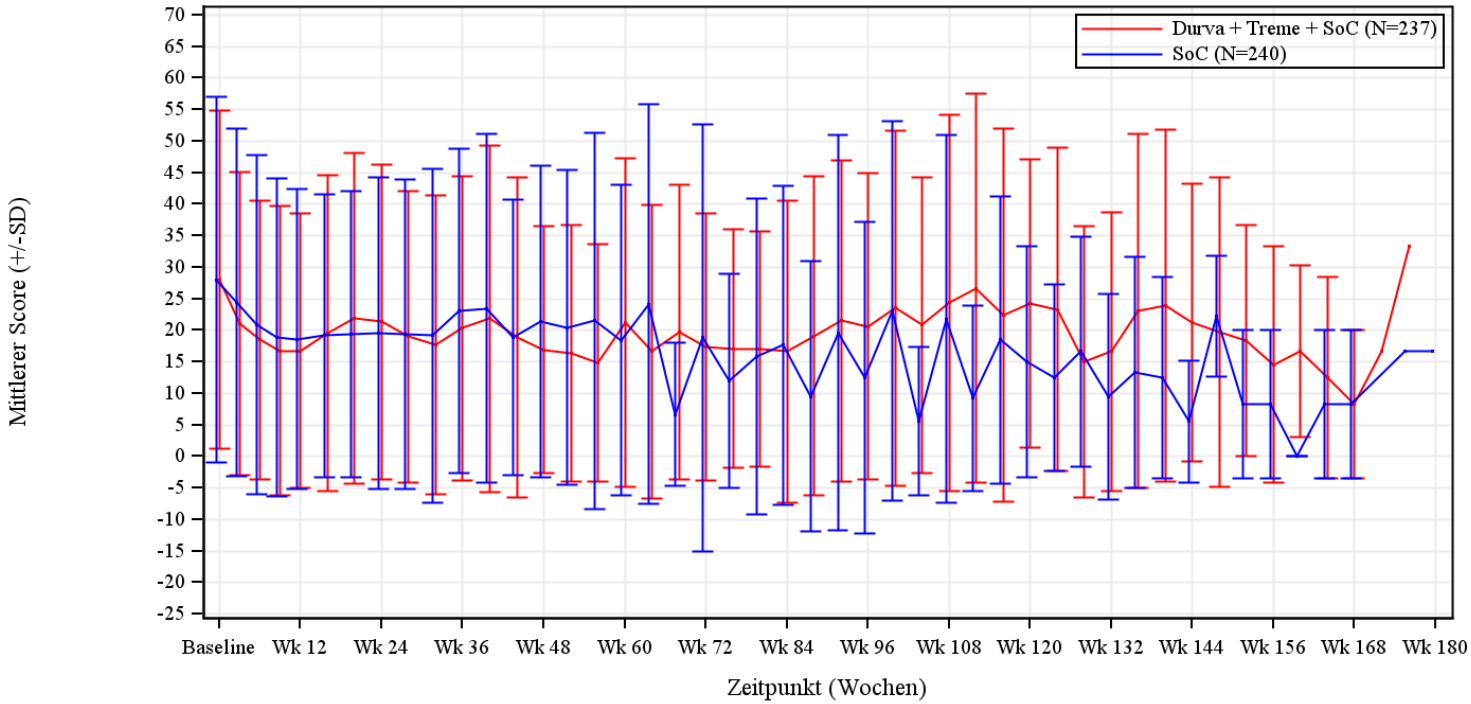
Figure 9.9.3.2 Mean change from baseline of EORTC QLQ-C30 pain (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs375g.sas Executed : 2022-10-17T222530

Table 9.10.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	30,1 (27,35)	-1,7 (1,50)	209	30,5 (28,35)	-0,7 (1,49)	-1,0 (2,11) [-5,1; 3,2]	0,6421
Woche 6	170	28,8 (25,88)	-2,7 (1,71)	183	28,8 (26,56)	0,0 (1,66)	-2,7 (2,38) [-7,4; 2,0]	0,2566
Woche 9	167	29,1 (26,93)	0,6 (1,79)	159	27,0 (26,03)	0,7 (1,81)	-0,1 (2,54) [-5,1; 4,9]	0,9714
Woche 12	158	28,5 (27,34)	1,0 (1,92)	147	28,1 (26,95)	0,4 (1,96)	0,6 (2,74) [-4,8; 6,0]	0,8361
Woche 16	148	27,3 (26,67)	0,3 (1,85)	137	25,3 (24,76)	1,9 (1,91)	-1,6 (2,65) [-6,8; 3,6]	0,5514
Woche 20	139	27,1 (26,79)	-1,5 (1,95)	113	24,5 (23,58)	-0,2 (2,10)	-1,3 (2,87) [-7,0; 4,3]	0,6483
Woche 24	118	29,4 (28,30)	1,6 (2,02)	94	24,8 (25,37)	0,4 (2,18)	1,1 (2,98) [-4,7; 7,0]	0,7007

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs285g.sas Executed : 2022-10-17T212246

Table 9.10.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	26,3 (26,95)	0,7 (2,12)	88	23,9 (25,24)	1,1 (2,30)	-0,4 (3,13) [-6,6; 5,8]	0,9011
Woche 32	95	26,3 (26,14)	-0,6 (2,29)	64	22,9 (25,80)	-1,8 (2,71)	1,2 (3,54) [-5,8; 8,2]	0,7321
Durchschnitt über alle Visiten	212	30,2 (27,55)	-0,3 (1,28)	217	30,6 (28,19)	0,2 (1,31)	-0,5 (1,83) [-4,1; 3,1]	0,8018
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,8022

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs285g.sas Executed : 2022-10-17T212246

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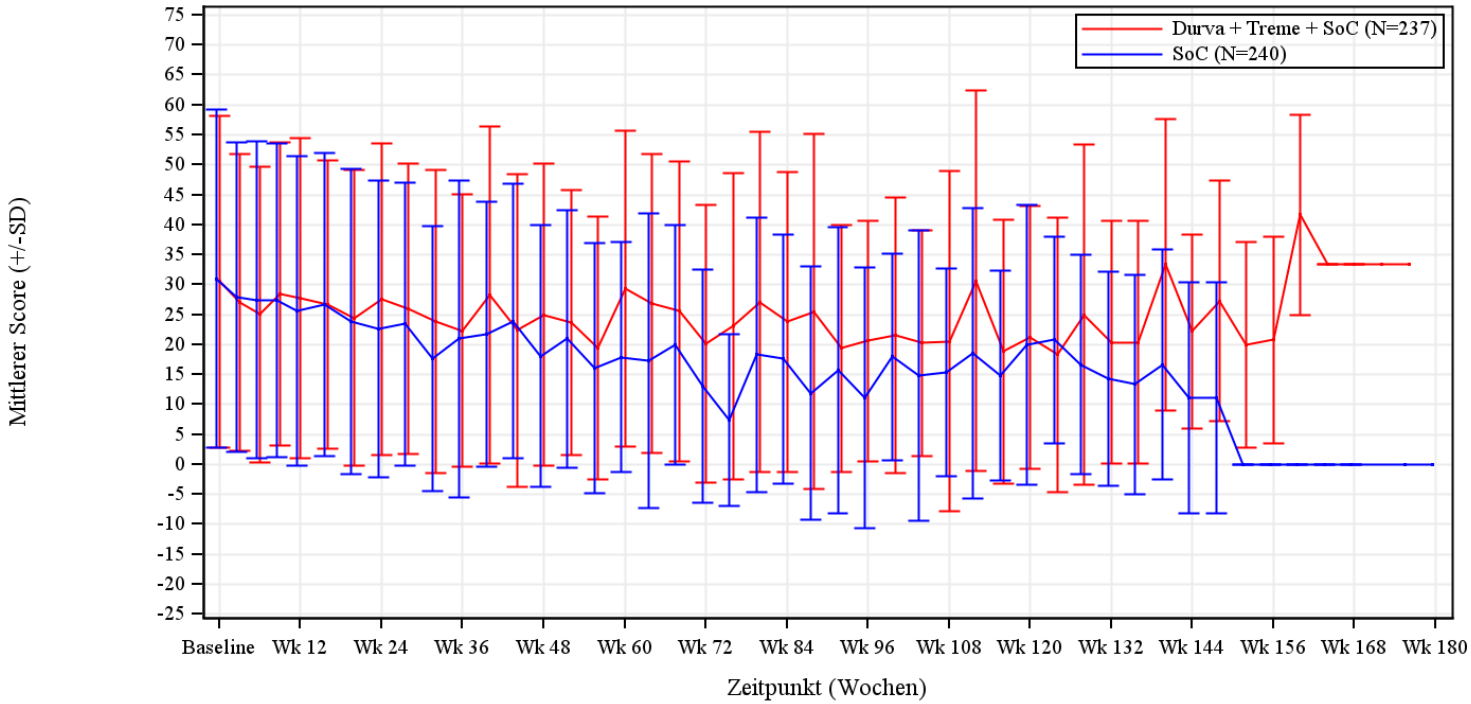
Figure 9.10.3.2 Mean change from baseline of EORTC QLQ-C30 dyspnoea (individual symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs385g.sas Executed : 2022-10-17T223006

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Table 9.11.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	24,9 (28,79)	-1,7 (1,67)	209	24,6 (29,65)	-0,7 (1,65)	-1,0 (2,35) [-5,6; 3,6]	0,6696
Woche 6	170	23,5 (28,93)	-1,9 (1,88)	183	25,5 (29,95)	-1,5 (1,82)	-0,4 (2,62) [-5,5; 4,8]	0,8882
Woche 9	167	23,8 (28,60)	-3,6 (1,75)	159	23,5 (28,45)	-3,3 (1,77)	-0,3 (2,49) [-5,2; 4,6]	0,9015
Woche 12	158	23,4 (27,78)	-4,9 (1,78)	147	21,8 (26,65)	-1,8 (1,82)	-3,1 (2,54) [-8,1; 1,9]	0,2270
Woche 16	148	25,5 (29,19)	-0,3 (1,98)	137	23,6 (28,63)	-3,3 (2,05)	3,0 (2,85) [-2,6; 8,6]	0,2971
Woche 20	139	25,7 (28,46)	-4,4 (1,93)	113	23,9 (30,04)	-3,9 (2,07)	-0,4 (2,83) [-6,0; 5,1]	0,8778
Woche 24	118	25,1 (28,56)	0,5 (2,04)	94	24,1 (28,67)	-3,1 (2,23)	3,6 (3,02) [-2,4; 9,5]	0,2386

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs295g.sas Executed : 2022-10-17T212703

Table 9.11.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	24,0 (29,18)	-4,1 (2,02)	88	22,0 (28,09)	-3,2 (2,18)	-0,8 (2,97) [-6,7; 5,0]	0,7752
Woche 32	95	23,5 (28,30)	-0,3 (2,40)	64	20,8 (27,54)	-1,6 (2,81)	1,3 (3,69) [-6,0; 8,6]	0,7260
Durchschnitt über alle Visiten	212	25,2 (28,96)	-2,3 (1,28)	217	25,3 (30,05)	-2,5 (1,31)	0,2 (1,83) [-3,4; 3,8]	0,9131
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9133

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs295g.sas Executed : 2022-10-17T212703

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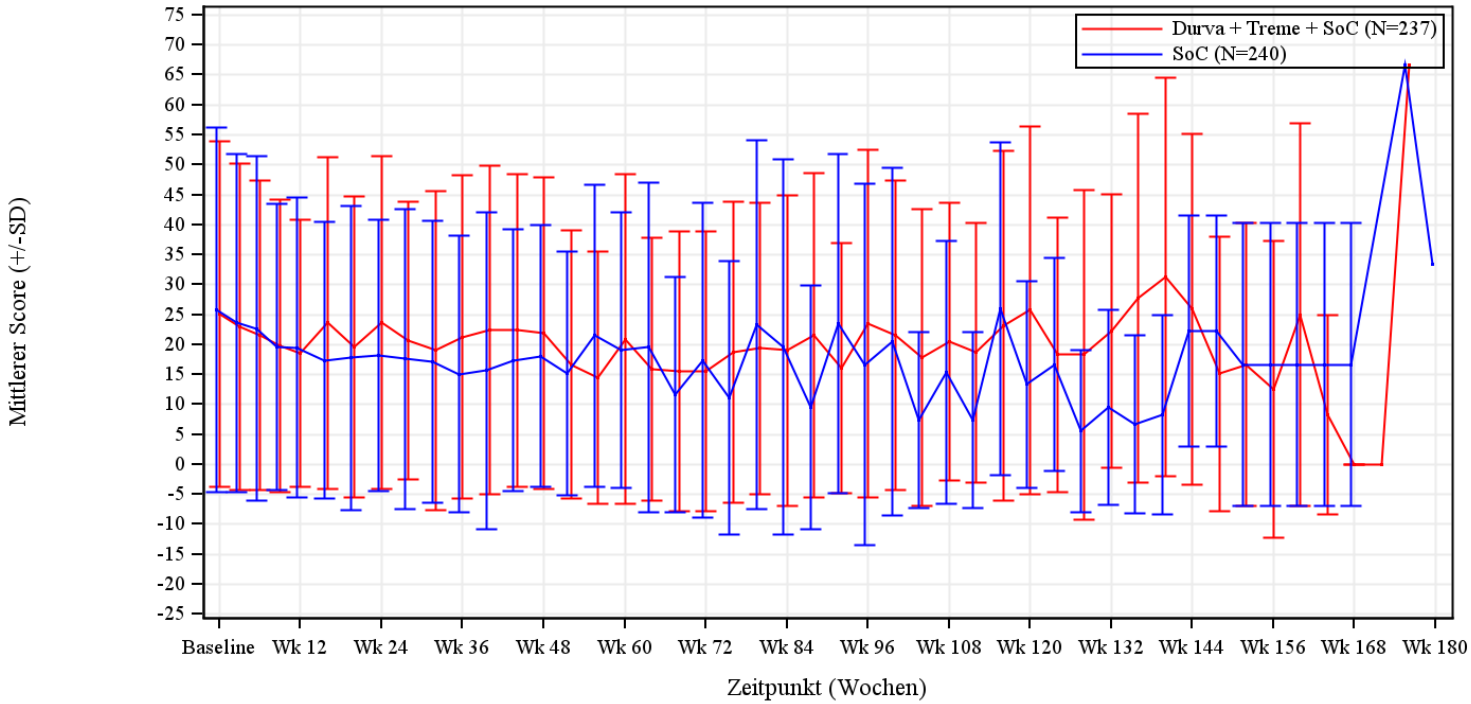
Figure 9.11.3.2 Mean change from baseline of EORTC QLQ-C30 insomnia (individual symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs395g.sas Executed : 2022-10-17T223508

Table 9.12.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	20,2 (27,26)	1,6 (1,73)	209	22,8 (27,85)	0,6 (1,72)	1,0 (2,44) [-3,8; 5,8]	0,6802
Woche 6	170	18,4 (26,15)	1,0 (1,92)	183	23,1 (28,48)	0,1 (1,87)	0,9 (2,68) [-4,4; 6,2]	0,7349
Woche 9	167	19,2 (26,23)	-1,3 (1,91)	159	21,0 (27,44)	-0,4 (1,93)	-1,0 (2,72) [-6,3; 4,4]	0,7205
Woche 12	158	17,7 (24,58)	0,0 (2,02)	147	19,7 (24,60)	0,5 (2,06)	-0,5 (2,88) [-6,1; 5,2]	0,8699
Woche 16	148	17,1 (24,43)	0,9 (1,95)	137	20,0 (25,71)	0,4 (2,01)	0,5 (2,81) [-5,0; 6,1]	0,8513
Woche 20	139	18,0 (24,82)	0,3 (1,91)	113	20,9 (26,43)	1,7 (2,07)	-1,4 (2,81) [-6,9; 4,1]	0,6191
Woche 24	118	20,3 (25,80)	0,7 (2,09)	94	21,6 (26,19)	-0,1 (2,31)	0,7 (3,12) [-5,4; 6,9]	0,8108

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation. SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2005g.sas Executed : 2022-10-17T213104

Table 9.12.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	18,6 (24,94)	-2,9 (2,02)	88	19,7 (24,05)	-2,8 (2,20)	-0,2 (2,99) [-6,1; 5,7]	0,9575
Woche 32	95	15,8 (24,23)	-1,5 (2,48)	64	19,8 (25,00)	-1,1 (2,94)	-0,4 (3,85) [-8,0; 7,1]	0,9078
Durchschnitt über alle Visiten	212	20,3 (27,59)	-0,1 (1,22)	217	23,3 (28,47)	-0,1 (1,26)	0,0 (1,76) [-3,5; 3,4]	0,9868
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9869

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation. SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2005g.sas Executed : 2022-10-17T213104

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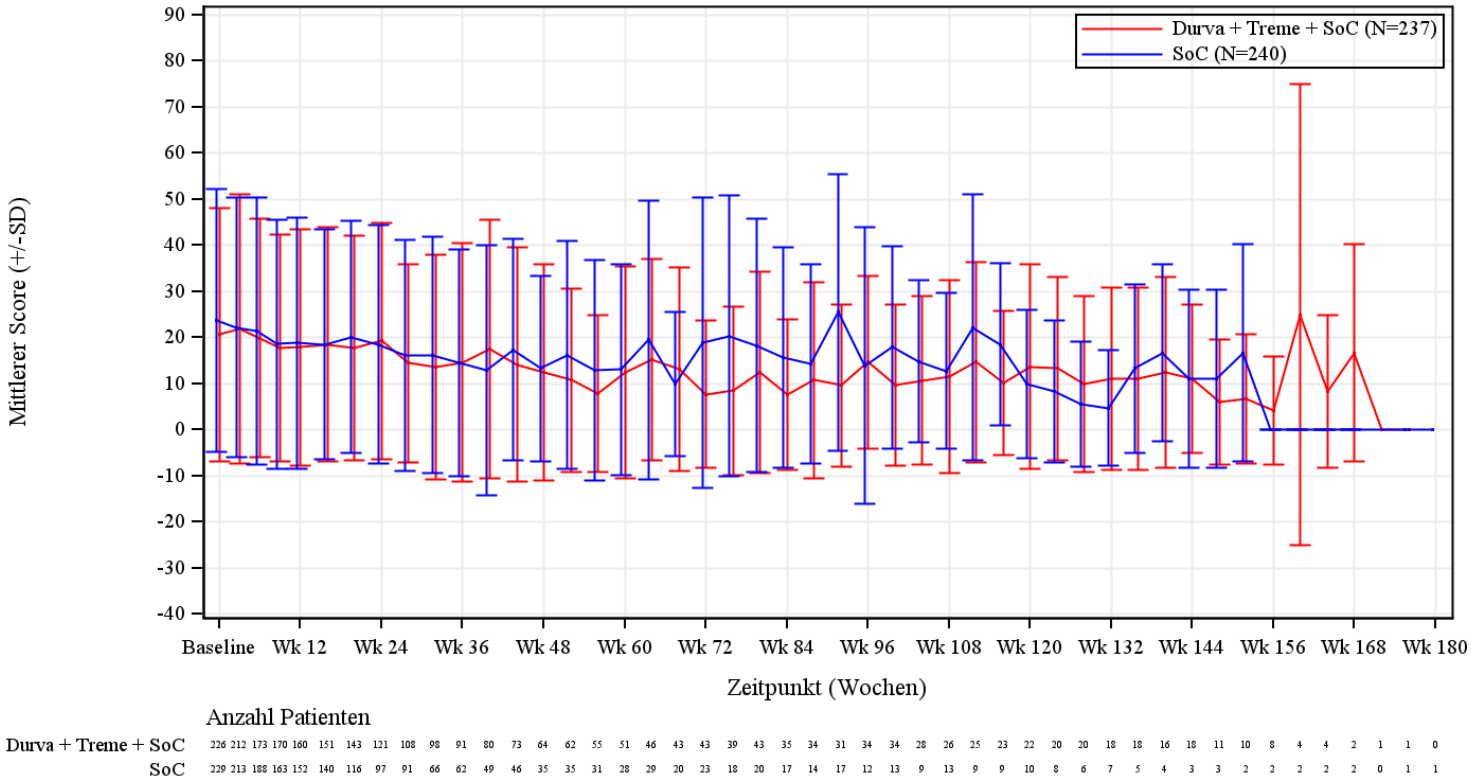
Figure 9.12.3.2 Mean change from baseline of EORTC QLQ-C30 loss of appetite (individual symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3005g.sas Executed : 2022-10-17T223944

Table 9.13.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	15,5 (26,47)	-0,1 (1,69)	209	17,2 (27,75)	2,9 (1,67)	-3,0 (2,37) [-7,7; 1,6]	0,2034
Woche 6	170	15,5 (25,93)	-1,9 (1,81)	183	16,6 (27,04)	3,0 (1,75)	-4,9 (2,52) [-9,9; 0,0]	0,0512
Woche 9	167	16,4 (27,59)	-0,9 (1,74)	159	16,4 (28,03)	1,9 (1,76)	-2,8 (2,48) [-7,7; 2,0]	0,2540
Woche 12	158	16,0 (26,53)	-1,9 (1,91)	147	15,4 (26,82)	1,5 (1,96)	-3,4 (2,74) [-8,7; 2,0]	0,2216
Woche 16	148	15,8 (26,50)	-1,9 (1,75)	137	16,5 (28,62)	-0,4 (1,80)	-1,5 (2,51) [-6,5; 3,4]	0,5469
Woche 20	139	16,1 (26,72)	-1,5 (2,00)	113	14,5 (25,54)	1,6 (2,18)	-3,1 (2,96) [-8,9; 2,7]	0,2909
Woche 24	118	16,1 (27,81)	1,6 (1,97)	94	15,2 (26,62)	0,3 (2,15)	1,3 (2,92) [-4,4; 7,1]	0,6515

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation. SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2105g.sas Executed : 2022-10-17T213519

Table 9.13.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

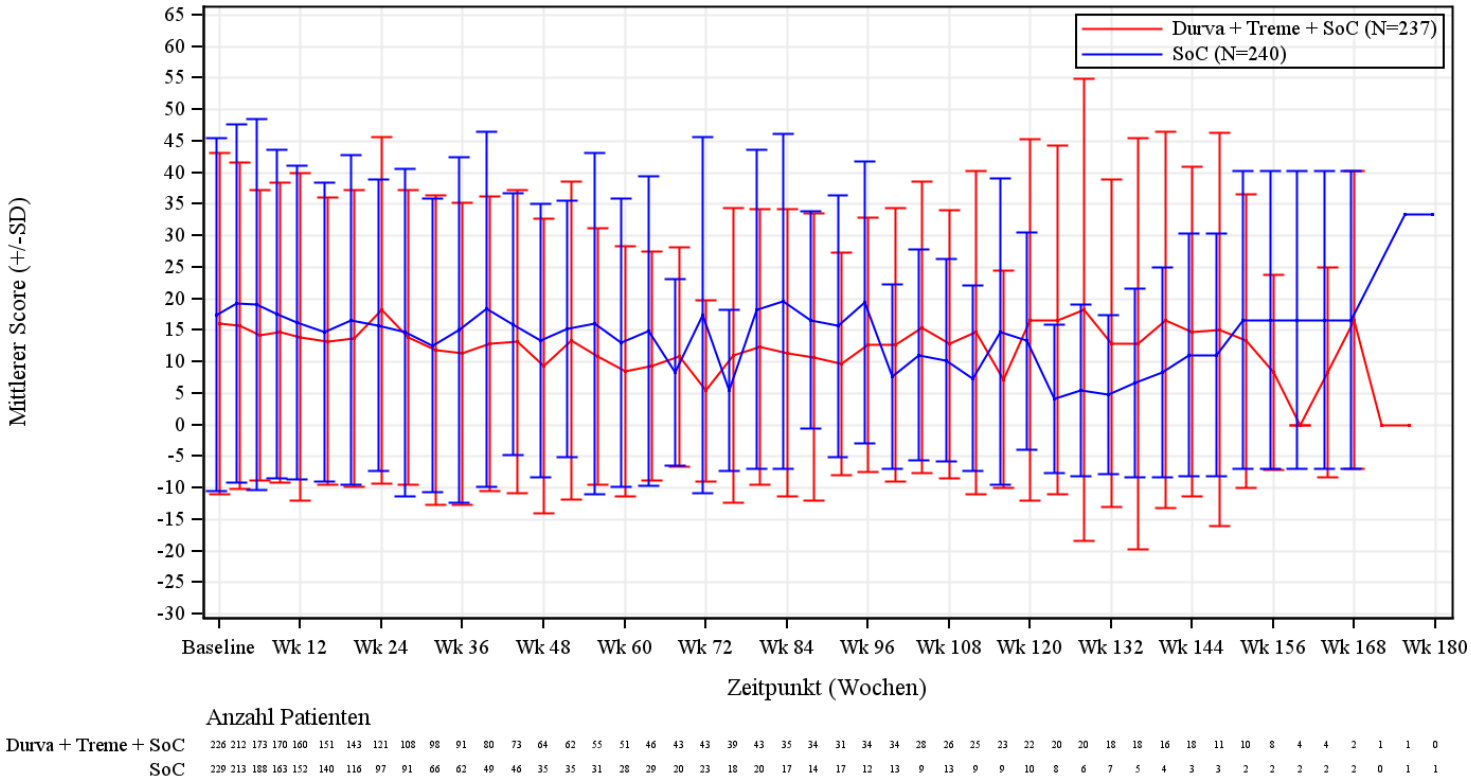
	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	17,3 (28,63)	-2,1 (1,98)	88	15,5 (25,75)	-1,0 (2,15)	-1,1 (2,92) [-6,8; 4,7]	0,7132
Woche 32	95	13,3 (24,50)	-1,2 (2,07)	64	15,1 (26,51)	-2,6 (2,42)	1,3 (3,18) [-4,9; 7,6]	0,6752
Durchschnitt über alle Visiten	212	15,7 (26,84)	-1,1 (1,22)	217	16,7 (27,43)	0,8 (1,26)	-1,9 (1,75) [-5,4; 1,5]	0,2770
Hedges' g SMD							-0,1 (0,10) [-0,3; 0,1]	0,2776

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation. SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2105g.sas Executed : 2022-10-17T213519

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 1

Figure 9.13.3.2 Mean change from baseline of EORTC QLQ-C30 constipation (individual symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3105g.sas Executed : 2022-10-17T224440

Table 9.14.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 diarrhoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	6,1 (15,96)	1,3 (1,11)	209	5,7 (13,44)	1,0 (1,11)	0,4 (1,57) [-2,7; 3,4]	0,8204
Woche 6	170	6,5 (15,51)	1,4 (1,10)	183	6,2 (13,91)	-1,6 (1,06)	3,0 (1,53) [0,0; 6,0]	0,0533
Woche 9	167	6,0 (14,77)	2,0 (1,25)	159	5,7 (13,63)	-0,8 (1,28)	2,9 (1,79) [-0,7; 6,4]	0,1103
Woche 12	158	5,3 (13,83)	0,8 (1,08)	147	5,2 (12,76)	-0,7 (1,12)	1,5 (1,56) [-1,6; 4,5]	0,3513
Woche 16	148	6,3 (15,23)	-0,7 (1,11)	137	5,6 (13,14)	-0,6 (1,15)	-0,1 (1,60) [-3,3; 3,0]	0,9404
Woche 20	139	6,0 (14,61)	0,5 (1,13)	113	5,9 (13,53)	-2,3 (1,22)	2,8 (1,66) [-0,5; 6,1]	0,0907
Woche 24	118	6,8 (15,44)	1,6 (1,41)	94	5,7 (13,51)	-2,7 (1,55)	4,3 (2,10) [0,2; 8,4]	0,0417

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2115g.sas Executed : 2022-10-17T213947

Table 9.14.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 diarrhoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	5,4 (14,02)	-1,5 (1,06)	88	5,7 (13,58)	-1,4 (1,15)	-0,1 (1,56) [-3,2; 2,9]	0,9242
Woche 32	95	6,0 (15,36)	-2,0 (1,18)	64	4,7 (11,68)	-1,9 (1,40)	-0,1 (1,83) [-3,7; 3,6]	0,9768
Durchschnitt über alle Visiten	212	6,1 (15,87)	0,4 (0,66)	217	5,8 (13,48)	-1,2 (0,69)	1,6 (0,96) [-0,3; 3,5]	0,0939
Hedges' g SMD							0,2 (0,10) [0,0; 0,4]	0,0942

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2115g.sas Executed : 2022-10-17T213947

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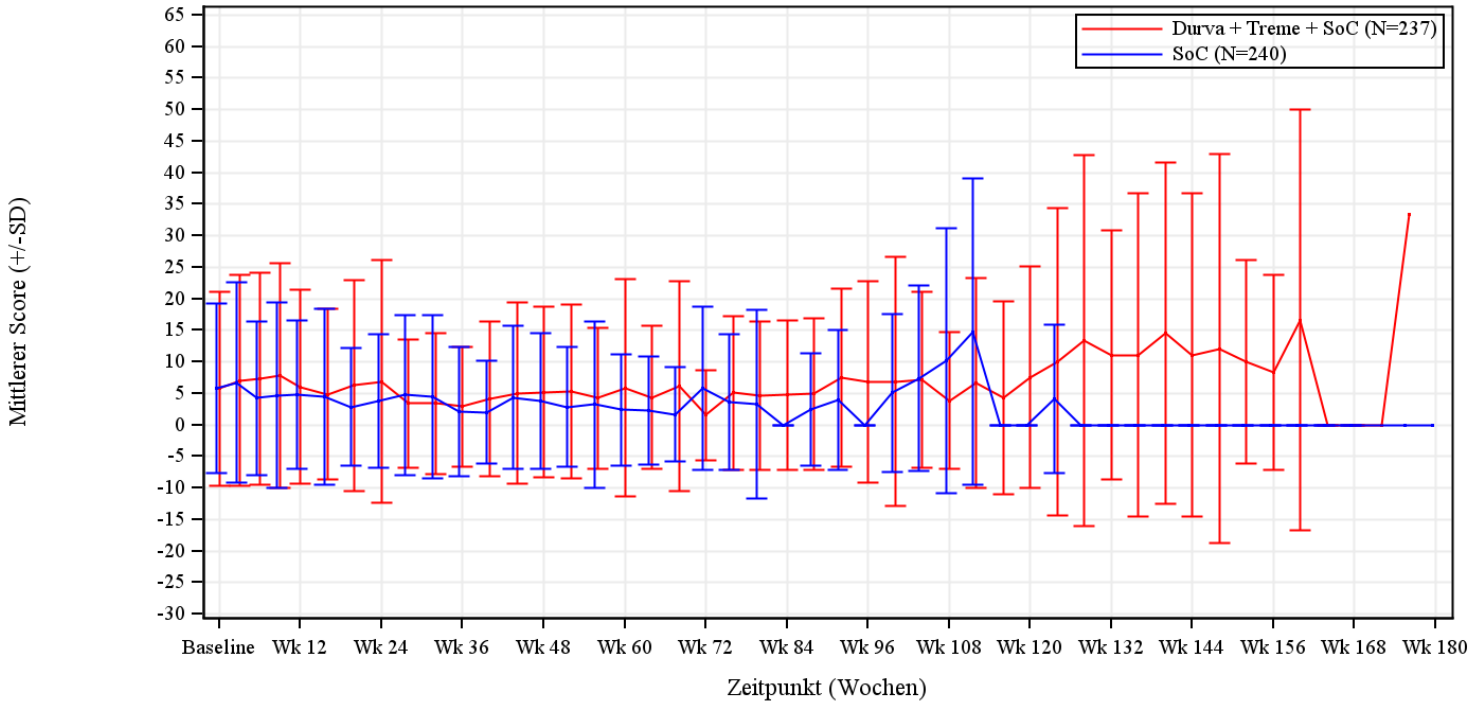
Figure 9.14.3.2 Mean change from baseline of EORTC QLQ-C30 diarrhoea (individual symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3115g.sas Executed : 2022-10-17T224902

Table 9.15.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	18,6 (26,63)	-1,0 (1,49)	209	22,8 (29,16)	-0,4 (1,48)	-0,6 (2,10) [-4,7; 3,5]	0,7748
Woche 6	170	17,3 (25,44)	-1,7 (1,65)	183	22,8 (29,82)	-3,0 (1,61)	1,3 (2,31) [-3,2; 5,9]	0,5718
Woche 9	167	18,6 (27,53)	-0,7 (1,59)	159	22,0 (29,25)	-1,4 (1,60)	0,7 (2,26) [-3,7; 5,1]	0,7569
Woche 12	158	18,8 (27,24)	-0,4 (1,70)	147	22,4 (28,98)	0,7 (1,73)	-1,1 (2,43) [-5,9; 3,7]	0,6442
Woche 16	148	18,2 (27,58)	-0,9 (1,92)	137	21,9 (28,13)	1,3 (1,98)	-2,2 (2,76) [-7,6; 3,3]	0,4334
Woche 20	139	17,5 (26,42)	2,3 (1,90)	113	22,7 (29,64)	0,0 (2,04)	2,3 (2,79) [-3,2; 7,8]	0,4118
Woche 24	118	16,9 (26,78)	2,7 (2,06)	94	22,3 (28,25)	-1,2 (2,21)	3,9 (3,03) [-2,1; 9,8]	0,2016

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2125g.sas Executed : 2022-10-17T214340

Table 9.15.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	18,3 (27,82)	2,7 (1,93)	88	20,8 (27,83)	-0,4 (2,06)	3,1 (2,83) [-2,5; 8,6]	0,2805
Woche 32	95	17,9 (27,85)	1,0 (1,99)	64	22,4 (32,01)	0,4 (2,28)	0,6 (3,02) [-5,3; 6,6]	0,8367
Durchschnitt über alle Visiten	212	18,7 (26,98)	0,4 (1,30)	217	23,3 (29,70)	-0,4 (1,32)	0,9 (1,86) [-2,8; 4,5]	0,6338
Hedges' g SMD							0,0 (0,10) [-0,1; 0,2]	0,6339

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2125g.sas Executed : 2022-10-17T214340

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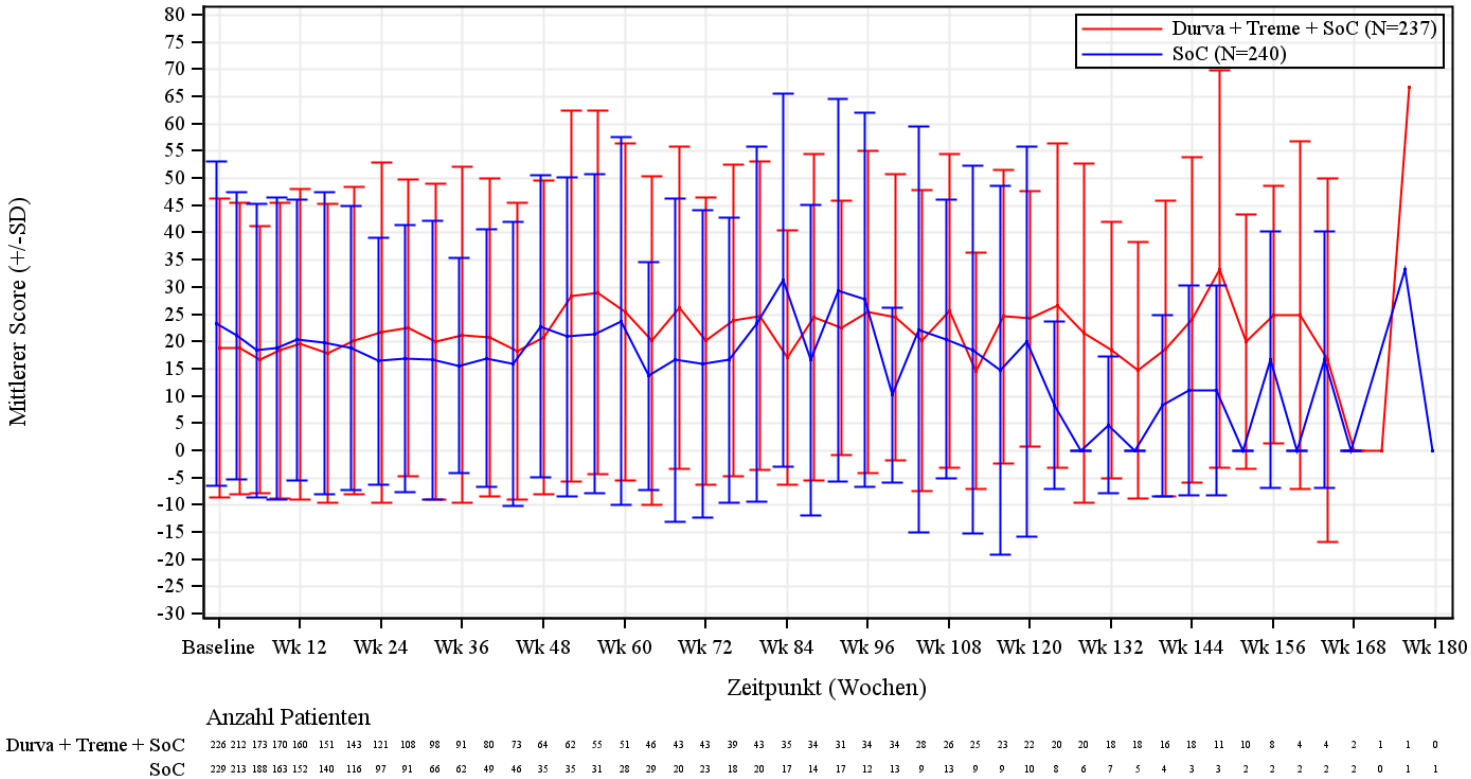
Figure 9.15.3.2 Mean change from baseline of EORTC QLQ-C30 financial difficulties score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3125g.sas Executed : 2022-10-17T225814

Anhang 4-G 1.1.2: EORTC QLQ-LC13 - Symptomskalen

Table 10.2.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	26,0 (21,26)	-1,3 (1,15)	208	24,3 (21,11)	0,8 (1,14)	-2,1 (1,61) [-5,3; 1,1]	0,1956
Woche 6	170	24,8 (20,41)	-0,3 (1,20)	181	22,7 (18,95)	0,3 (1,17)	-0,6 (1,67) [-3,9; 2,7]	0,7100
Woche 9	166	25,2 (21,06)	-0,4 (1,30)	159	21,1 (17,99)	2,8 (1,31)	-3,2 (1,85) [-6,8; 0,4]	0,0839
Woche 12	158	24,1 (20,52)	1,5 (1,41)	147	21,5 (18,79)	4,0 (1,43)	-2,5 (2,01) [-6,4; 1,5]	0,2149
Woche 16	147	23,7 (20,01)	1,9 (1,53)	137	20,6 (17,13)	4,3 (1,57)	-2,4 (2,19) [-6,7; 1,9]	0,2701
Woche 20	137	24,7 (19,99)	0,3 (1,46)	112	19,7 (16,25)	3,6 (1,55)	-3,3 (2,14) [-7,5; 0,9]	0,1226
Woche 24	118	25,0 (21,45)	0,7 (1,48)	94	20,2 (17,99)	3,1 (1,61)	-2,4 (2,20) [-6,7; 2,0]	0,2809

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc205g.sas Executed : 2022-10-17T231047

Table 10.2.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	23,7 (21,35)	1,7 (1,57)	88	19,9 (19,22)	3,2 (1,70)	-1,6 (2,32) [-6,1; 3,0]	0,4995
Woche 32	95	21,6 (20,27)	-0,1 (1,69)	64	18,6 (18,99)	0,3 (2,00)	-0,5 (2,61) [-5,6; 4,7]	0,8546
Durchschnitt über alle Visiten	212	26,0 (21,36)	0,4 (1,00)	216	24,2 (20,92)	2,5 (1,02)	-2,1 (1,43) [-4,9; 0,8]	0,1503
Hedges' g SMD							-0,1 (0,10) [-0,3; 0,1]	0,1507

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc205g.sas Executed : 2022-10-17T231047

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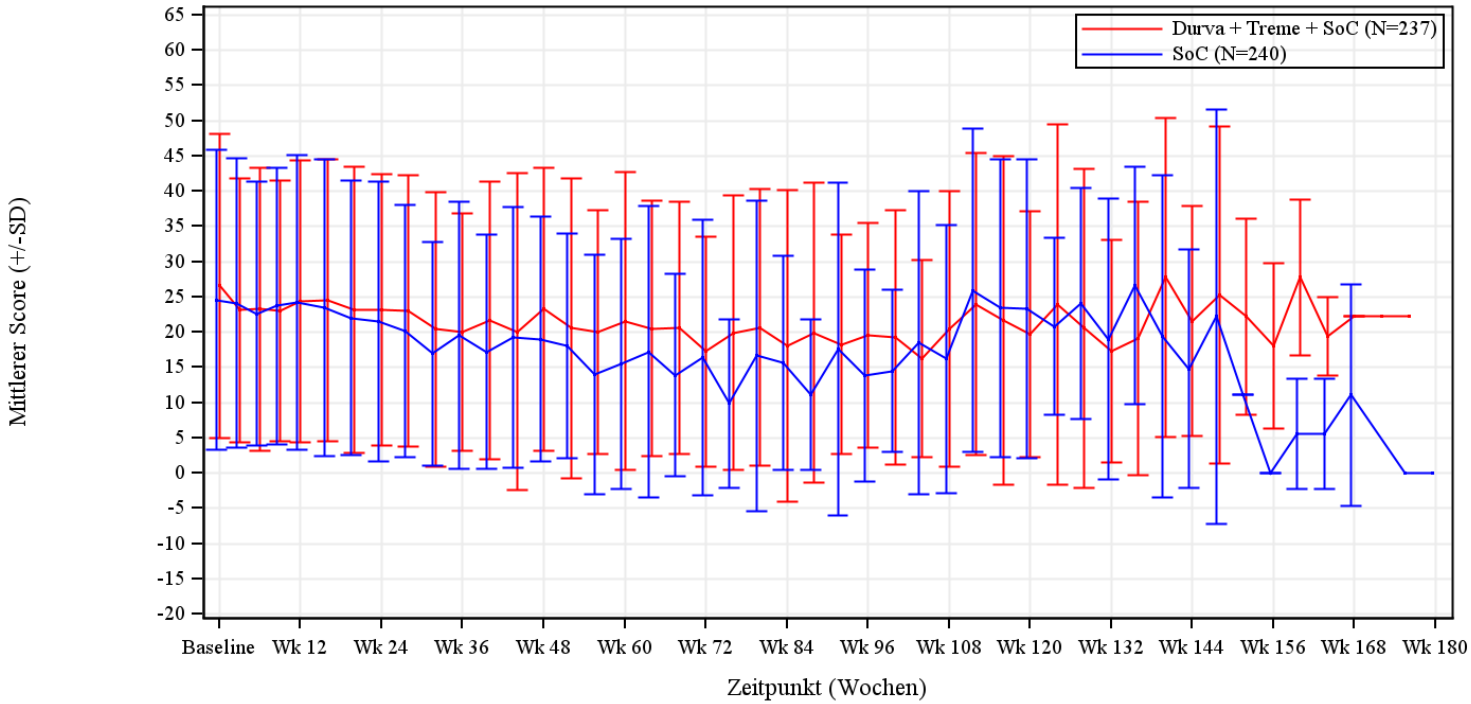
Figure 10.2.3.2 Mean change from baseline of EORTC QLQ-LC13 dyspnoea score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc305g.sas Executed : 2022-10-17T235516

Table 10.3.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	19,6 (23,73)	-3,4 (1,55)	208	23,6 (27,91)	-3,8 (1,54)	0,5 (2,19) [-3,8; 4,7]	0,8361
Woche 6	170	18,4 (22,65)	-4,5 (1,51)	181	23,2 (27,70)	-7,0 (1,48)	2,5 (2,12) [-1,7; 6,6]	0,2415
Woche 9	166	19,9 (23,49)	-5,4 (1,47)	159	19,5 (25,52)	-5,6 (1,49)	0,2 (2,10) [-3,9; 4,3]	0,9246
Woche 12	158	19,0 (22,37)	-5,4 (1,57)	147	19,7 (24,91)	-5,0 (1,61)	-0,5 (2,24) [-4,9; 4,0]	0,8379
Woche 16	147	19,7 (23,65)	-2,8 (1,57)	137	19,5 (24,47)	-4,2 (1,61)	1,4 (2,25) [-3,1; 5,8]	0,5476
Woche 20	137	19,2 (23,82)	-2,7 (1,70)	112	19,9 (25,88)	-4,8 (1,83)	2,1 (2,50) [-2,8; 7,0]	0,4042
Woche 24	118	19,2 (23,23)	0,0 (1,79)	94	19,1 (23,18)	-4,1 (1,95)	4,1 (2,64) [-1,1; 9,3]	0,1250

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 10.3.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	18,9 (23,58)	-4,6 (1,80)	88	17,4 (24,75)	-3,7 (1,96)	-1,0 (2,66) [-6,2; 4,3]	0,7138
Woche 32	95	17,2 (21,67)	-4,6 (1,91)	64	18,8 (25,80)	-5,5 (2,25)	0,8 (2,95) [-5,0; 6,6]	0,7798
Durchschnitt über alle Visiten	212	19,5 (23,79)	-3,7 (1,08)	216	23,3 (28,16)	-4,8 (1,11)	1,1 (1,55) [-1,9; 4,2]	0,4736
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,4741

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc215g.sas Executed : 2022-10-17T231517

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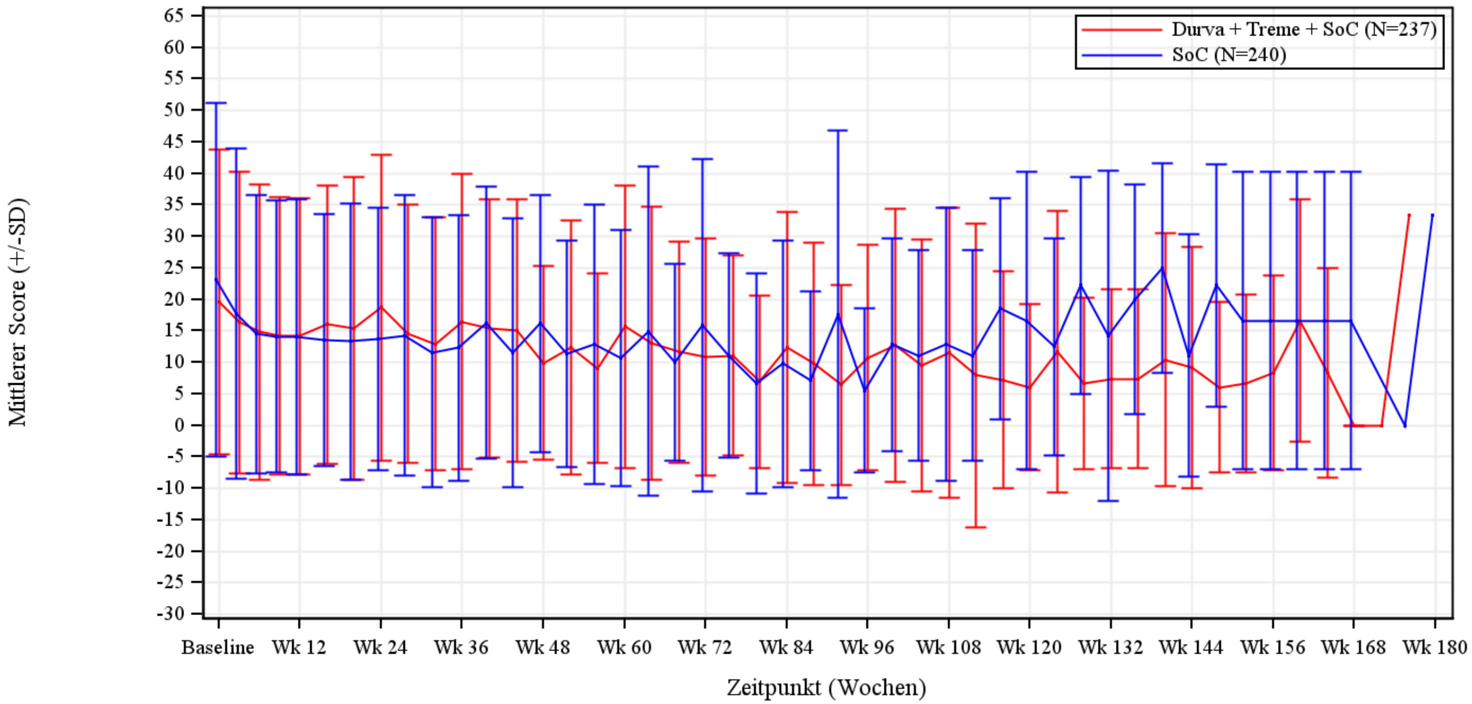
Figure 10.3.3.2 Mean change from baseline of EORTC QLQ-LC13 pain (chest) (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Anzahl Patienten

Durva + Treme + SoC	226	212	173	169	160	150	141	121	108	98	91	80	73	64	62	55	51	46	43	43	39	43	35	34	31	34	34	28	26	25	23	22	20	20	18	18	16	18	11	10	8	4	4	2	1	1	0
SoC	229	212	186	163	152	140	115	97	91	66	62	49	46	35	35	31	28	29	20	23	18	20	17	14	17	12	13	9	13	9	9	10	8	6	7	5	4	3	3	2	2	2	2	2	0	1	1

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc315g.sas Executed : 2022-10-17T235929

Table 10.4.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	17,3 (27,09)	-3,2 (1,37)	208	17,1 (27,80)	-1,6 (1,36)	-1,6 (1,93) [-5,4; 2,2]	0,4159
Woche 6	170	15,9 (26,94)	-5,4 (1,41)	181	17,1 (27,13)	-5,3 (1,37)	0,0 (1,97) [-3,9; 3,8]	0,9854
Woche 9	166	16,5 (26,65)	-3,8 (1,44)	159	15,1 (24,79)	-2,8 (1,45)	-1,0 (2,04) [-5,0; 3,0]	0,6229
Woche 12	158	15,8 (25,71)	-4,6 (1,56)	147	15,9 (25,38)	-1,9 (1,60)	-2,7 (2,24) [-7,1; 1,7]	0,2306
Woche 16	147	17,0 (27,41)	1,2 (1,75)	137	15,1 (25,23)	-0,7 (1,80)	1,8 (2,51) [-3,1; 6,8]	0,4625
Woche 20	137	17,3 (28,04)	1,1 (1,83)	112	17,0 (27,58)	-0,6 (1,98)	1,7 (2,69) [-3,6; 7,0]	0,5346
Woche 24	118	15,8 (27,81)	1,5 (2,01)	94	16,7 (27,11)	0,7 (2,21)	0,8 (2,99) [-5,0; 6,7]	0,7769

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc225g.sas Executed : 2022-10-17T232007

Table 10.4.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	16,7 (28,63)	1,5 (2,08)	88	17,0 (26,74)	-0,9 (2,24)	2,4 (3,06) [-3,6; 8,4]	0,4277
Woche 32	95	13,7 (25,49)	-0,6 (2,10)	64	15,6 (27,84)	-0,7 (2,43)	0,1 (3,21) [-6,2; 6,4]	0,9710
Durchschnitt über alle Visiten	212	17,3 (26,85)	-1,4 (1,14)	216	17,0 (27,47)	-1,5 (1,18)	0,2 (1,64) [-3,0; 3,4]	0,9130
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9132

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc225g.sas Executed : 2022-10-17T232007

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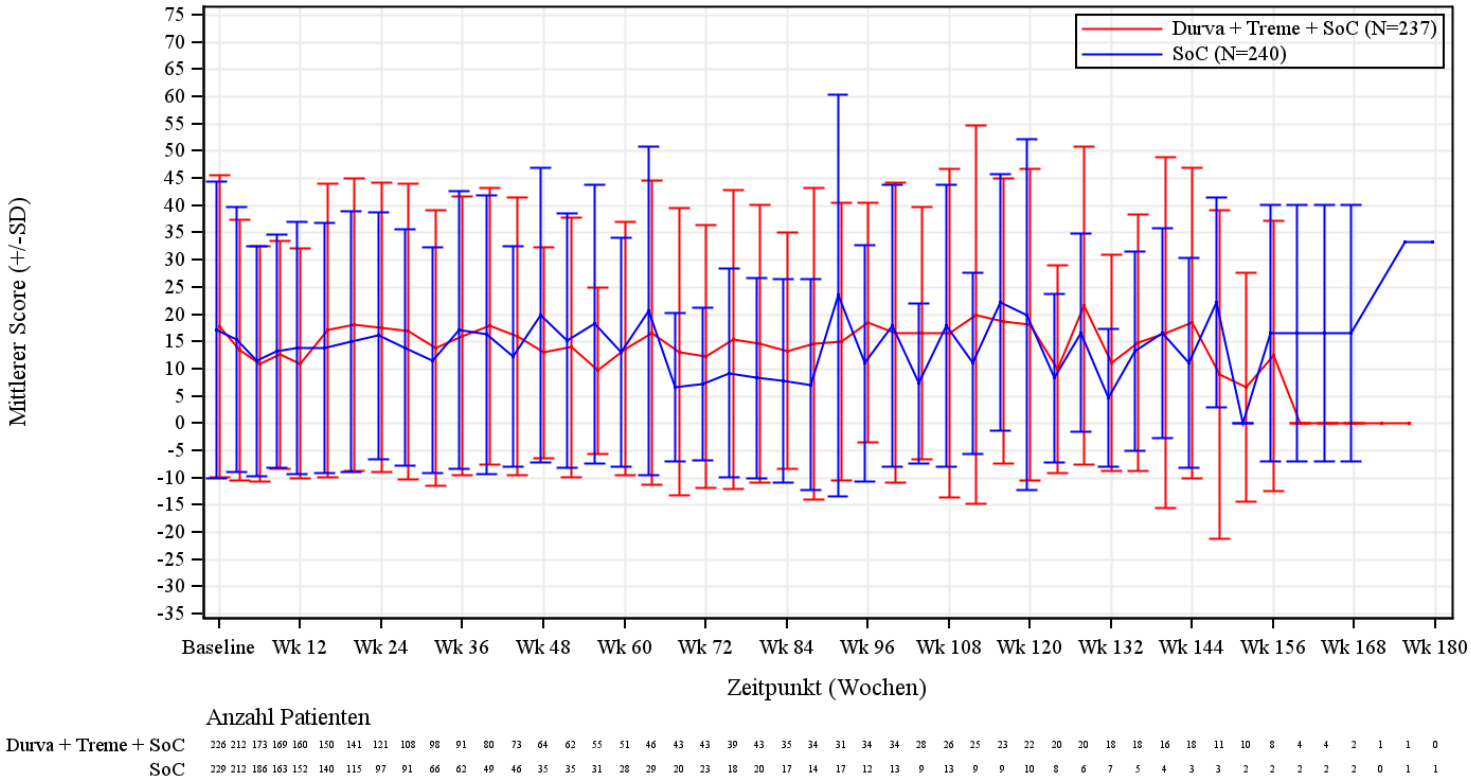
Figure 10.4.3.2 Mean change from baseline of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc325g.sas Executed : 2022-10-18T000339

Table 10.5.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	20,2 (26,46)	-2,2 (1,60)	208	24,5 (28,98)	-1,0 (1,59)	-1,2 (2,26) [-5,6; 3,3]	0,6008
Woche 6	170	20,2 (25,72)	-3,3 (1,69)	181	24,7 (28,63)	-4,0 (1,66)	0,7 (2,37) [-4,0; 5,3]	0,7764
Woche 9	166	18,9 (25,53)	-6,2 (1,71)	159	23,7 (28,40)	-1,8 (1,72)	-4,5 (2,43) [-9,2; 0,3]	0,0674
Woche 12	158	18,6 (25,65)	-5,7 (1,72)	147	21,5 (26,11)	-2,1 (1,75)	-3,5 (2,46) [-8,4; 1,3]	0,1495
Woche 16	147	20,0 (26,65)	-3,5 (1,79)	137	22,4 (28,33)	-2,4 (1,84)	-1,1 (2,57) [-6,2; 3,9]	0,6572
Woche 20	137	20,7 (26,55)	-2,8 (1,95)	112	22,9 (27,59)	0,3 (2,09)	-3,1 (2,86) [-8,7; 2,5]	0,2775
Woche 24	118	20,3 (27,92)	-1,3 (2,22)	94	21,6 (27,09)	1,1 (2,44)	-2,5 (3,30) [-9,0; 4,0]	0,4580

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc235g.sas Executed : 2022-10-17T232419

Table 10.5.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	19,9 (27,29)	-2,2 (2,04)	88	21,2 (28,22)	-1,9 (2,21)	-0,3 (3,01) [-6,2; 5,7]	0,9239
Woche 32	95	17,9 (25,18)	-2,9 (2,22)	64	22,9 (30,79)	3,0 (2,65)	-5,8 (3,46) [-12,7; 1,0]	0,0935
Durchschnitt über alle Visiten	212	20,1 (26,24)	-3,3 (1,18)	216	24,7 (29,24)	-1,0 (1,22)	-2,4 (1,70) [-5,7; 1,0]	0,1646
Hedges' g SMD							-0,1 (0,10) [-0,3; 0,1]	0,1645

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc235g.sas Executed : 2022-10-17T232419

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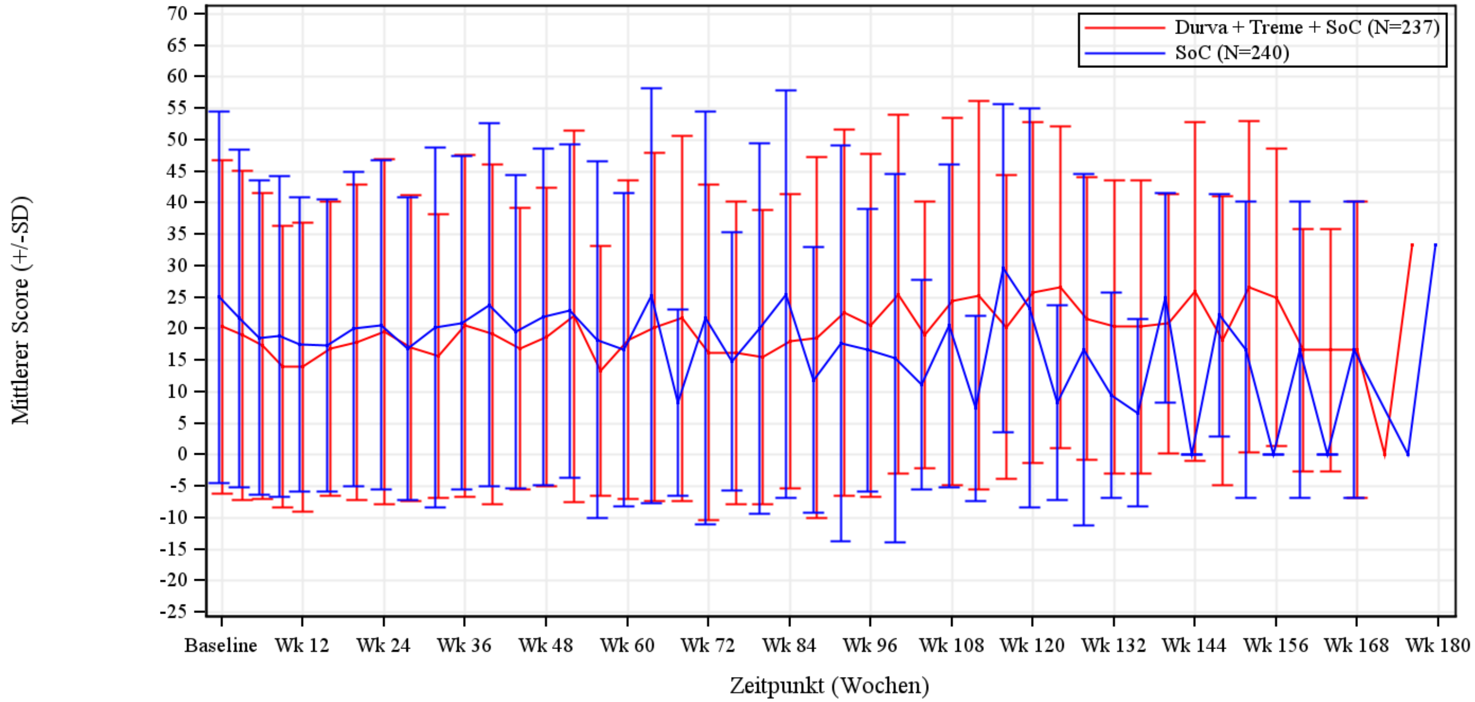
Figure 10.5.3.2 Mean change from baseline of EORTC QLQ-LC13 pain (other) (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Anzahl Patienten

Durva + Treme + SoC	226	212	173	169	160	150	141	121	108	98	91	80	73	64	62	55	51	46	43	43	39	43	35	34	31	34	34	28	26	25	23	22	20	20	18	18	16	18	11	10	8	4	4	2	1	1	0
SoC	229	212	186	163	152	140	115	97	91	66	62	49	46	35	35	31	28	29	20	23	18	20	17	14	17	12	13	9	13	9	9	10	8	6	7	5	4	3	3	2	2	2	2	2	0	1	1

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc335g.sas Executed : 2022-10-18T000825

Table 10.6.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	36,4 (26,87)	-1,8 (1,51)	208	38,3 (28,79)	-6,4 (1,50)	4,6 (2,13) [0,4; 8,8]	0,0321
Woche 6	170	34,5 (26,37)	-5,3 (1,71)	181	38,5 (28,07)	-7,5 (1,67)	2,3 (2,39) [-2,4; 7,0]	0,3457
Woche 9	166	34,9 (26,92)	-6,7 (1,58)	159	35,8 (27,70)	-10,2 (1,60)	3,5 (2,25) [-0,9; 7,9]	0,1231
Woche 12	158	34,6 (26,84)	-8,1 (1,64)	147	37,6 (29,27)	-9,4 (1,68)	1,3 (2,35) [-3,4; 5,9]	0,5913
Woche 16	147	34,7 (26,99)	-7,9 (1,91)	137	36,5 (27,97)	-7,3 (1,97)	-0,5 (2,75) [-6,0; 4,9]	0,8437
Woche 20	137	33,6 (27,56)	-7,2 (1,89)	112	37,5 (26,89)	-11,8 (2,03)	4,6 (2,78) [-0,9; 10,1]	0,0983
Woche 24	118	33,6 (27,39)	-8,9 (1,98)	94	37,9 (28,75)	-12,3 (2,18)	3,4 (2,95) [-2,4; 9,3]	0,2443

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc245g.sas Executed : 2022-10-17T232844

Table 10.6.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	32,4 (25,63)	-5,6 (2,22)	88	36,0 (29,57)	-3,4 (2,42)	-2,2 (3,28) [-8,7; 4,3]	0,5058
Woche 32	95	31,9 (26,59)	-8,6 (2,27)	64	36,5 (29,53)	-6,4 (2,66)	-2,2 (3,50) [-9,1; 4,7]	0,5302
Durchschnitt über alle Visiten	212	36,3 (27,28)	-6,7 (1,18)	216	38,4 (28,75)	-8,3 (1,22)	1,6 (1,70) [-1,7; 5,0]	0,3374
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,3379

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc245g.sas Executed : 2022-10-17T232844

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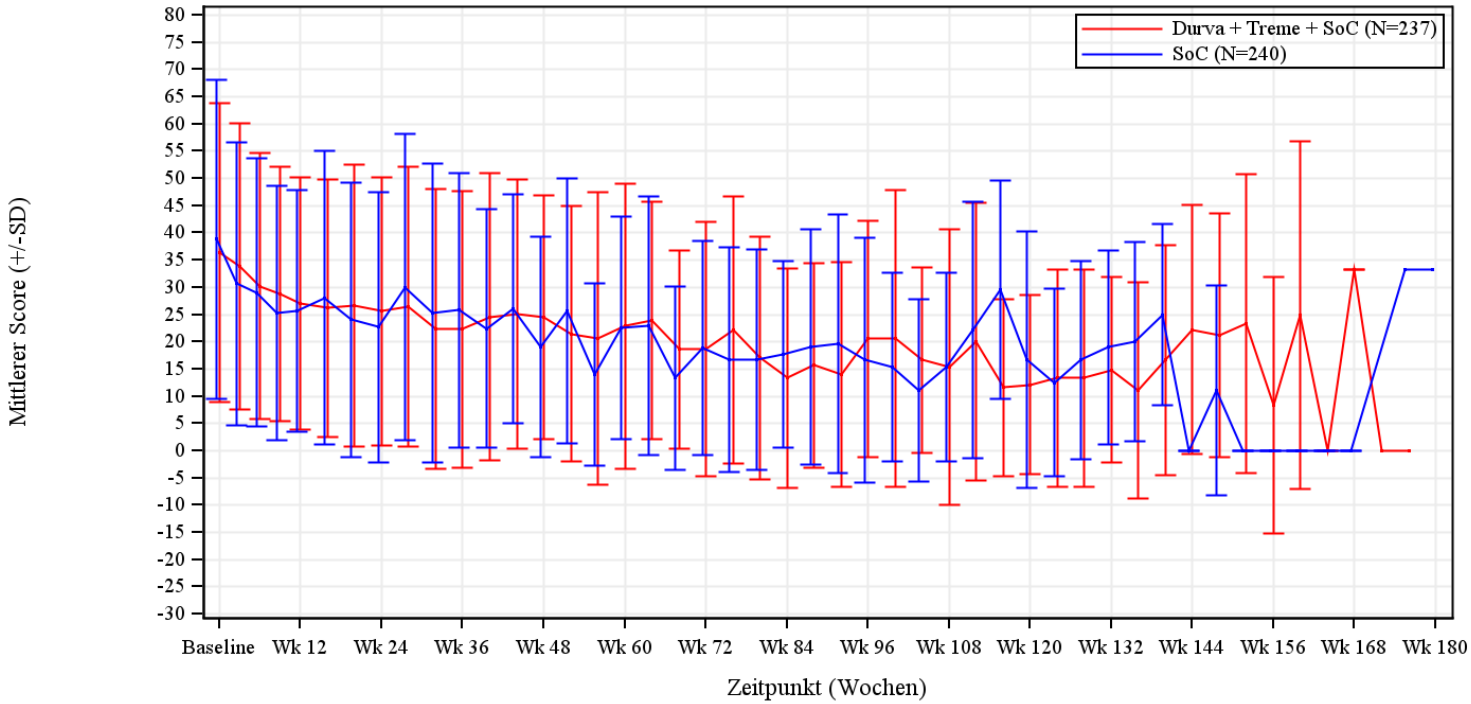
Figure 10.6.3.2 Mean change from baseline of EORTC QLQ-LC13 cough (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc345g.sas Executed : 2022-10-18T001322

Table 10.7.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	6,1 (16,30)	-2,0 (0,89)	208	8,3 (19,52)	-2,1 (0,88)	0,1 (1,25) [-2,3; 2,6]	0,9087
Woche 6	170	5,3 (14,67)	-4,0 (0,80)	181	8,1 (18,81)	-2,7 (0,78)	-1,2 (1,12) [-3,5; 1,0]	0,2674
Woche 9	166	5,6 (15,41)	-4,9 (0,67)	159	7,3 (18,24)	-3,0 (0,67)	-1,9 (0,95) [-3,8; 0,0]	0,0469
Woche 12	158	4,6 (14,31)	-4,4 (0,72)	147	8,8 (20,02)	-3,3 (0,74)	-1,0 (1,03) [-3,1; 1,0]	0,3153
Woche 16	147	5,4 (15,13)	-5,2 (0,62)	137	6,3 (16,93)	-3,4 (0,64)	-1,8 (0,90) [-3,5; 0,0]	0,0515
Woche 20	137	4,9 (14,31)	-4,5 (0,57)	112	8,0 (20,13)	-4,8 (0,60)	0,2 (0,83) [-1,4; 1,9]	0,7737
Woche 24	118	4,5 (13,72)	-3,6 (0,98)	94	7,8 (19,20)	-1,9 (1,08)	-1,7 (1,46) [-4,6; 1,2]	0,2504

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc255g.sas Executed : 2022-10-17T233248

Table 10.7.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	3,8 (12,56)	-0,3 (1,40)	88	8,3 (20,99)	-0,2 (1,55)	-0,2 (2,10) [-4,3; 4,0]	0,9395
Woche 32	95	1,8 (7,48)	-3,1 (1,05)	64	10,4 (22,91)	-2,2 (1,23)	-0,8 (1,64) [-4,1; 2,4]	0,6125
Durchschnitt über alle Visiten	212	6,0 (16,09)	-3,5 (0,52)	216	8,0 (19,22)	-2,6 (0,55)	-0,9 (0,76) [-2,4; 0,6]	0,2272
Hedges' g SMD							-0,1 (0,10) [-0,3; 0,1]	0,2263

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc255g.sas Executed : 2022-10-17T233248

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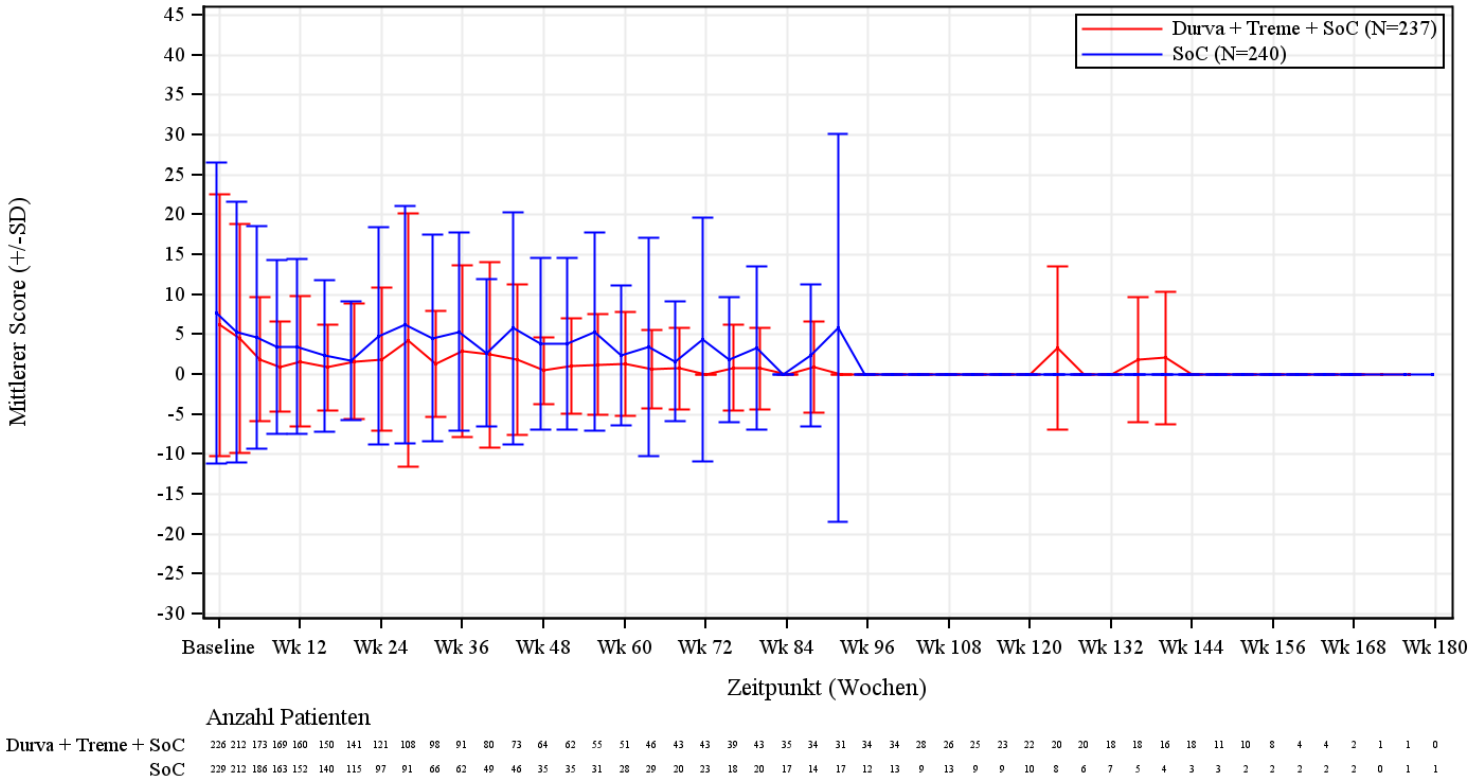
Figure 10.7.3.2 Mean change from baseline of EORTC QLQ-LC13 hemoptysis (symptom) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc355g.sas Executed : 2022-10-18T001743

Table 10.8.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	5,8 (16,41)	2,6 (1,27)	208	5,0 (15,43)	3,5 (1,26)	-0,9 (1,78) [-4,4; 2,6]	0,6272
Woche 6	170	5,7 (16,23)	2,7 (1,21)	181	5,5 (16,30)	1,9 (1,18)	0,8 (1,69) [-2,6; 4,1]	0,6492
Woche 9	166	5,0 (14,96)	4,1 (1,27)	159	3,8 (12,98)	1,9 (1,29)	2,2 (1,81) [-1,4; 5,7]	0,2336
Woche 12	158	4,6 (14,80)	1,5 (1,30)	147	4,8 (15,11)	3,0 (1,34)	-1,6 (1,87) [-5,3; 2,1]	0,4003
Woche 16	147	5,0 (15,29)	3,4 (1,38)	137	4,9 (16,44)	2,5 (1,42)	0,8 (1,99) [-3,1; 4,8]	0,6713
Woche 20	137	4,9 (14,87)	2,7 (1,45)	112	5,4 (17,65)	2,6 (1,57)	0,0 (2,14) [-4,2; 4,3]	0,9814
Woche 24	118	4,8 (15,27)	1,1 (1,44)	94	5,3 (17,15)	1,5 (1,60)	-0,4 (2,16) [-4,6; 3,9]	0,8697

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc265g.sas Executed : 2022-10-17T233649

Table 10.8.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	4,5 (14,73)	0,3 (1,32)	88	4,9 (16,41)	0,6 (1,41)	-0,3 (1,93) [-4,1; 3,5]	0,8917
Woche 32	95	2,5 (12,15)	-0,9 (1,17)	64	3,6 (14,69)	0,3 (1,38)	-1,2 (1,80) [-4,8; 2,4]	0,5060
Durchschnitt über alle Visiten	212	5,7 (16,21)	1,9 (0,80)	216	4,8 (15,17)	2,0 (0,82)	0,0 (1,15) [-2,3; 2,2]	0,9664
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9665

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc265g.sas Executed : 2022-10-17T233649

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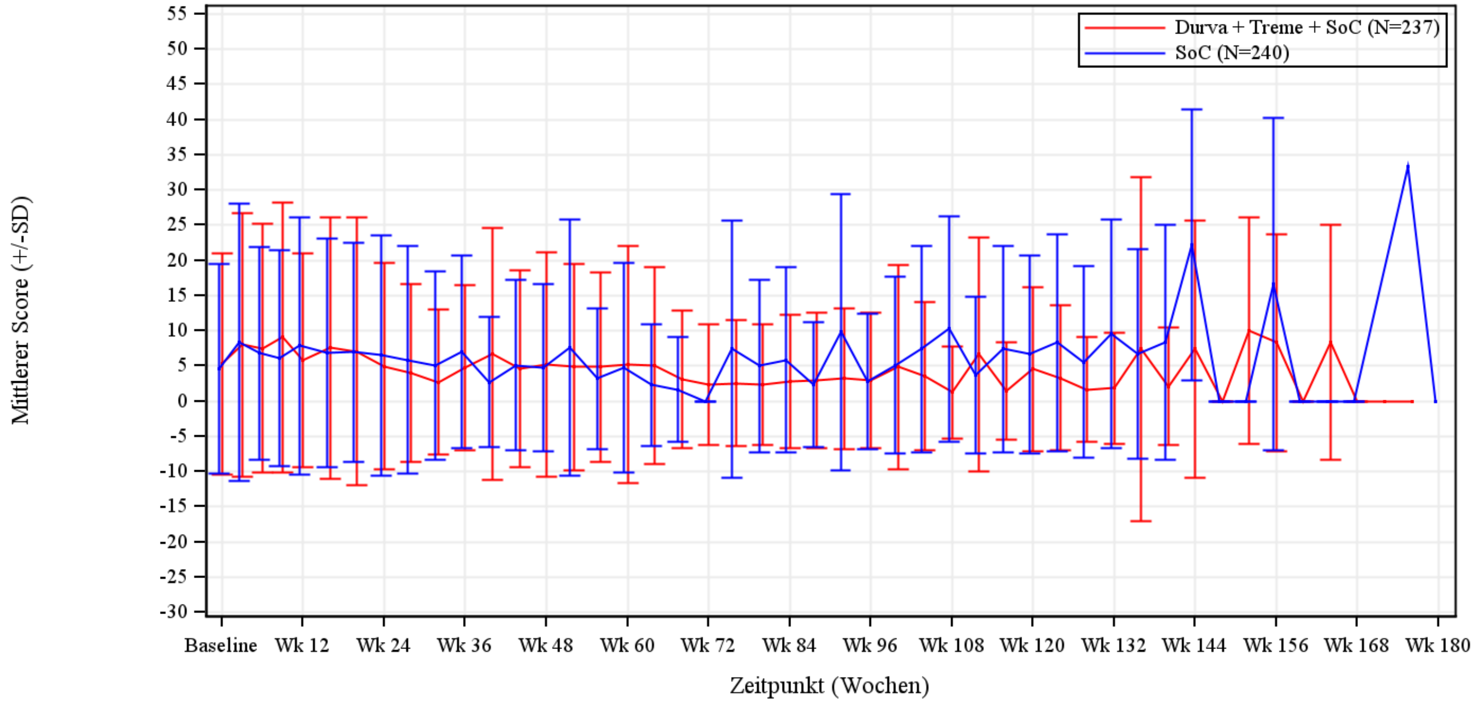
Figure 10.8.3.2 Mean change from baseline of EORTC QLQ-LC13 sore mouth score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Anzahl Patienten

Durva + Treme + SoC	226	212	173	169	160	150	141	121	108	98	91	80	73	64	62	55	51	46	43	43	39	43	35	34	31	34	34	28	26	25	23	22	20	20	18	18	16	18	11	10	8	4	4	2	1	1	0
SoC	229	212	186	163	152	140	115	97	91	66	62	49	46	35	35	31	28	29	20	23	18	20	17	14	17	12	13	9	13	9	9	10	8	6	7	5	4	3	3	2	2	2	2	2	0	1	1

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc365g.sas Executed : 2022-10-18T002234

Table 10.9.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	9,1 (20,66)	0,5 (1,33)	208	9,5 (20,50)	1,7 (1,32)	-1,2 (1,87) [-4,9; 2,4]	0,5055
Woche 6	170	7,5 (18,04)	-0,7 (1,16)	181	9,6 (20,35)	-0,6 (1,14)	-0,1 (1,62) [-3,3; 3,1]	0,9381
Woche 9	166	7,0 (17,91)	0,7 (1,27)	159	6,7 (16,68)	0,9 (1,29)	-0,2 (1,81) [-3,8; 3,4]	0,9096
Woche 12	158	6,5 (17,83)	0,0 (1,14)	147	6,6 (15,43)	0,4 (1,17)	-0,4 (1,63) [-3,6; 2,9]	0,8262
Woche 16	147	7,0 (18,39)	1,6 (1,29)	137	7,3 (18,40)	1,0 (1,33)	0,6 (1,86) [-3,0; 4,3]	0,7388
Woche 20	137	7,3 (18,40)	-0,1 (1,22)	112	6,8 (17,41)	-0,9 (1,32)	0,9 (1,80) [-2,7; 4,4]	0,6358
Woche 24	118	8,2 (19,46)	1,0 (1,43)	94	5,3 (14,09)	-2,7 (1,60)	3,7 (2,15) [-0,6; 7,9]	0,0903

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc275g.sas Executed : 2022-10-17T234121

Table 10.9.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	7,4 (17,96)	-1,3 (1,28)	88	4,9 (15,61)	-1,7 (1,37)	0,4 (1,88) [-3,3; 4,1]	0,8453
Woche 32	95	6,3 (17,05)	-2,8 (1,03)	64	4,7 (15,56)	-2,1 (1,22)	-0,7 (1,59) [-3,8; 2,5]	0,6828
Durchschnitt über alle Visiten	212	8,8 (20,42)	-0,1 (0,76)	216	9,3 (20,25)	-0,4 (0,78)	0,3 (1,09) [-1,8; 2,5]	0,7663
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,7667

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc275g.sas Executed : 2022-10-17T234121

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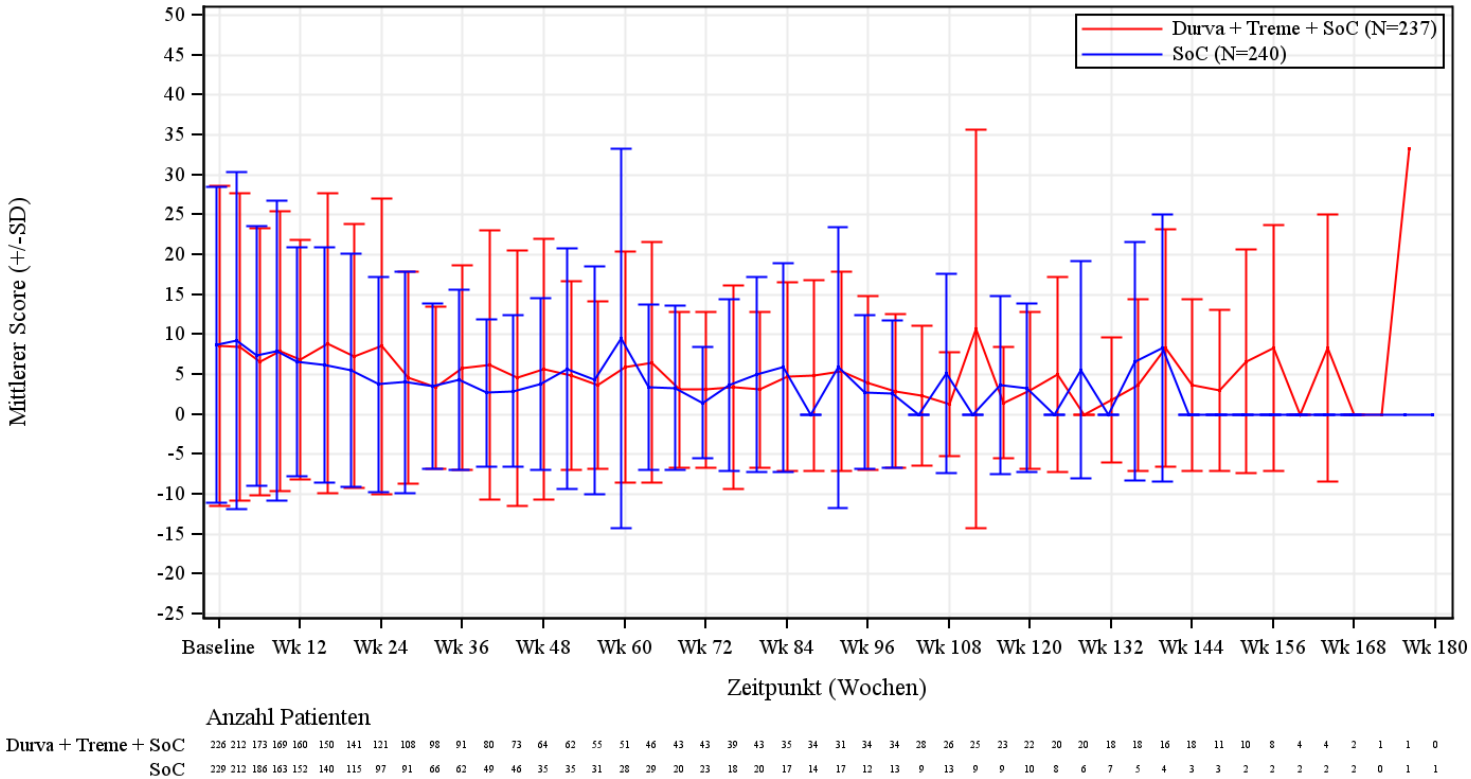
Figure 10.9.3.2 Mean change from baseline of EORTC QLQ-LC13 dysphagia score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc375g.sas Executed : 2022-10-18T075513

Table 10.10.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	10,7 (20,93)	0,1 (1,28)	208	9,6 (18,05)	1,7 (1,27)	-1,6 (1,80) [-5,1; 2,0]	0,3862
Woche 6	170	10,8 (21,33)	1,5 (1,33)	181	11,0 (19,26)	1,8 (1,29)	-0,2 (1,85) [-3,9; 3,4]	0,8993
Woche 9	166	9,6 (21,10)	2,5 (1,42)	159	9,4 (18,04)	3,2 (1,44)	-0,6 (2,02) [-4,6; 3,3]	0,7545
Woche 12	158	8,4 (18,79)	1,7 (1,59)	147	10,2 (18,14)	5,4 (1,62)	-3,7 (2,27) [-8,2; 0,8]	0,1045
Woche 16	147	9,8 (20,72)	4,5 (1,71)	137	9,0 (16,91)	5,3 (1,76)	-0,8 (2,45) [-5,6; 4,0]	0,7405
Woche 20	137	9,0 (19,18)	5,7 (1,67)	112	10,7 (18,02)	4,0 (1,80)	1,8 (2,46) [-3,0; 6,6]	0,4676
Woche 24	118	8,8 (19,21)	7,8 (2,00)	94	10,6 (18,43)	5,7 (2,20)	2,0 (2,98) [-3,8; 7,9]	0,4924

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc285g.sas Executed : 2022-10-17T234559

Table 10.10.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	8,0 (18,86)	8,2 (2,23)	88	9,1 (17,31)	9,9 (2,40)	-1,8 (3,27) [-8,2; 4,7]	0,5885
Woche 32	95	7,7 (17,16)	7,3 (2,08)	64	7,8 (15,42)	9,5 (2,39)	-2,1 (3,16) [-8,4; 4,1]	0,5029
Durchschnitt über alle Visiten	212	10,4 (20,71)	4,4 (1,17)	216	10,0 (18,39)	5,2 (1,20)	-0,8 (1,67) [-4,1; 2,5]	0,6424
Hedges' g SMD							0,0 (0,10) [-0,2; 0,1]	0,6429

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc285g.sas Executed : 2022-10-17T234559

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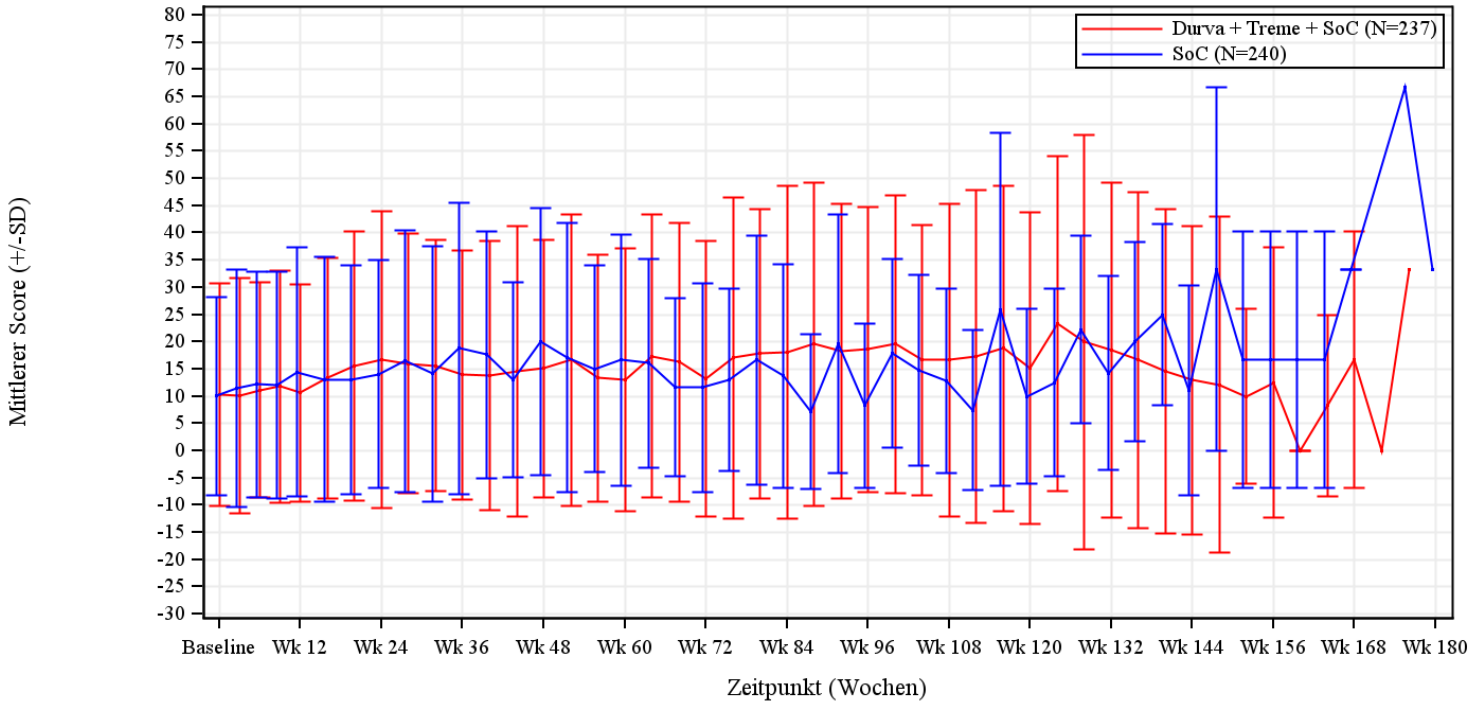
Figure 10.10.3.2 Mean change from baseline of EORTC QLQ-LC13 peripheral neuropathy score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc385g.sas Executed : 2022-10-18T080004

Table 10.11.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	5,0 (15,85)	7,4 (1,53)	208	7,4 (17,62)	3,5 (1,52)	3,9 (2,15) [-0,3; 8,1]	0,0709
Woche 6	170	4,5 (13,54)	8,9 (1,63)	181	7,6 (17,87)	5,3 (1,59)	3,6 (2,29) [-0,9; 8,1]	0,1151
Woche 9	166	4,2 (13,32)	9,8 (1,77)	159	7,8 (18,06)	8,2 (1,78)	1,6 (2,51) [-3,3; 6,6]	0,5152
Woche 12	158	4,9 (15,43)	9,4 (1,71)	147	7,0 (17,55)	7,8 (1,74)	1,5 (2,45) [-3,3; 6,3]	0,5328
Woche 16	147	5,0 (15,29)	7,2 (1,75)	137	7,3 (17,49)	9,7 (1,79)	-2,5 (2,51) [-7,4; 2,4]	0,3222
Woche 20	137	4,4 (13,29)	8,0 (1,81)	112	9,2 (19,09)	8,0 (1,95)	0,0 (2,67) [-5,2; 5,3]	0,9868
Woche 24	118	4,5 (14,40)	6,3 (1,74)	94	9,2 (19,19)	5,0 (1,93)	1,3 (2,61) [-3,9; 6,4]	0,6235

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc295g.sas Executed : 2022-10-17T235030

Table 10.11.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	5,1 (16,60)	4,5 (1,68)	88	9,1 (19,40)	2,7 (1,84)	1,8 (2,49) [-3,1; 6,7]	0,4684
Woche 32	95	3,9 (12,74)	2,3 (1,43)	64	9,4 (19,22)	0,7 (1,70)	1,6 (2,23) [-2,9; 6,0]	0,4864
Durchschnitt über alle Visiten	212	4,9 (15,64)	7,1 (1,07)	216	7,3 (17,43)	5,7 (1,10)	1,4 (1,54) [-1,6; 4,5]	0,3533
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,3530

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc295g.sas Executed : 2022-10-17T235030

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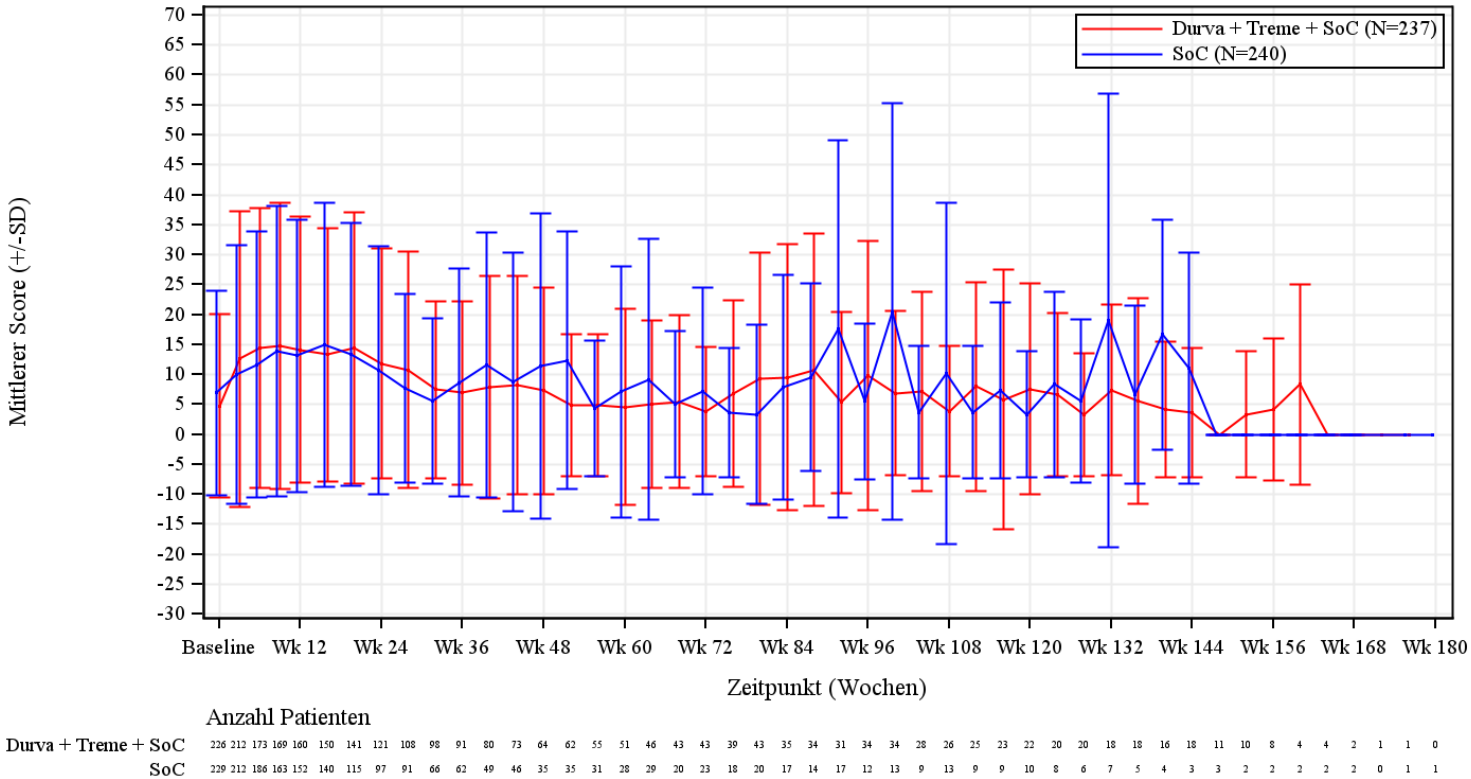
Figure 10.11.3.2 Mean change from baseline of EORTC QLQ-LC13 alopecia score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc395g.sas Executed : 2022-10-18T080709

Anhang 4-G 1.1.3: EQ-5D-5L VAS - Gesundheitszustand

Table 11.2.3.1 Summary of analysis of change from baseline (MMRM) of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	68,4 (16,56)	-0,1 (1,00)	207	66,9 (18,28)	0,6 (1,00)	-0,7 (1,42) [-3,5; 2,1]	0,6116
Woche 6	170	68,9 (17,10)	1,1 (1,10)	180	67,1 (18,15)	1,5 (1,08)	-0,4 (1,54) [-3,5; 2,6]	0,7802
Woche 9	166	68,9 (17,34)	2,3 (1,06)	159	68,6 (18,56)	1,2 (1,07)	1,0 (1,51) [-1,9; 4,0]	0,4970
Woche 12	158	69,3 (17,21)	1,1 (1,18)	147	68,1 (17,84)	0,0 (1,20)	1,0 (1,68) [-2,3; 4,3]	0,5360
Woche 16	147	69,6 (17,29)	-2,1 (1,36)	137	68,9 (17,78)	0,0 (1,40)	-2,0 (1,95) [-5,9; 1,8]	0,2991
Woche 20	137	69,2 (17,20)	-0,5 (1,32)	112	70,2 (18,08)	-1,6 (1,40)	1,1 (1,93) [-2,7; 4,9]	0,5702
Woche 24	118	69,5 (17,86)	-0,4 (1,39)	94	68,9 (19,52)	0,3 (1,49)	-0,7 (2,04) [-4,7; 3,3]	0,7303

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va205g.sas Executed : 2022-10-18T082205

Table 11.2.3.1 Summary of analysis of change from baseline (MMRM) of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	69,2 (16,94)	-0,8 (1,32)	88	69,7 (18,96)	1,4 (1,41)	-2,2 (1,93) [-6,0; 1,6]	0,2486
Woche 32	95	69,9 (16,58)	-0,7 (1,51)	64	70,3 (19,94)	-1,7 (1,73)	1,1 (2,30) [-3,5; 5,6]	0,6460
Durchschnitt über alle Visiten	212	68,2 (16,99)	0,0 (0,91)	216	66,9 (18,16)	0,2 (0,93)	-0,2 (1,31) [-2,8; 2,4]	0,8714
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,8716

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va205g.sas Executed : 2022-10-18T082205

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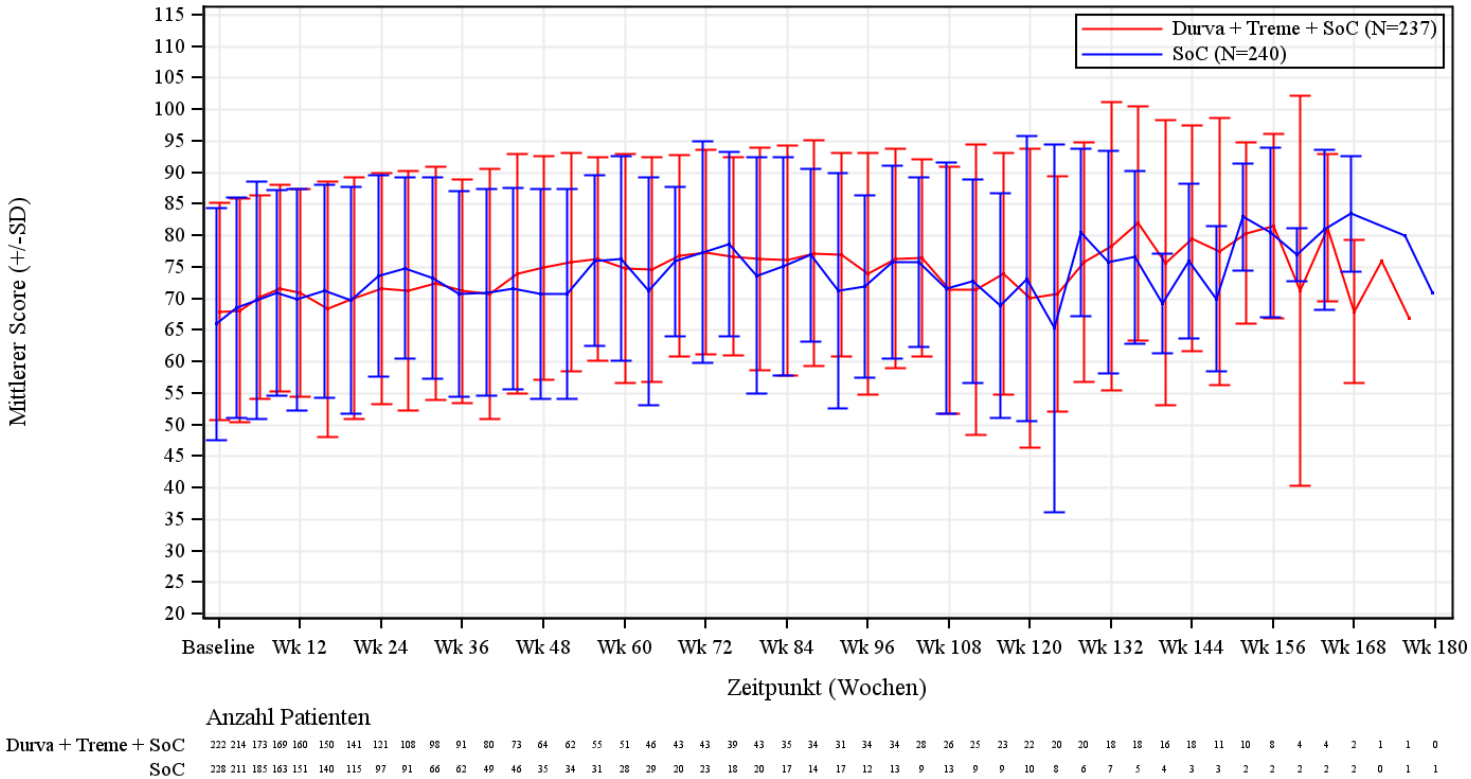
Figure 11.2.3.2 Mean change from baseline in EQ-5D VAS score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va305g.sas Executed : 2022-10-18T082700

Anhang 4-G 1.1.4: PGIC – Gesundheitszustand

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Table 12.2.3.1 Summary of analysis of change from baseline (MMRM) of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	182	NA	3,1 (0,07)	180	NA	3,3 (0,08)	-0,2 (0,11) [-0,4; 0,0]	0,0505
Woche 6	170	NA	2,8 (0,08)	182	NA	3,0 (0,08)	-0,2 (0,11) [-0,4; 0,0]	0,0666
Woche 9	169	NA	2,7 (0,08)	162	NA	3,0 (0,08)	-0,4 (0,12) [-0,6; -0,1]	0,0021
Woche 12	159	NA	2,7 (0,09)	150	NA	3,1 (0,09)	-0,4 (0,12) [-0,7; -0,2]	0,0007
Woche 16	150	NA	2,8 (0,09)	139	NA	3,1 (0,10)	-0,3 (0,13) [-0,6; 0,0]	0,0255
Woche 20	141	NA	2,8 (0,10)	113	NA	3,1 (0,11)	-0,3 (0,15) [-0,6; 0,0]	0,0447
Woche 24	121	NA	2,8 (0,10)	97	NA	3,0 (0,11)	-0,2 (0,15) [-0,5; 0,1]	0,1894

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group. NA Not applicable.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables.

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Table 12.2.3.1 Summary of analysis of change from baseline (MMRM) of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	108	NA	2,9 (0,11)	91	NA	3,0 (0,12)	-0,2 (0,16) [-0,5; 0,2]	0,3410
Woche 32	98	NA	2,7 (0,11)	66	NA	3,1 (0,12)	-0,4 (0,16) [-0,7; -0,1]	0,0178
Woche 36	91	NA	3,0 (0,12)	62	NA	3,2 (0,14)	-0,2 (0,18) [-0,6; 0,1]	0,1771
Durchschnitt über alle Visiten	210	NA	2,8 (0,07)	214	NA	3,1 (0,07)	-0,3 (0,10) [-0,5; -0,1]	0,0045
Hedges' g SMD							-0,3 (0,10) [-0,5; -0,1]	0,0045

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group. NA Not applicable.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables.

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Anhang 4-G 1.1.5: EORTC QLQ-C30 – Globaler Gesundheitsstatus

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Table 9.16.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	60,8 (19,54)	1,0 (1,06)	209	60,7 (18,75)	0,5 (1,05)	0,5 (1,49) [-2,4; 3,5]	0,7242
Woche 6	170	63,6 (18,01)	1,1 (1,35)	183	60,6 (19,06)	-0,5 (1,31)	1,6 (1,89) [-2,1; 5,3]	0,3955
Woche 9	167	61,4 (18,40)	3,0 (1,32)	159	62,6 (18,86)	-0,7 (1,34)	3,7 (1,88) [0,0; 7,4]	0,0486
Woche 12	158	61,6 (18,73)	2,3 (1,29)	147	62,1 (18,17)	-0,7 (1,31)	3,0 (1,84) [-0,6; 6,6]	0,1012
Woche 16	148	62,2 (18,91)	-1,1 (1,40)	137	63,0 (19,01)	0,8 (1,45)	-1,9 (2,01) [-5,9; 2,0]	0,3372
Woche 20	139	62,5 (19,15)	0,7 (1,43)	113	63,6 (18,90)	0,6 (1,54)	0,1 (2,10) [-4,0; 4,3]	0,9519
Woche 24	118	62,4 (19,90)	-0,4 (1,46)	94	62,7 (20,00)	1,2 (1,60)	-1,6 (2,16) [-5,8; 2,7]	0,4676

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 9.16.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	61,8 (18,38)	1,5 (1,57)	88	65,3 (18,69)	0,2 (1,70)	1,3 (2,31) [-3,3; 5,8]	0,5866
Woche 32	95	62,6 (18,71)	0,6 (1,78)	64	67,2 (18,48)	-1,7 (2,12)	2,3 (2,77) [-3,1; 7,8]	0,4004
Durchschnitt über alle Visiten	212	60,8 (19,40)	1,0 (0,94)	217	60,6 (18,53)	0,0 (0,97)	1,0 (1,35) [-1,6; 3,7]	0,4536
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,4545

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2135g.sas Executed : 2022-10-17T214811

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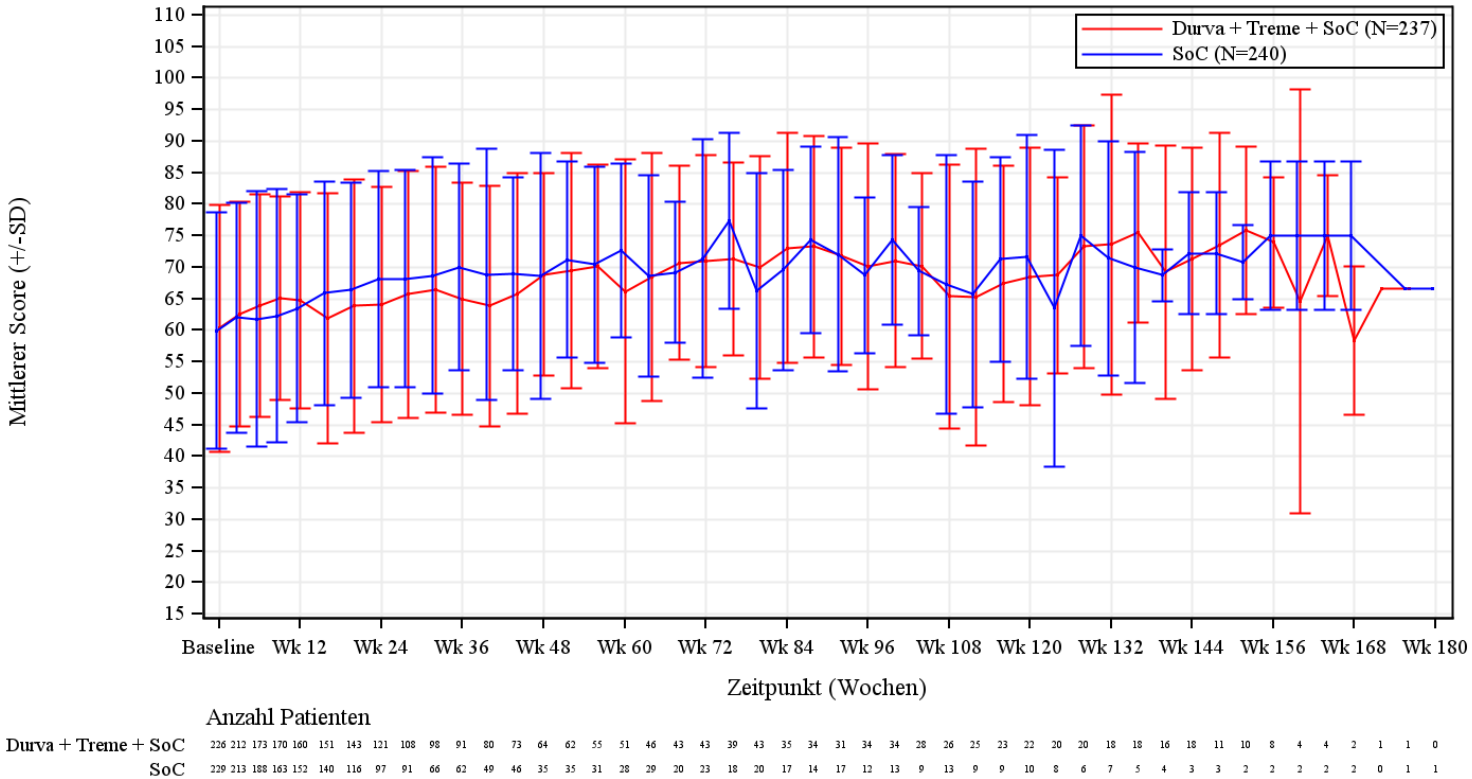
Figure 5.16.3.2 Mean change from baseline for EORTC QLQ-C30 in global health status score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3135g.sas Executed : 2022-09-30T221325

Anhang 4-G 1.1.6: EORTC QLQ-C30 – Funktionsskalen

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Table 9.2.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	77,4 (18,57)	-0,1 (1,06)	209	76,1 (21,05)	-1,9 (1,06)	1,7 (1,50) [-1,2; 4,7]	0,2450
Woche 6	170	78,8 (17,32)	-0,2 (1,17)	183	76,6 (20,30)	-2,0 (1,14)	1,9 (1,63) [-1,3; 5,1]	0,2535
Woche 9	167	78,8 (17,46)	0,0 (1,24)	159	79,2 (18,81)	-3,8 (1,24)	3,9 (1,75) [0,4; 7,3]	0,0275
Woche 12	158	78,9 (17,92)	-0,3 (1,27)	147	78,5 (19,60)	-2,1 (1,29)	1,8 (1,81) [-1,7; 5,4]	0,3107
Woche 16	148	79,4 (17,32)	-2,2 (1,46)	137	79,0 (18,17)	-2,8 (1,49)	0,6 (2,09) [-3,5; 4,7]	0,7710
Woche 20	139	79,1 (17,69)	-1,9 (1,49)	113	79,6 (19,34)	-4,8 (1,58)	3,0 (2,17) [-1,3; 7,2]	0,1744
Woche 24	118	77,7 (18,86)	-2,7 (1,65)	94	79,2 (18,39)	-3,7 (1,79)	1,0 (2,43) [-3,8; 5,8]	0,6831

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 9.2.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	79,2 (18,05)	-2,7 (1,50)	88	80,2 (18,40)	-3,3 (1,62)	0,6 (2,20) [-3,7; 5,0]	0,7697
Woche 32	95	78,7 (19,28)	-2,7 (1,76)	64	81,5 (16,44)	-3,6 (2,02)	0,8 (2,68) [-4,5; 6,1]	0,7637
Durchschnitt über alle Visiten	212	77,3 (18,58)	-1,4 (1,04)	217	75,8 (20,88)	-3,1 (1,06)	1,7 (1,48) [-1,2; 4,6]	0,2510
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,2517

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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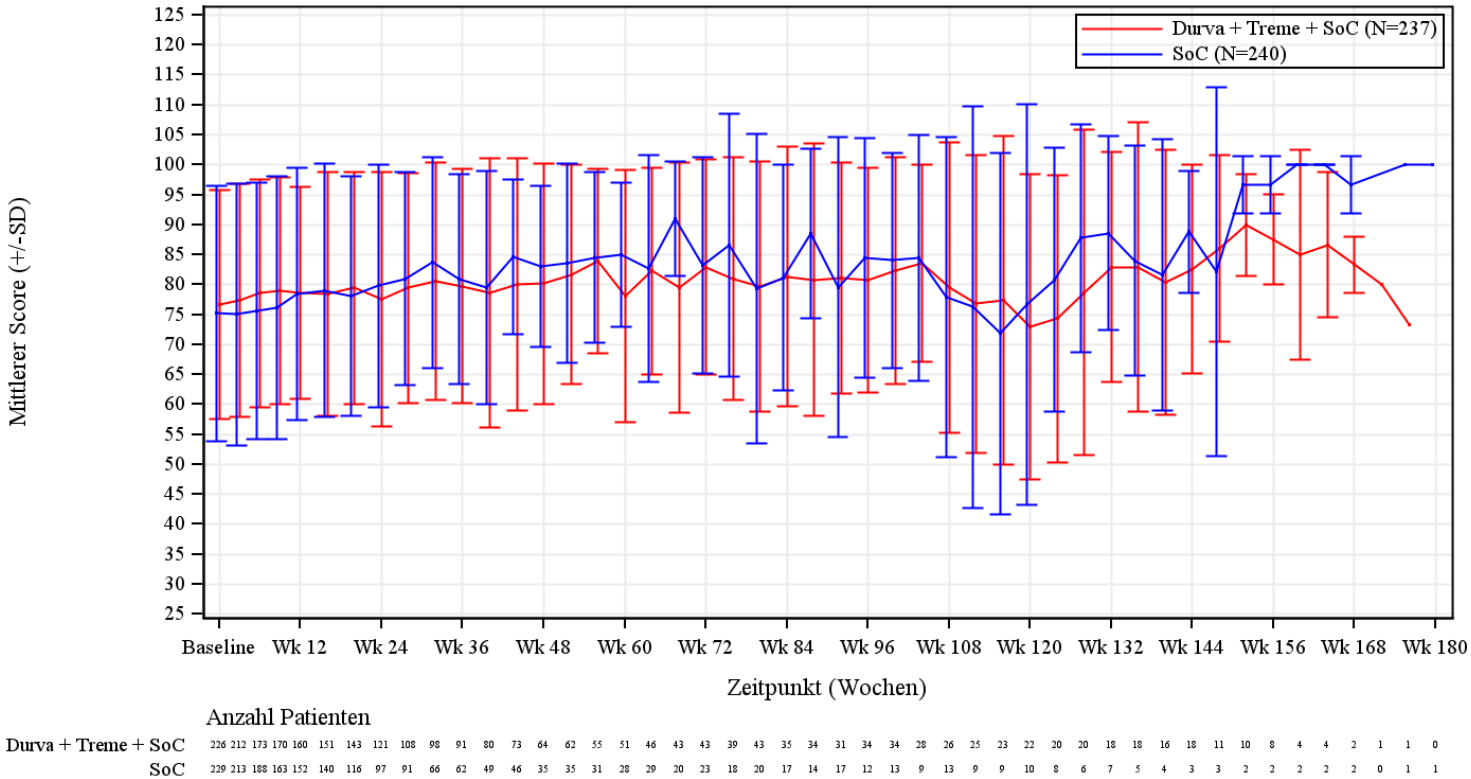
Figure 9.2.3.2 Mean change from baseline of EORTC QLQ-C30 physical (function) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs304g.sas Executed : 2022-10-17T215312

Table 9.3.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	75,0 (27,83)	0,1 (1,62)	209	75,0 (27,84)	-1,6 (1,61)	1,7 (2,28) [-2,8; 6,1]	0,4683
Woche 6	170	77,1 (26,08)	-1,2 (1,75)	183	75,7 (26,94)	-3,2 (1,71)	2,0 (2,45) [-2,8; 6,9]	0,4064
Woche 9	167	76,1 (26,79)	0,6 (1,75)	159	79,0 (24,54)	-4,4 (1,77)	5,0 (2,49) [0,1; 9,9]	0,0450
Woche 12	158	75,7 (27,75)	-0,6 (1,78)	147	78,0 (25,80)	-1,9 (1,81)	1,3 (2,54) [-3,7; 6,3]	0,6143
Woche 16	148	76,7 (27,75)	-1,8 (1,89)	137	78,5 (25,74)	-3,5 (1,94)	1,7 (2,71) [-3,6; 7,0]	0,5334
Woche 20	139	75,9 (27,60)	-1,1 (1,82)	113	79,4 (25,42)	-4,7 (1,93)	3,6 (2,65) [-1,6; 8,8]	0,1749
Woche 24	118	74,4 (28,55)	-4,7 (2,17)	94	79,4 (25,68)	-7,8 (2,33)	3,1 (3,18) [-3,1; 9,4]	0,3237

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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Table 9.3.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	75,2 (28,16)	-2,3 (2,07)	88	79,9 (27,12)	-2,2 (2,22)	0,0 (3,04) [-6,0; 5,9]	0,9890
Woche 32	95	76,3 (28,52)	-1,2 (2,27)	64	80,7 (25,58)	-8,6 (2,63)	7,4 (3,47) [0,6; 14,3]	0,0343
Durchschnitt über alle Visiten	212	75,2 (27,66)	-1,3 (1,39)	217	74,8 (27,78)	-4,2 (1,41)	2,9 (1,98) [-1,0; 6,8]	0,1484
Hedges' g SMD							0,1 (0,10) [0,0; 0,3]	0,1489

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

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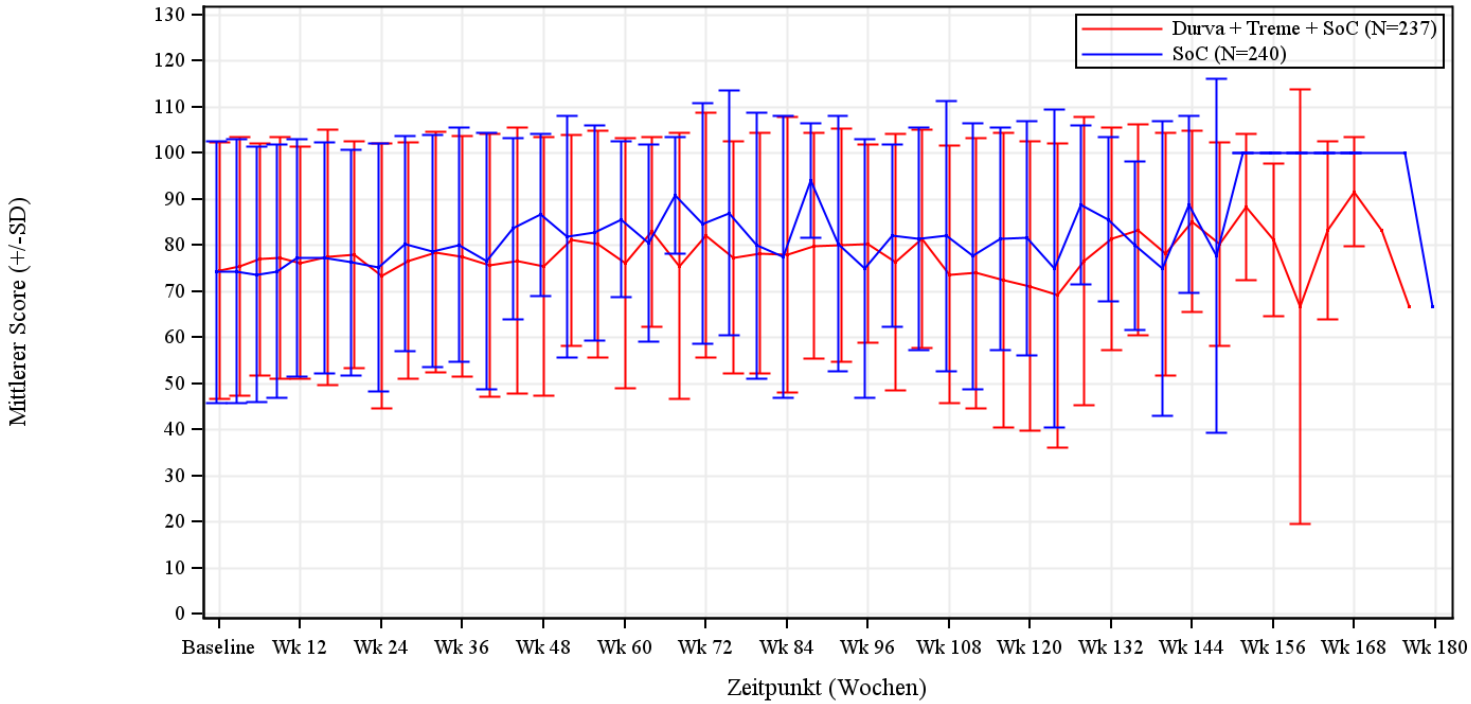
Figure 9.3.3.2 Mean change from baseline of EORTC QLQ-C30 role (function) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs315g.sas Executed : 2022-10-17T215753

Table 9.4.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	85,5 (20,34)	-1,1 (1,10)	209	85,6 (19,37)	1,1 (1,09)	-2,1 (1,54) [-5,2; 0,9]	0,1705
Woche 6	170	86,5 (20,43)	1,4 (1,24)	183	84,1 (20,21)	0,9 (1,21)	0,5 (1,73) [-2,9; 3,9]	0,7773
Woche 9	167	86,5 (20,03)	0,6 (1,24)	159	86,2 (18,10)	-1,5 (1,25)	2,2 (1,76) [-1,3; 5,6]	0,2197
Woche 12	158	86,0 (20,39)	0,2 (1,15)	147	86,6 (18,16)	-0,2 (1,17)	0,3 (1,64) [-2,9; 3,6]	0,8314
Woche 16	148	85,7 (20,85)	-0,1 (1,20)	137	86,7 (18,65)	1,0 (1,24)	-1,1 (1,73) [-4,5; 2,3]	0,5112
Woche 20	139	85,7 (20,52)	-0,3 (1,24)	113	85,8 (20,44)	-1,2 (1,32)	0,9 (1,81) [-2,7; 4,5]	0,6203
Woche 24	118	85,5 (21,41)	-2,0 (1,39)	94	85,6 (19,95)	-0,9 (1,52)	-1,1 (2,06) [-5,2; 2,9]	0,5882

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs225g.sas Executed : 2022-10-17T205749

Table 9.4.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

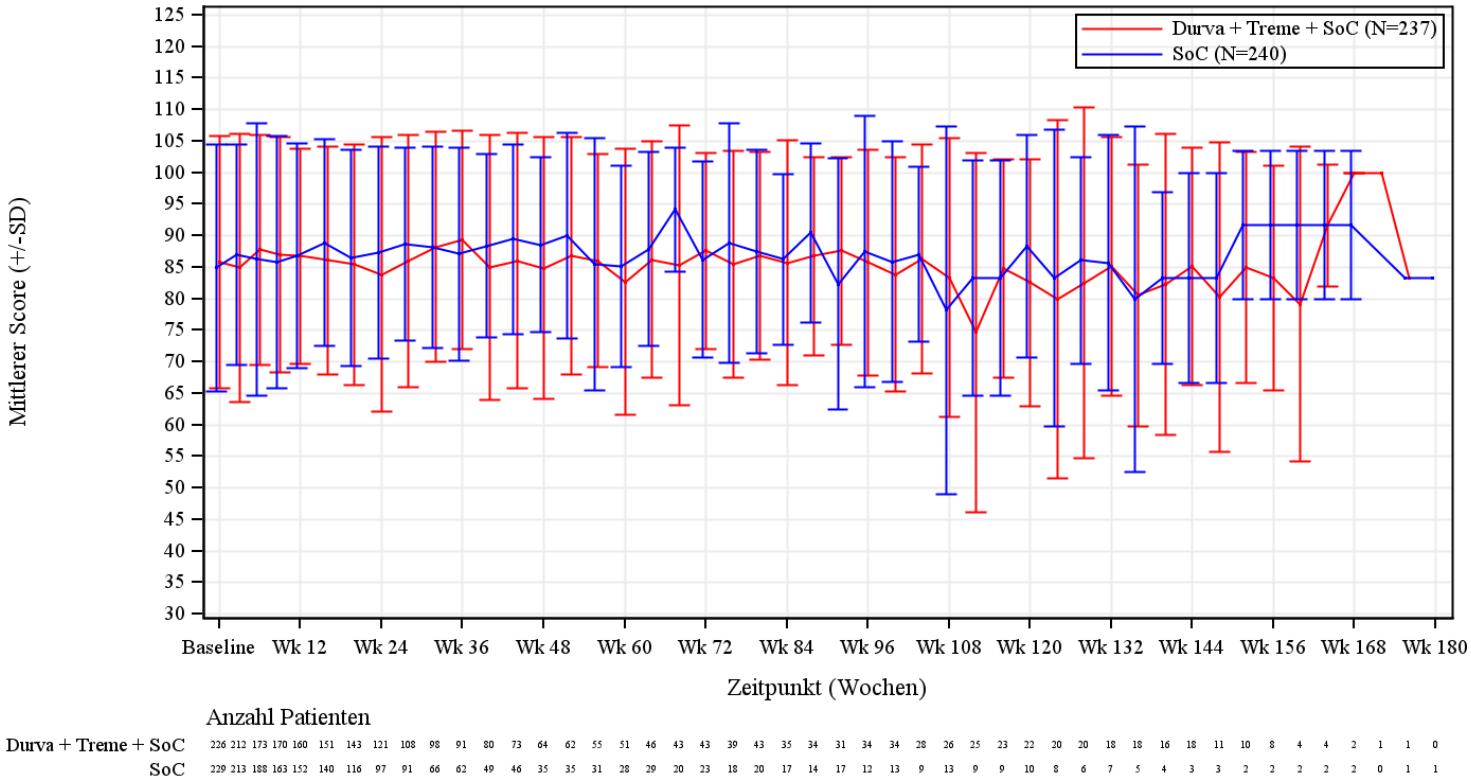
	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	84,8 (22,17)	-1,5 (1,49)	88	87,1 (17,46)	-0,2 (1,59)	-1,4 (2,18) [-5,7; 2,9]	0,5292
Woche 32	95	87,5 (20,19)	-0,3 (1,30)	64	87,2 (18,24)	-0,8 (1,51)	0,5 (1,99) [-3,4; 4,5]	0,7904
Durchschnitt über alle Visiten	212	85,7 (20,19)	-0,3 (0,87)	217	85,0 (19,57)	-0,2 (0,88)	-0,1 (1,24) [-2,6; 2,3]	0,9059
Hedges' g SMD							0,0 (0,10) [-0,2; 0,2]	0,9060

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs225g.sas Executed : 2022-10-17T205749

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 1

Figure 9.4.3.2 Mean change from baseline of EORTC QLQ-C30 cognitive (function) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs325g.sas Executed : 2022-10-17T220250

Table 9.5.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	78,4 (22,10)	4,0 (1,13)	209	78,9 (21,93)	2,5 (1,12)	1,6 (1,59) [-1,6; 4,7]	0,3288
Woche 6	170	81,0 (20,97)	4,0 (1,28)	183	76,8 (22,77)	2,7 (1,25)	1,4 (1,79) [-2,1; 4,9]	0,4410
Woche 9	167	79,2 (21,84)	4,8 (1,24)	159	78,4 (22,83)	1,9 (1,26)	2,9 (1,77) [-0,6; 6,4]	0,1008
Woche 12	158	79,6 (21,85)	3,1 (1,33)	147	78,8 (21,51)	-0,1 (1,35)	3,2 (1,90) [-0,5; 7,0]	0,0922
Woche 16	148	79,2 (22,28)	2,2 (1,29)	137	78,0 (21,79)	1,6 (1,33)	0,6 (1,85) [-3,0; 4,3]	0,7411
Woche 20	139	78,4 (21,79)	3,2 (1,29)	113	77,7 (21,49)	0,7 (1,39)	2,5 (1,90) [-1,3; 6,2]	0,1925
Woche 24	118	78,2 (22,54)	2,0 (1,42)	94	77,8 (22,62)	2,2 (1,56)	-0,1 (2,11) [-4,3; 4,0]	0,9531

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs235g.sas Executed : 2022-10-17T210142

Table 9.5.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	78,1 (23,37)	1,2 (1,52)	88	78,9 (22,24)	2,3 (1,65)	-1,1 (2,25) [-5,5; 3,3]	0,6254
Woche 32	95	81,1 (20,89)	1,4 (1,44)	64	79,3 (20,19)	2,5 (1,67)	-1,1 (2,21) [-5,5; 3,2]	0,6074
Durchschnitt über alle Visiten	212	79,0 (22,02)	2,9 (0,90)	217	78,1 (22,27)	1,8 (0,92)	1,1 (1,28) [-1,4; 3,6]	0,3980
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,3985

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs235g.sas Executed : 2022-10-17T210142

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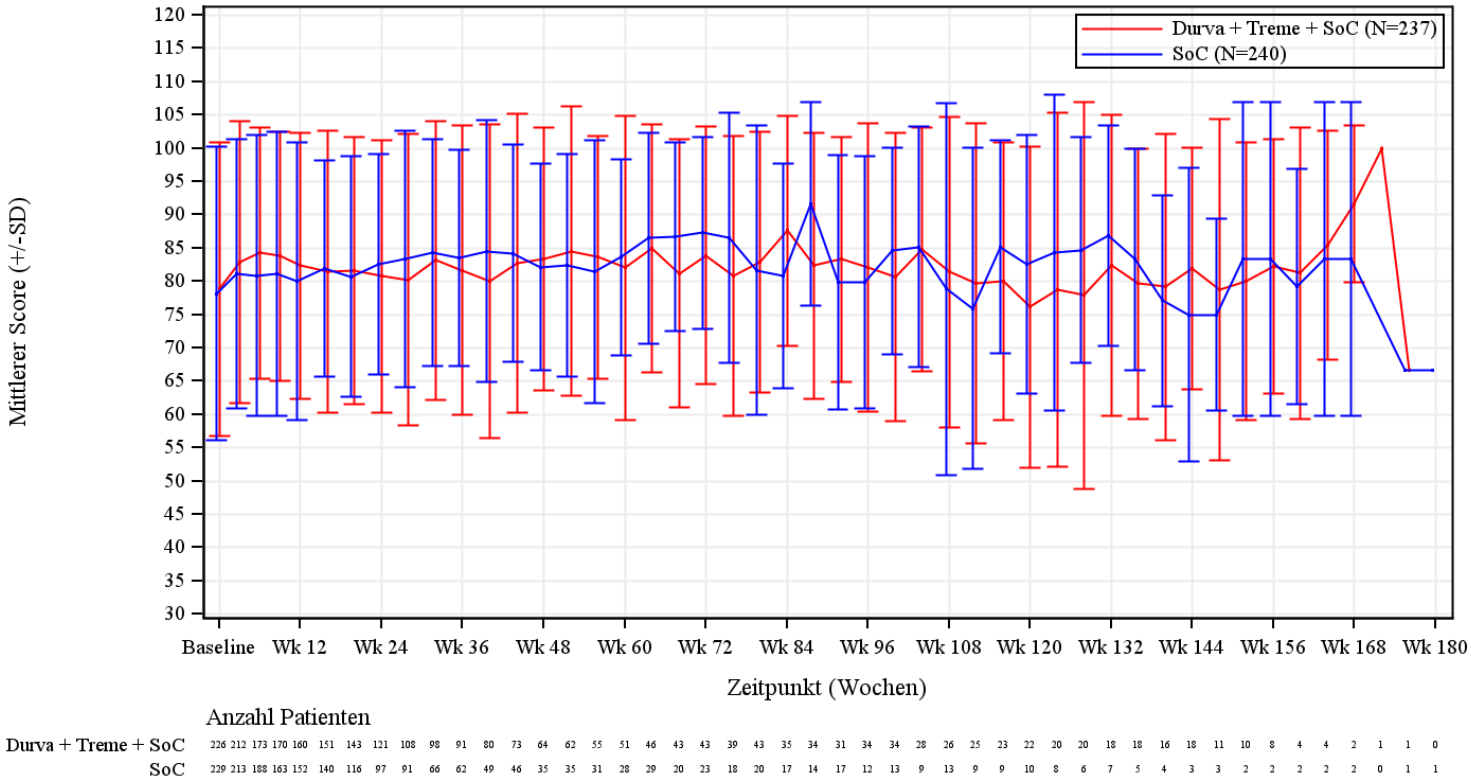
Figure 9.5.3.2 Mean change from baseline of EORTC QLQ-C30 emotional (function) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs335g.sas Executed : 2022-10-17T220740

Table 9.6.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 3	206	81,8 (24,00)	-0,6 (1,40)	209	80,3 (23,43)	-0,7 (1,39)	0,1 (1,98) [-3,8; 4,0]	0,9693
Woche 6	170	83,8 (22,68)	0,3 (1,58)	183	79,2 (24,27)	-1,3 (1,54)	1,6 (2,21) [-2,7; 5,9]	0,4688
Woche 9	167	83,1 (23,14)	0,1 (1,46)	159	81,2 (22,48)	-1,0 (1,48)	1,1 (2,08) [-3,0; 5,1]	0,6117
Woche 12	158	82,7 (23,56)	0,1 (1,50)	147	80,5 (23,44)	-2,0 (1,53)	2,1 (2,15) [-2,1; 6,3]	0,3299
Woche 16	148	82,4 (24,26)	-0,8 (1,76)	137	80,8 (22,13)	-4,1 (1,80)	3,3 (2,52) [-1,6; 8,3]	0,1887
Woche 20	139	82,5 (23,94)	-0,3 (1,60)	113	80,7 (22,67)	-1,8 (1,72)	1,5 (2,35) [-3,2; 6,1]	0,5339
Woche 24	118	83,5 (23,82)	-1,8 (1,75)	94	81,0 (22,08)	-2,0 (1,89)	0,3 (2,58) [-4,8; 5,3]	0,9222

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs245g.sas Executed : 2022-10-17T210551

Table 9.6.3.1 Summary of analysis of change from baseline (MMRM) of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

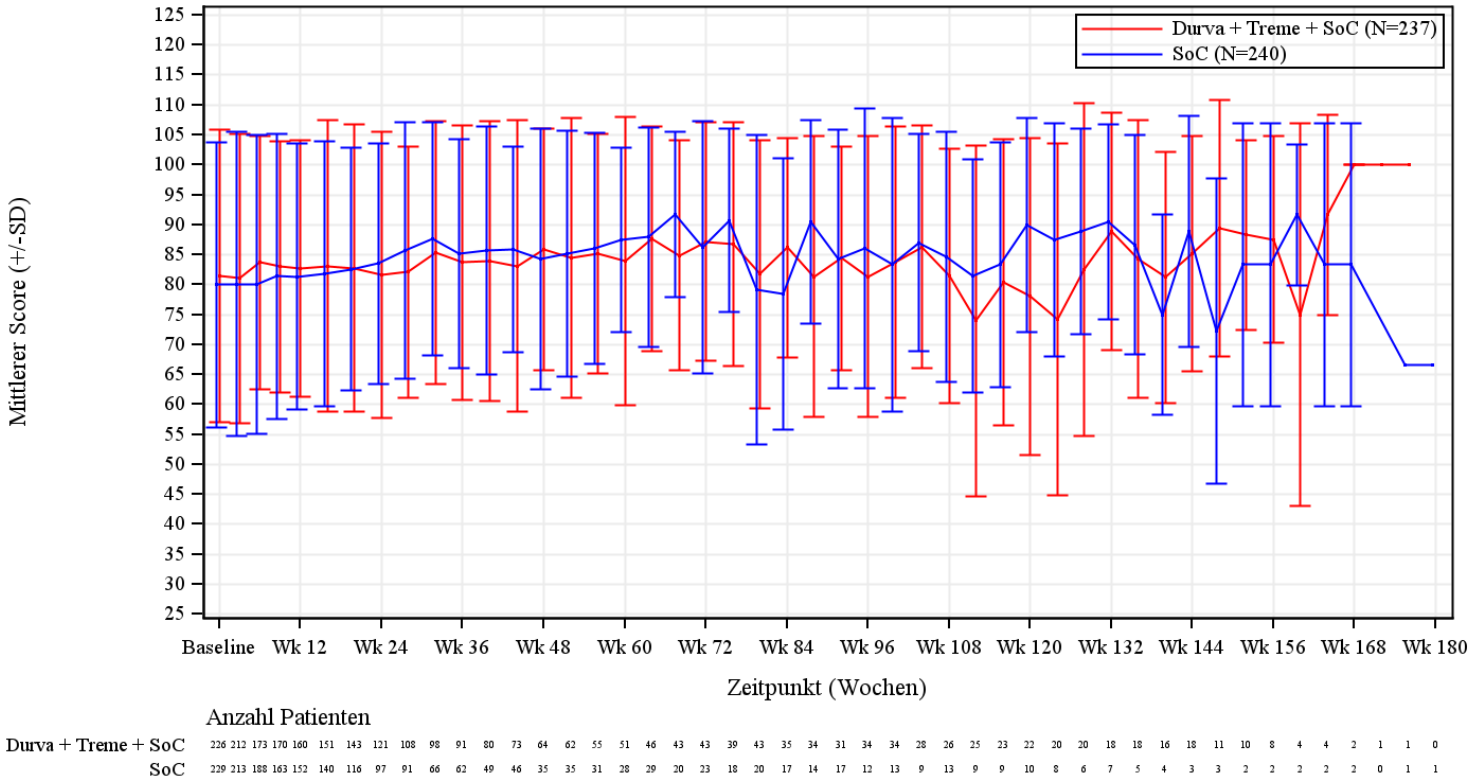
	Durva + Treme + SoC (N=237)			SoC (N=240)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD (SE) [95%-KI]	p-Wert
Woche 28	104	82,1 (24,32)	-1,4 (1,67)	88	81,3 (24,08)	-0,8 (1,80)	-0,6 (2,46) [-5,5; 4,2]	0,8010
Woche 32	95	84,6 (23,97)	0,8 (1,67)	64	82,6 (23,46)	-0,4 (1,91)	1,1 (2,54) [-3,9; 6,1]	0,6621
Durchschnitt über alle Visiten	212	82,1 (23,92)	-0,4 (1,15)	217	79,6 (23,93)	-1,6 (1,17)	1,2 (1,64) [-2,1; 4,4]	0,4842
Hedges' g SMD							0,1 (0,10) [-0,1; 0,3]	0,4845

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. SD Standard deviation.
SE Standard error. SMD Standardised mean difference. N Number of patients in treatment group.
[a] Number of patients with change from baseline at each timepoint in the Mixed Model for Repeated Measures (MMRM) analysis.
[b] Mean baseline score for patients with change from baseline at each timepoint in the MMRM analysis.
Visits with fewer than 25% of patients in each arm are excluded from the analysis, where percentages are calculated out of N.
An unstructured covariance matrix is used to model the within-subject error.
Mean change from baseline and estimated differences are estimated by restricted maximum likelihood estimation using a MMRM with treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a continuous covariate and the baseline by visit interaction.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs245g.sas Executed : 2022-10-17T210551

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 1

Figure 9.6.3.2 Mean change from baseline of EORTC QLQ-C30 social (function) score by visit
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
Error bars represent +/- one standard deviation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs345g.sas Executed : 2022-10-17T221207

Anhang 4-G 1.2: Kaplan-Meier-Kurven für unerwünschte Ereignisse nach SOC und PT

Anhang 4-G 1.2.1: Kaplan-Meier-Kurven für die Gesamtraten unerwünschter Ereignisse nach SOC und PT

Anhang 4-G 1.2.1.1: Unerwünschte Ereignisse nach SOC und PT

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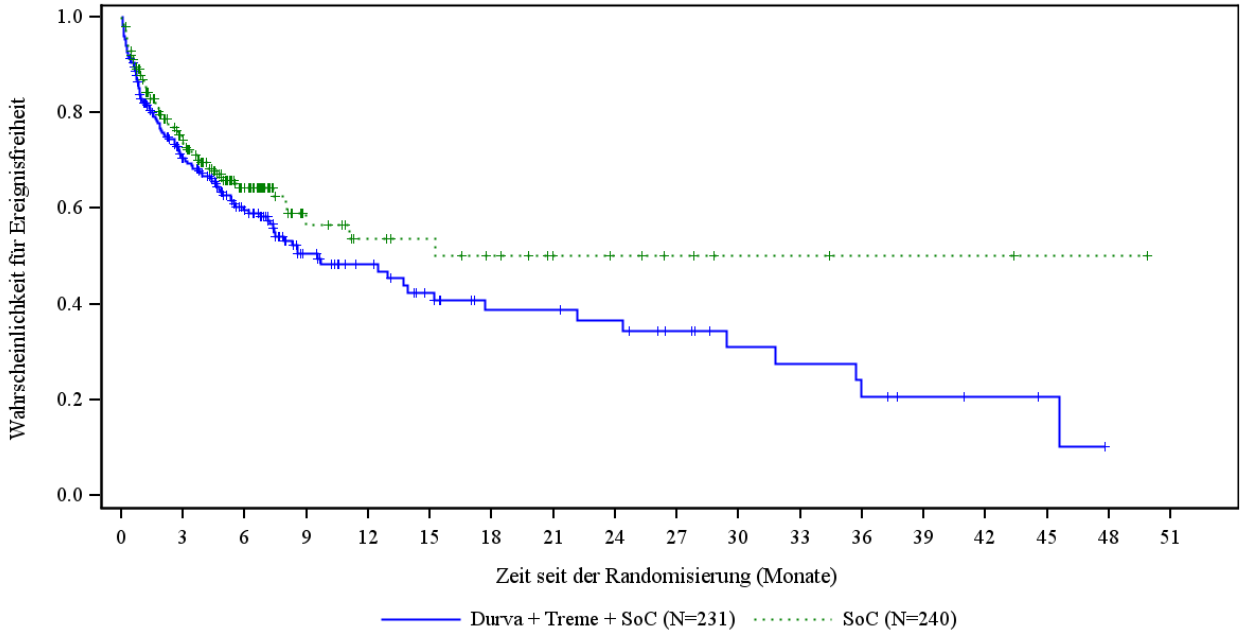
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Infektionen und parasitaere Erkrankungen



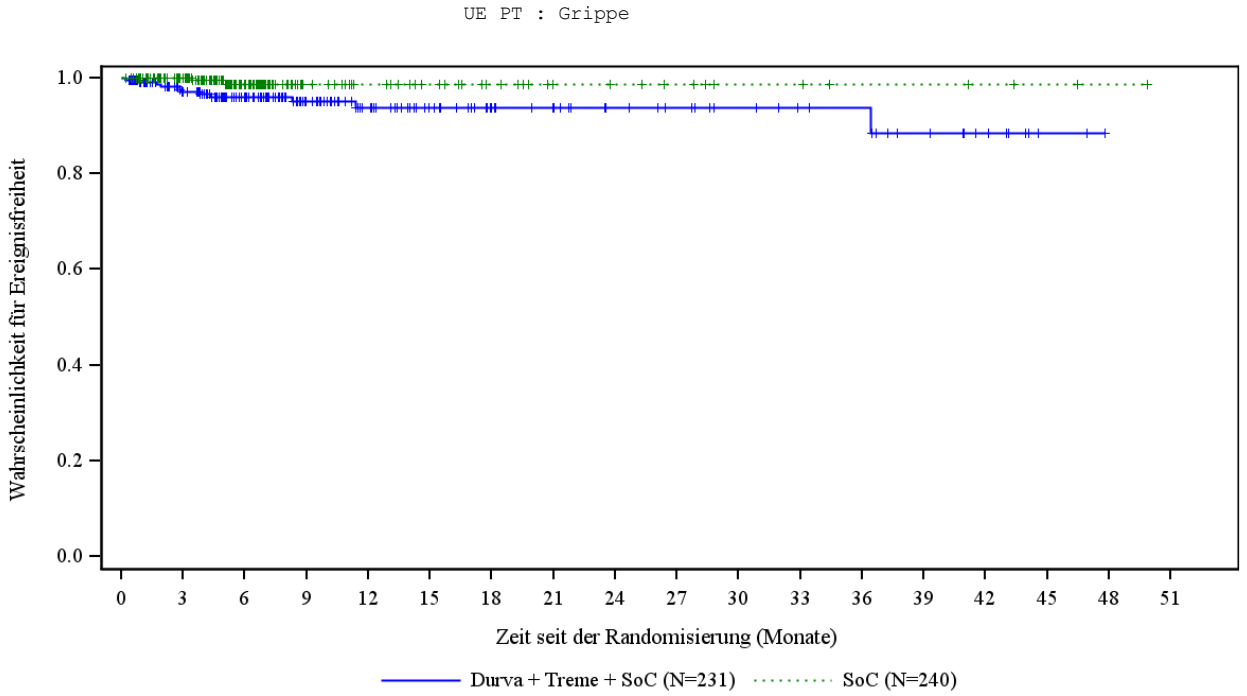
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	136	90	48	35	26	19	19	17	13	9	8	6	4	3	2	0	0
SoC	240	144	72	23	17	15	12	8	7	5	3	3	2	2	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

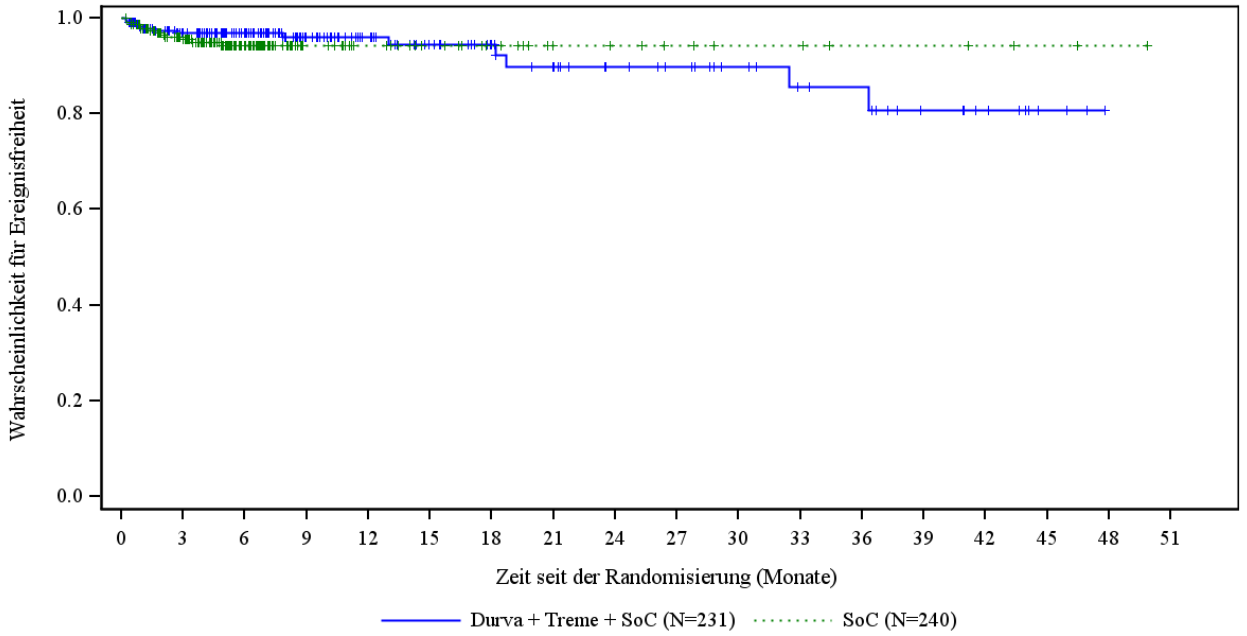
Durva + Treme + SoC	231	186	137	91	66	51	39	35	29	26	22	19	18	12	8	2	0	0
SoC	240	189	108	38	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Harnwegsinfektion



Anzahl an Patienten unter Risiko

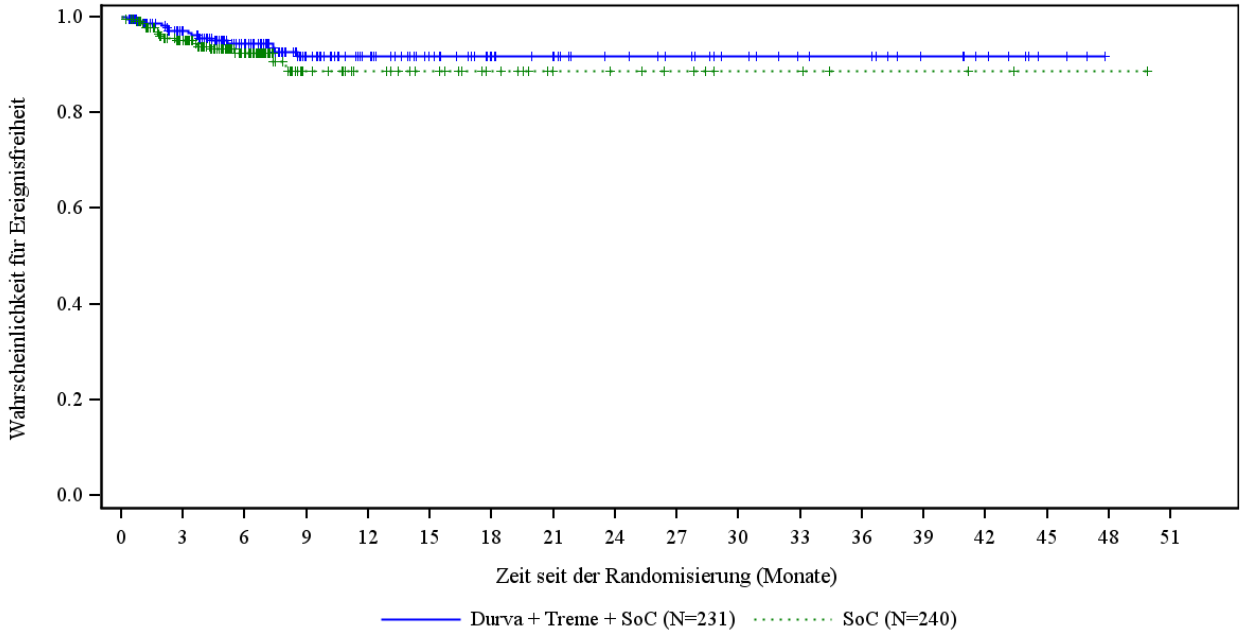
Durva + Treme + SoC	231	186	140	92	68	53	43	37	31	28	23	19	18	11	8	3	0	0
SoC	240	183	104	36	28	22	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Infektion der oberen Atemwege



Anzahl an Patienten unter Risiko

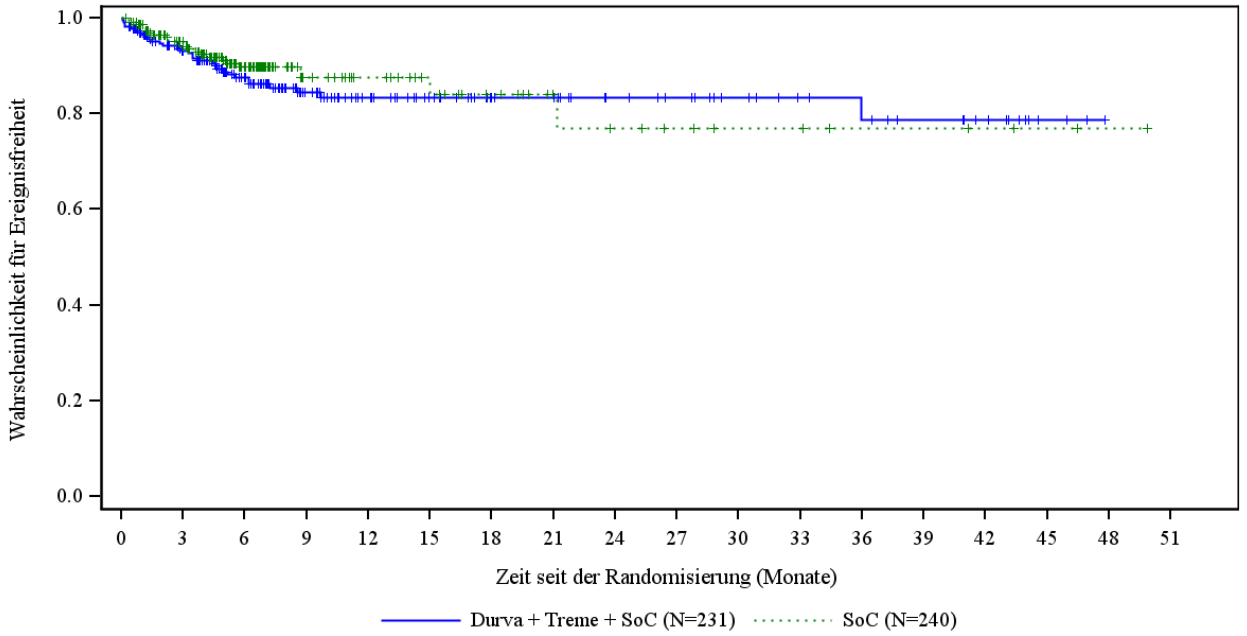
Durva + Treme + SoC	231	186	137	88	66	52	40	36	30	27	22	18	17	11	8	3	0	0
SoC	240	178	100	35	28	23	17	11	10	8	5	5	3	3	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Pneumonie



Anzahl an Patienten unter Risiko

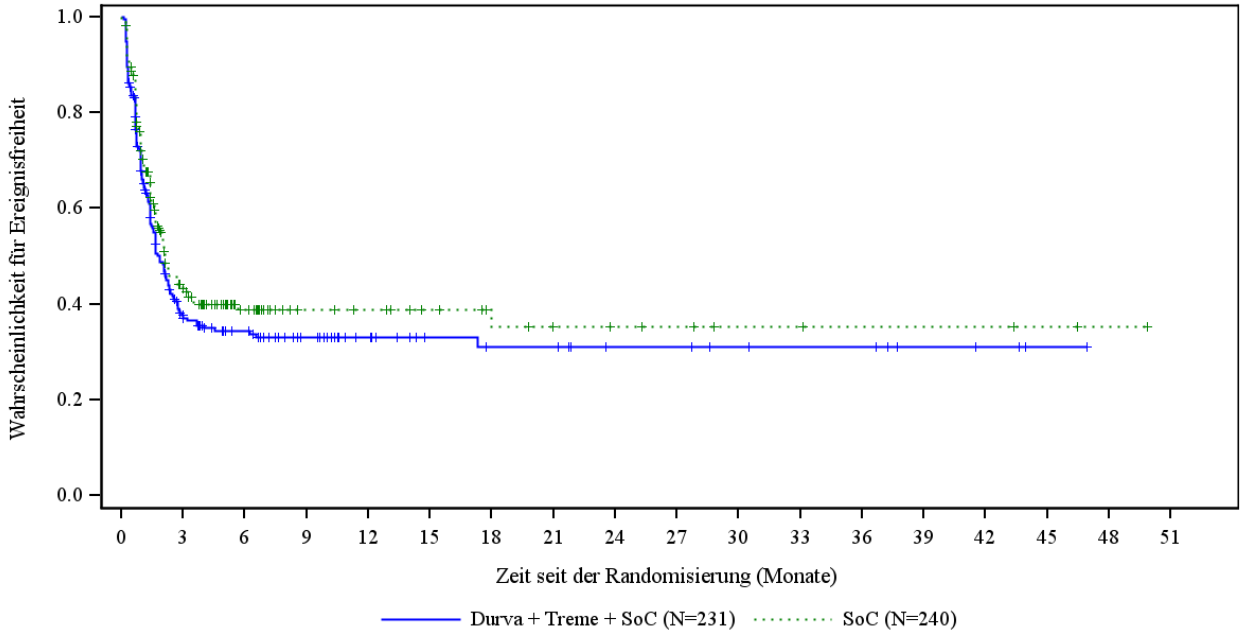
Durva + Treme + SoC	231	182	132	85	61	50	39	38	31	28	23	19	17	13	10	3	0	0
SoC	240	183	104	38	30	24	18	12	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen des Blutes und des Lymphsystems



Anzahl an Patienten unter Risiko

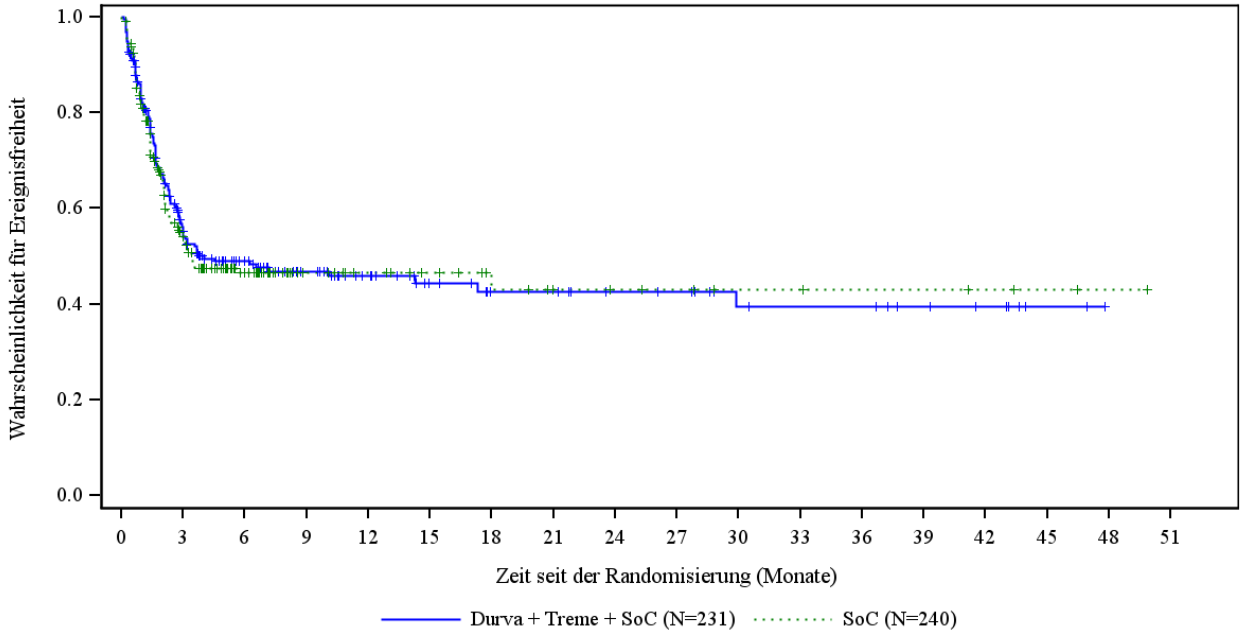
Durva + Treme + SoC	231	72	53	34	23	16	14	14	10	10	8	7	7	4	3	1	0	0
SoC	240	80	40	20	18	14	10	8	7	6	4	4	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Anaemie



Anzahl an Patienten unter Risiko

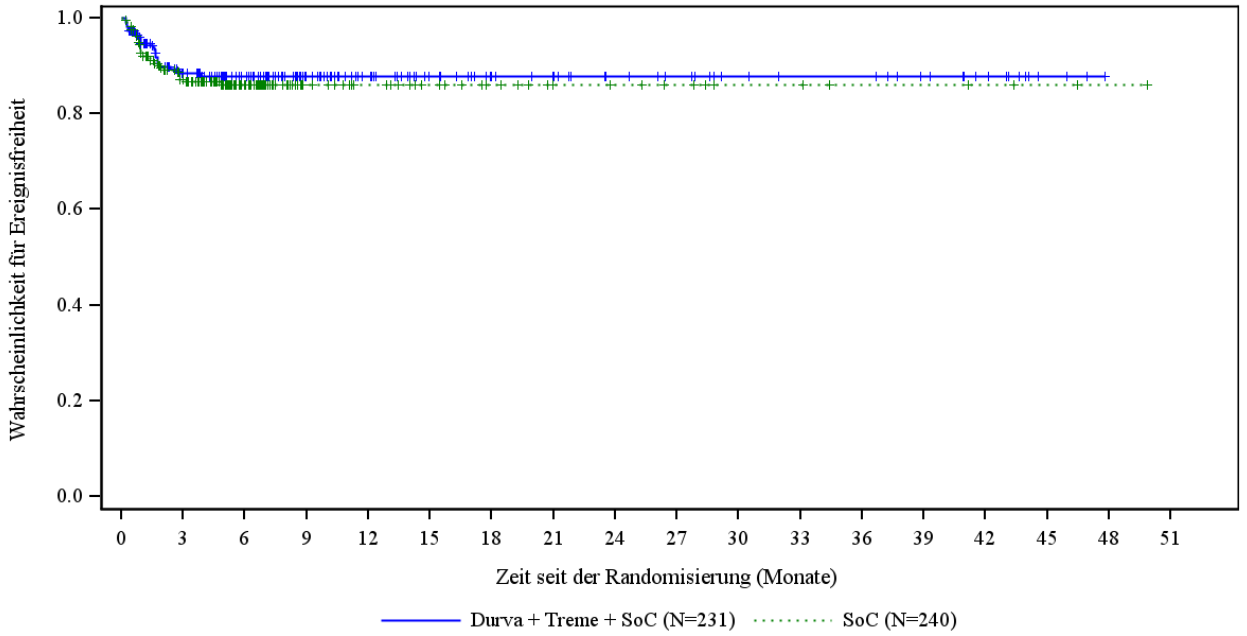
Durva + Treme + SoC	231	109	75	52	38	28	22	22	18	17	12	11	11	8	6	2	0	0
SoC	240	102	54	26	21	17	12	9	8	7	5	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Leukopenie



Anzahl an Patienten unter Risiko

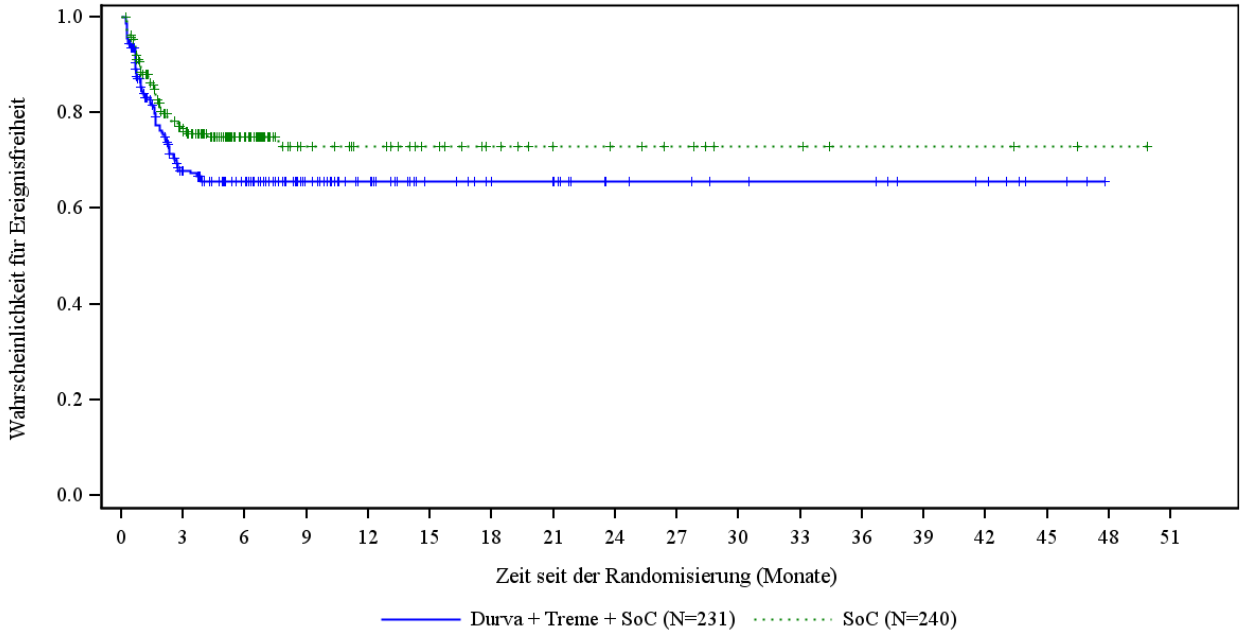
Durva + Treme + SoC	231	169	127	85	62	48	38	35	29	26	21	19	19	14	10	3	0	0
SoC	240	165	92	35	28	22	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Neutropenie



Anzahl an Patienten unter Risiko

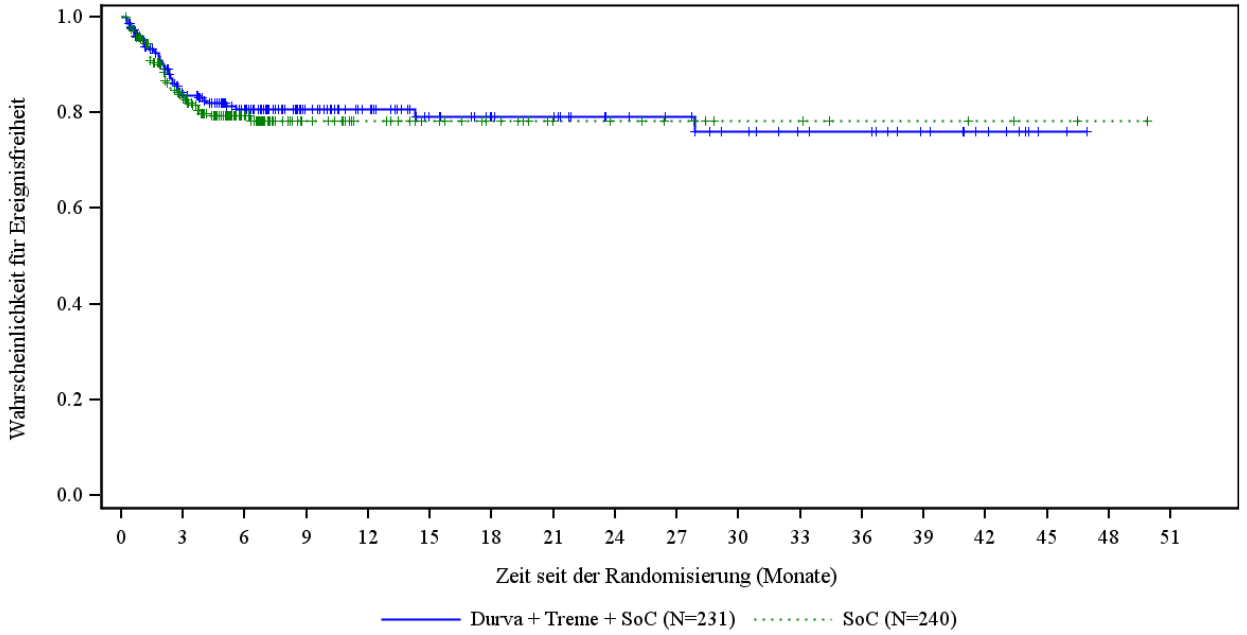
Durva + Treme + SoC	231	125	92	58	42	29	24	23	16	15	13	12	12	8	7	3	0	0
SoC	240	141	74	31	26	20	15	11	10	8	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Thrombozytopenie



Anzahl an Patienten unter Risiko

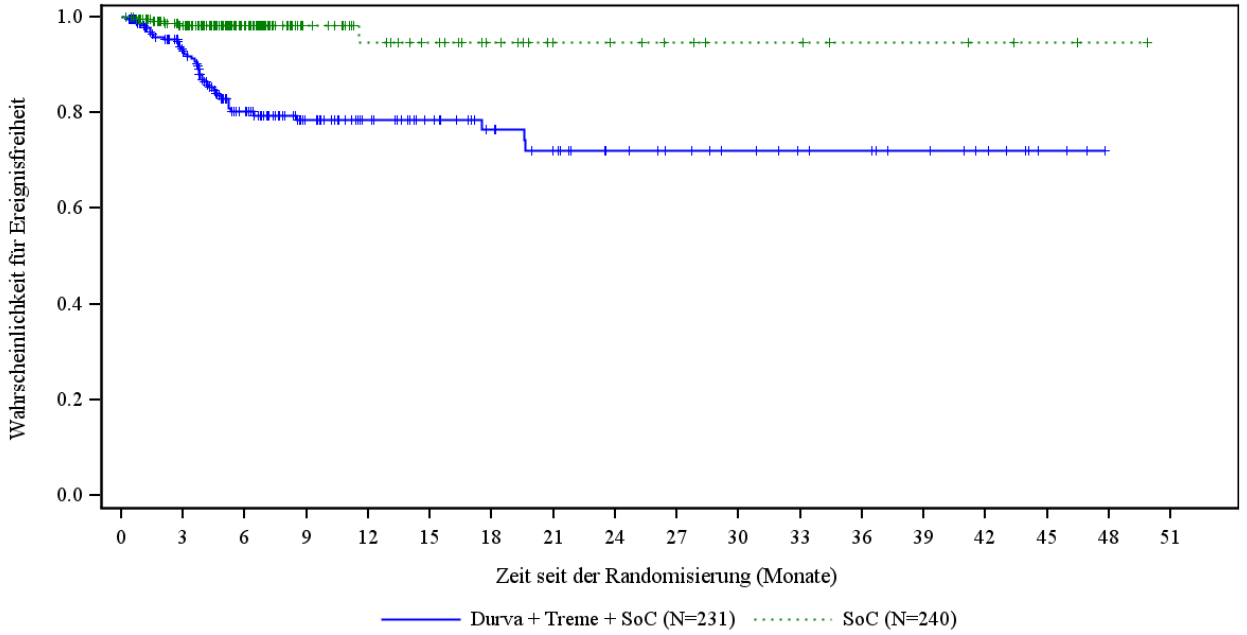
Durva + Treme + SoC	231	162	120	80	60	45	38	37	30	28	23	19	18	12	8	2	0	0
SoC	240	161	88	38	29	23	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Endokrine Erkrankungen



Anzahl an Patienten unter Risiko

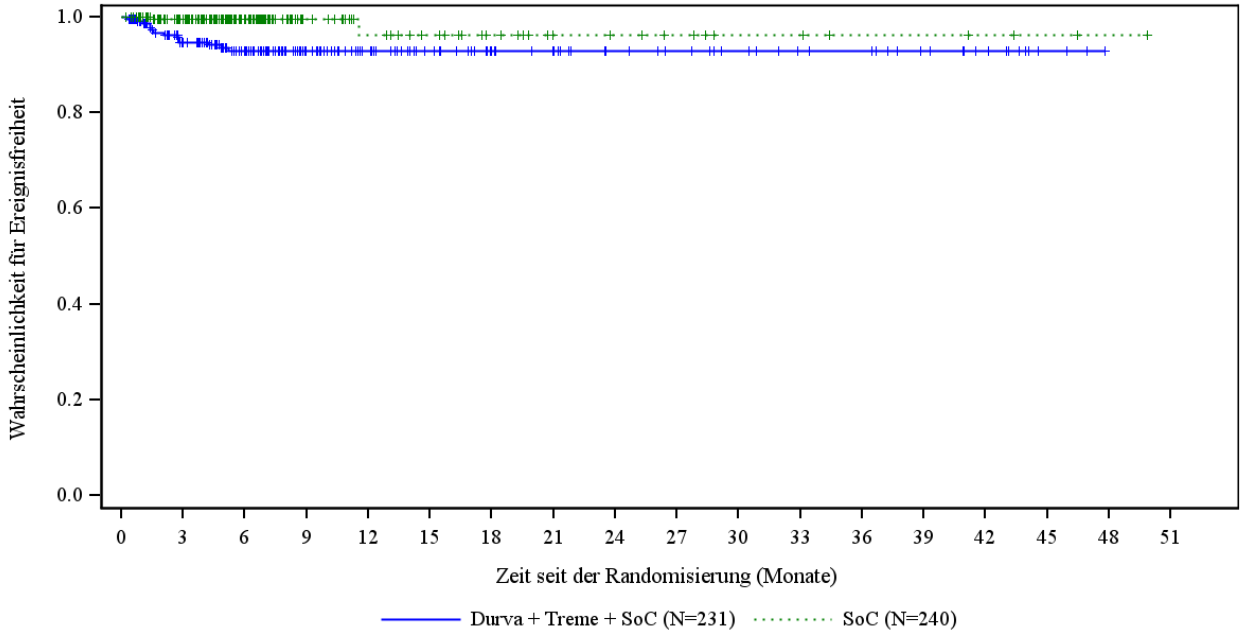
Durva + Treme + SoC	231	178	114	77	57	45	36	30	24	21	18	15	14	11	8	3	0	0
SoC	240	185	106	38	28	23	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Hyperthyroidismus



Anzahl an Patienten unter Risiko

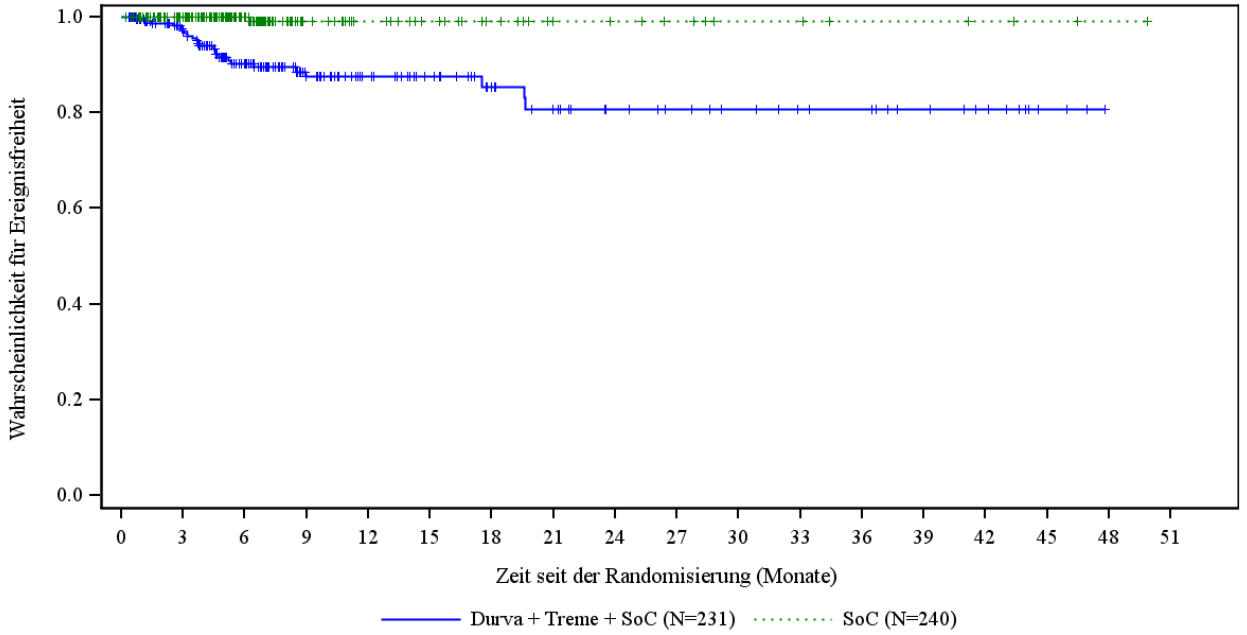
Durva + Treme + SoC	231	181	133	90	68	53	42	38	31	28	24	20	19	14	10	3	0	0
SoC	240	188	109	39	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Hypothyreose



Anzahl an Patienten unter Risiko

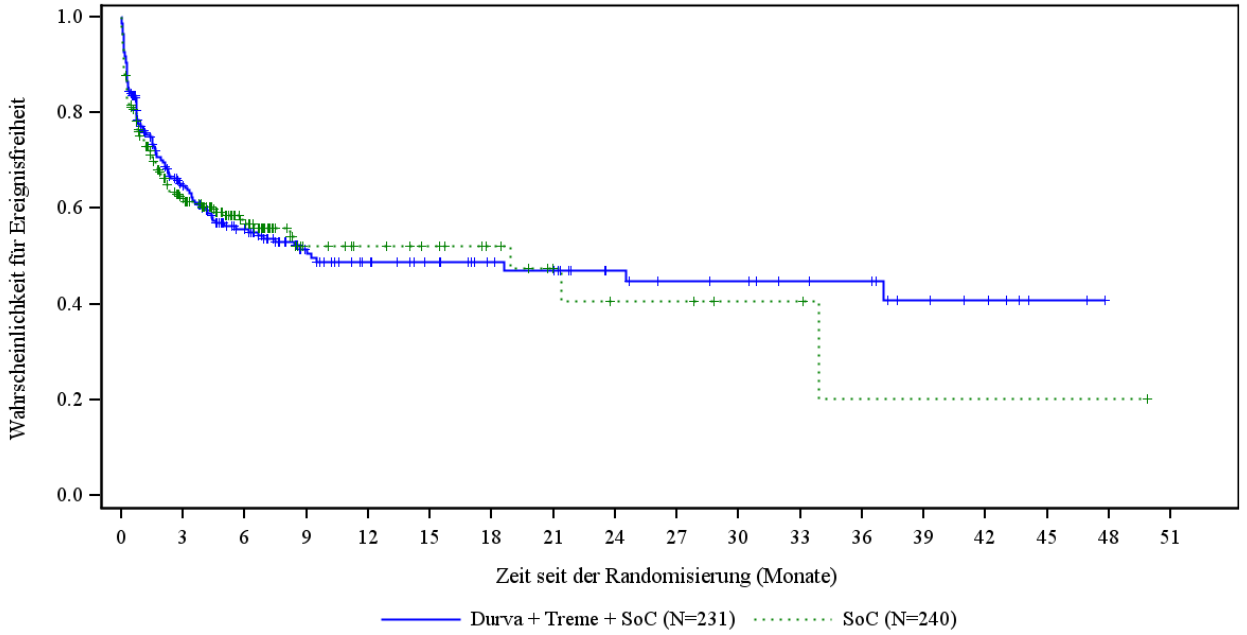
Durva + Treme + SoC	231	187	128	83	61	49	38	32	26	23	20	17	16	12	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Stoffwechsel- und Ernaehrungsstoerungen



Anzahl an Patienten unter Risiko

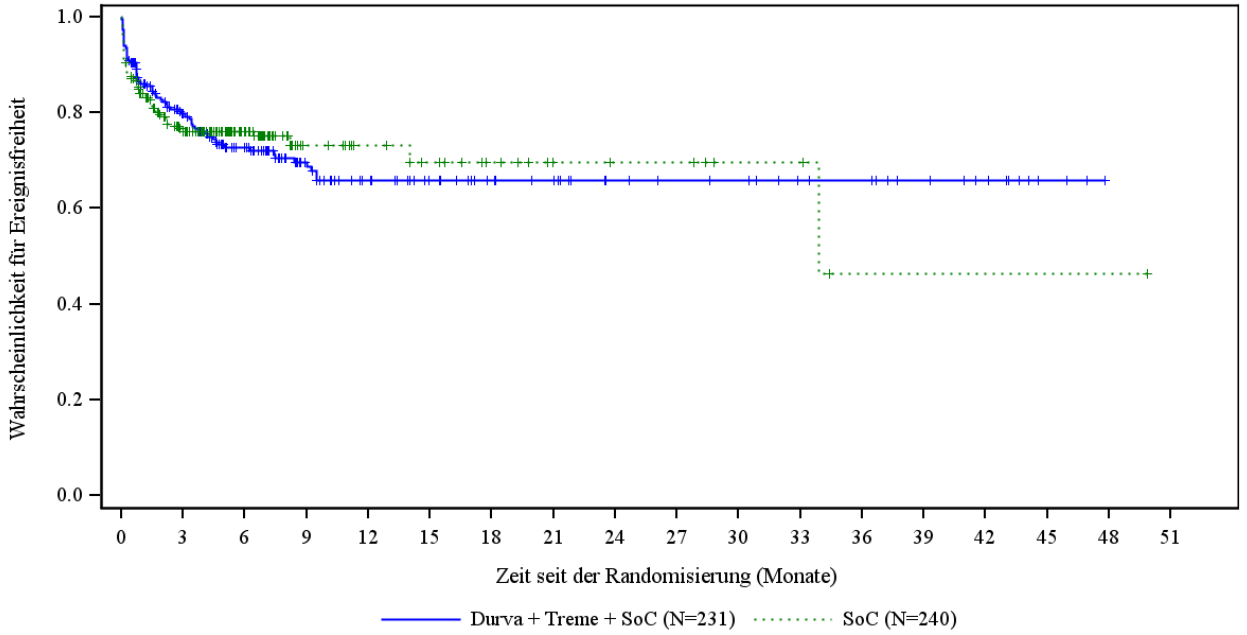
Durva + Treme + SoC	231	126	89	58	43	36	30	28	21	18	17	14	13	8	6	2	0	0
SoC	240	122	66	23	19	16	12	7	5	5	3	3	1	1	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Appetit vermindert



Anzahl an Patienten unter Risiko

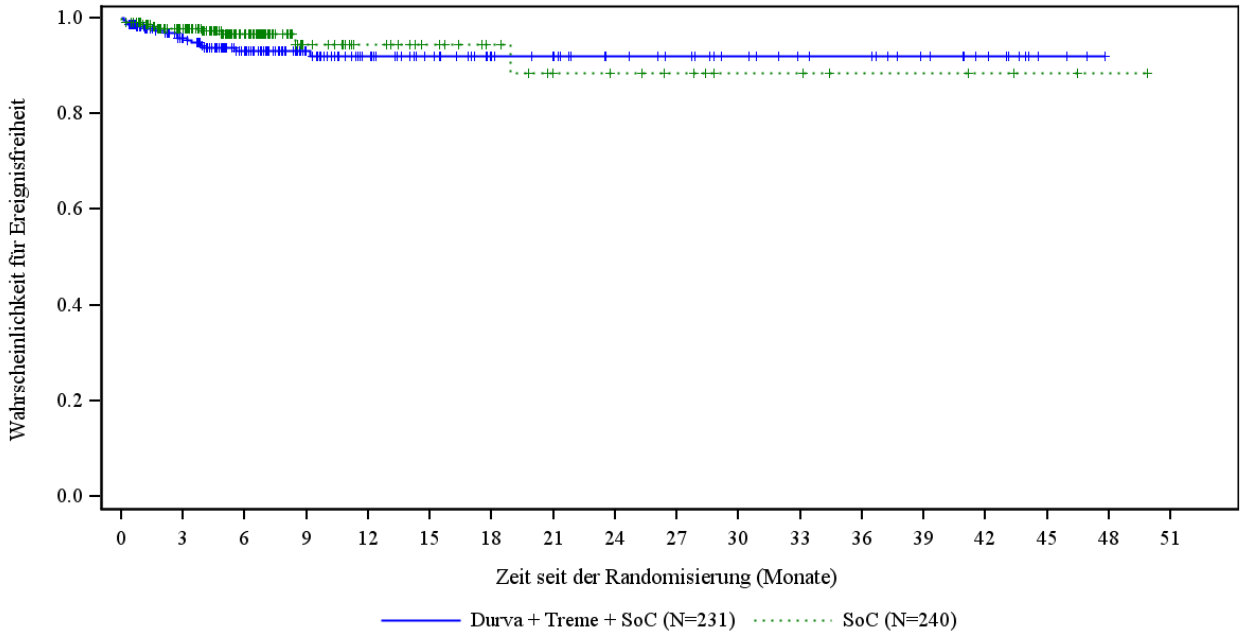
Durva + Treme + SoC	231	154	112	74	53	42	34	31	24	22	21	17	16	12	9	3	0	0
SoC	240	147	82	28	22	18	13	8	7	7	4	4	1	1	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Hyperglykaemie



Anzahl an Patienten unter Risiko

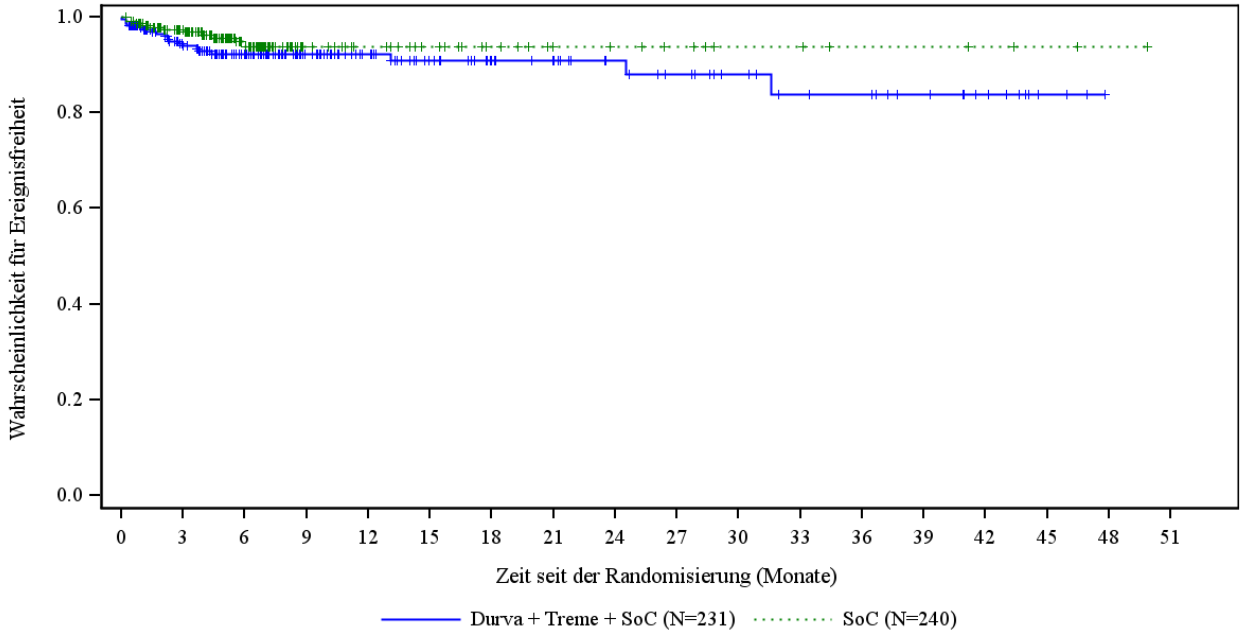
Durva + Treme + SoC	231	185	137	91	67	54	42	39	32	29	24	20	19	14	10	3	0	0
SoC	240	184	107	37	28	22	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Hypokaliaemie



Anzahl an Patienten unter Risiko

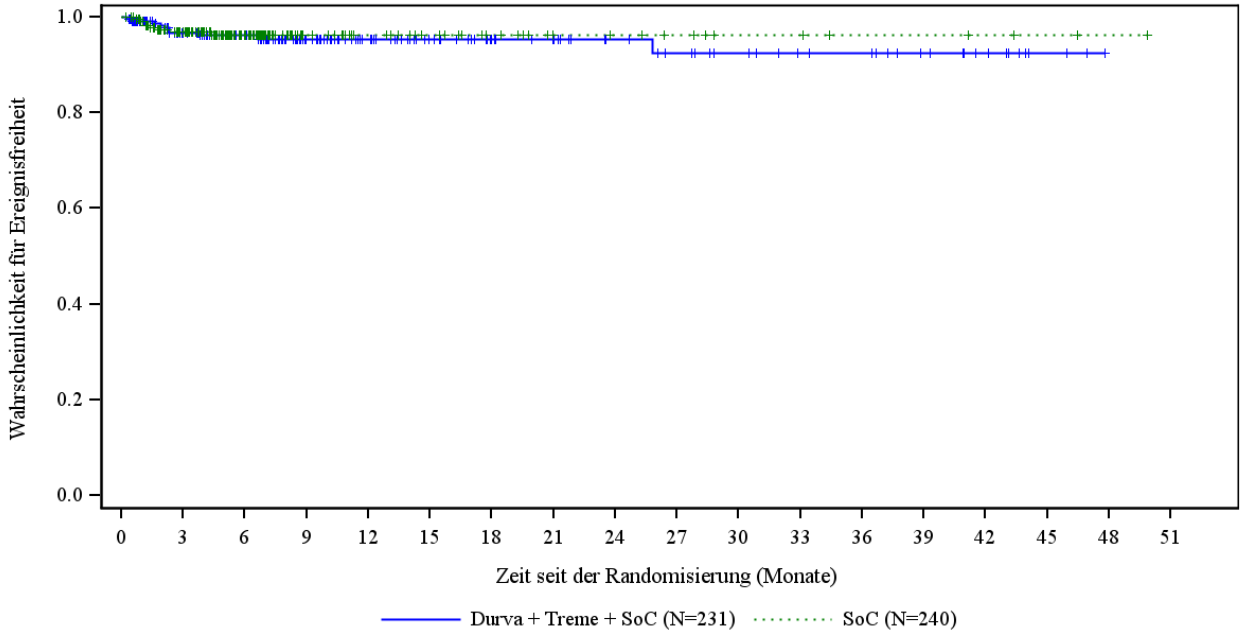
Durva + Treme + SoC	231	184	138	93	70	54	43	39	32	28	23	19	18	13	9	3	0	0
SoC	240	184	105	36	29	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Hypomagnesiaemie



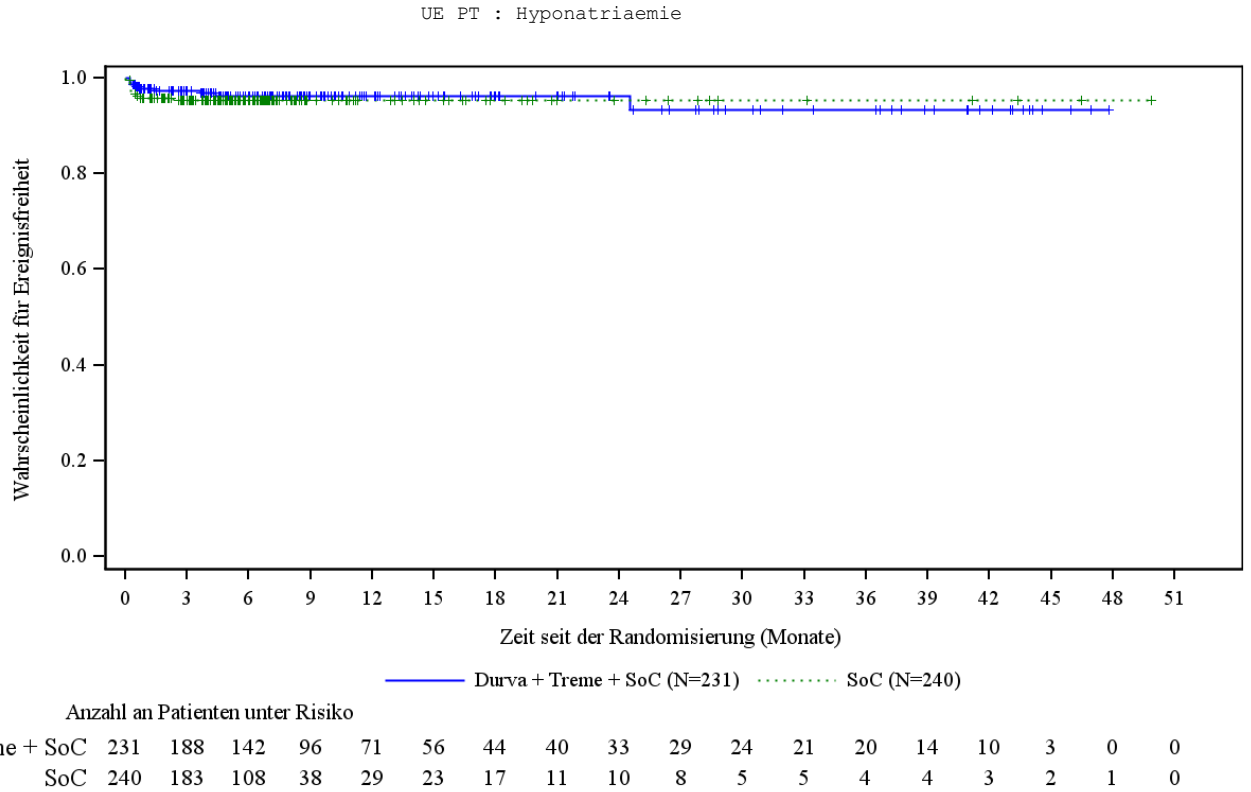
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	141	94	70	54	43	39	32	28	24	20	19	13	9	3	0	0
SoC	240	183	106	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

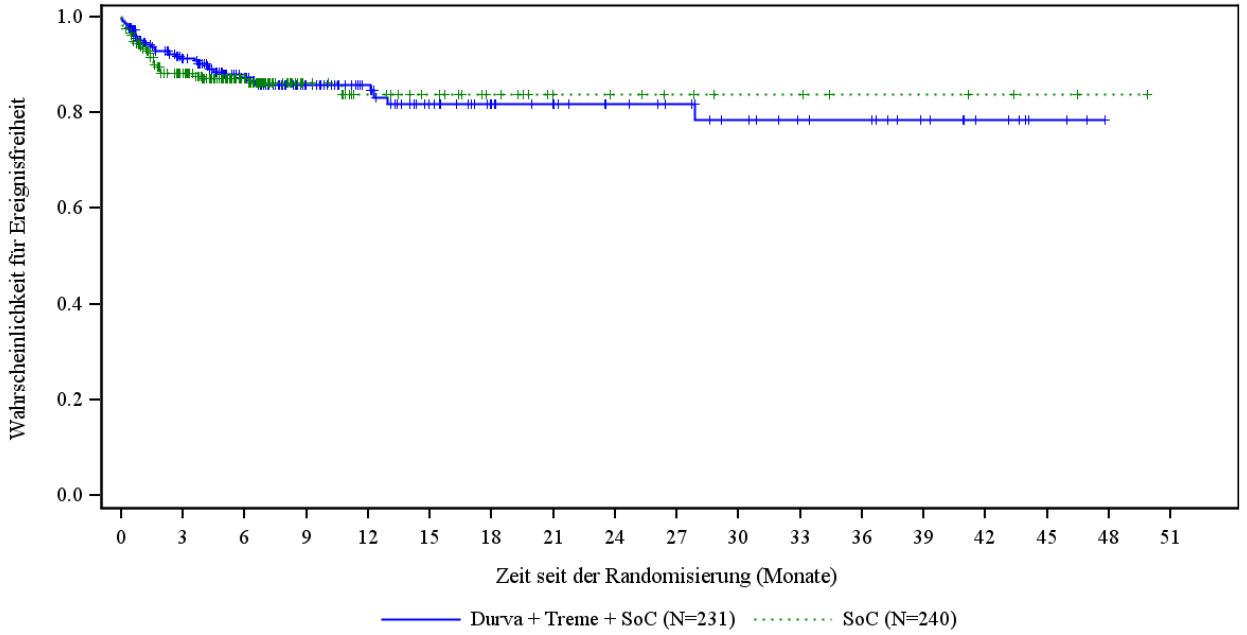


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Psychiatrische Erkrankungen



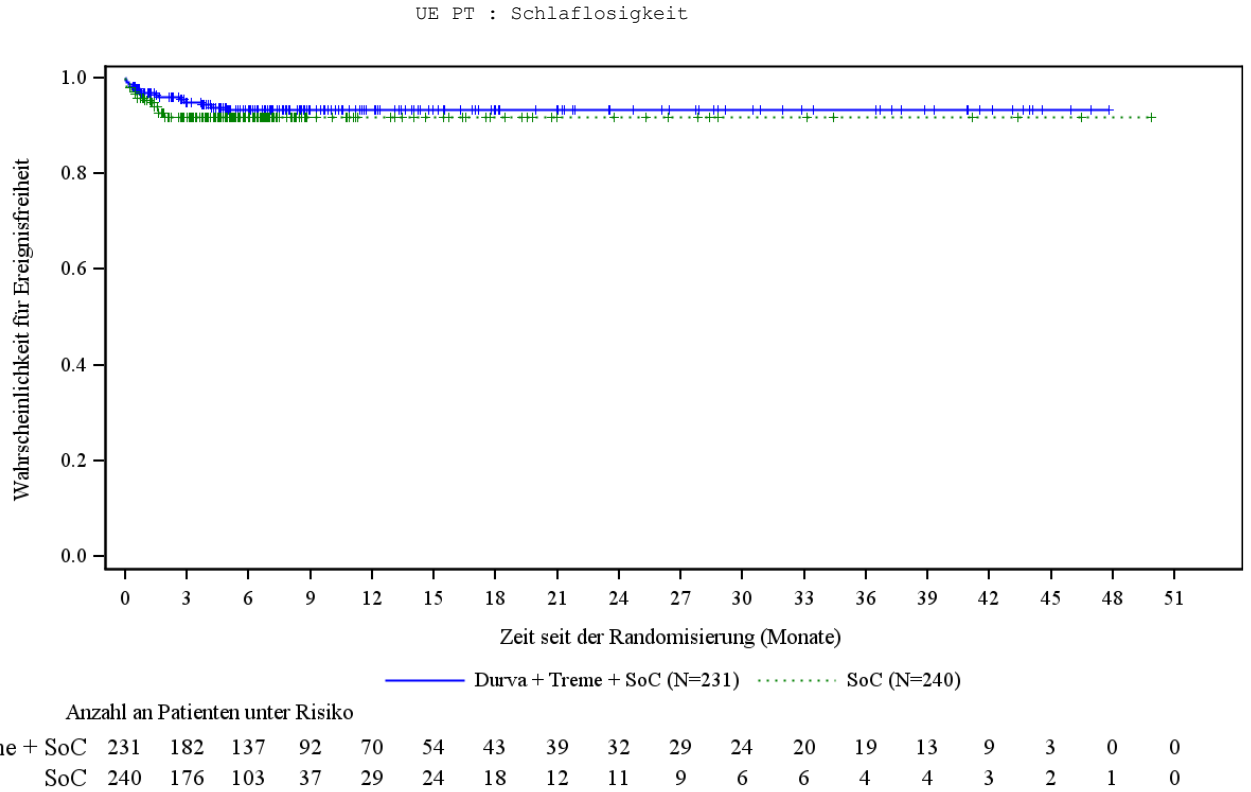
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	177	129	88	67	49	39	35	30	27	22	18	17	11	7	3	0	0
SoC	240	170	101	37	28	23	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

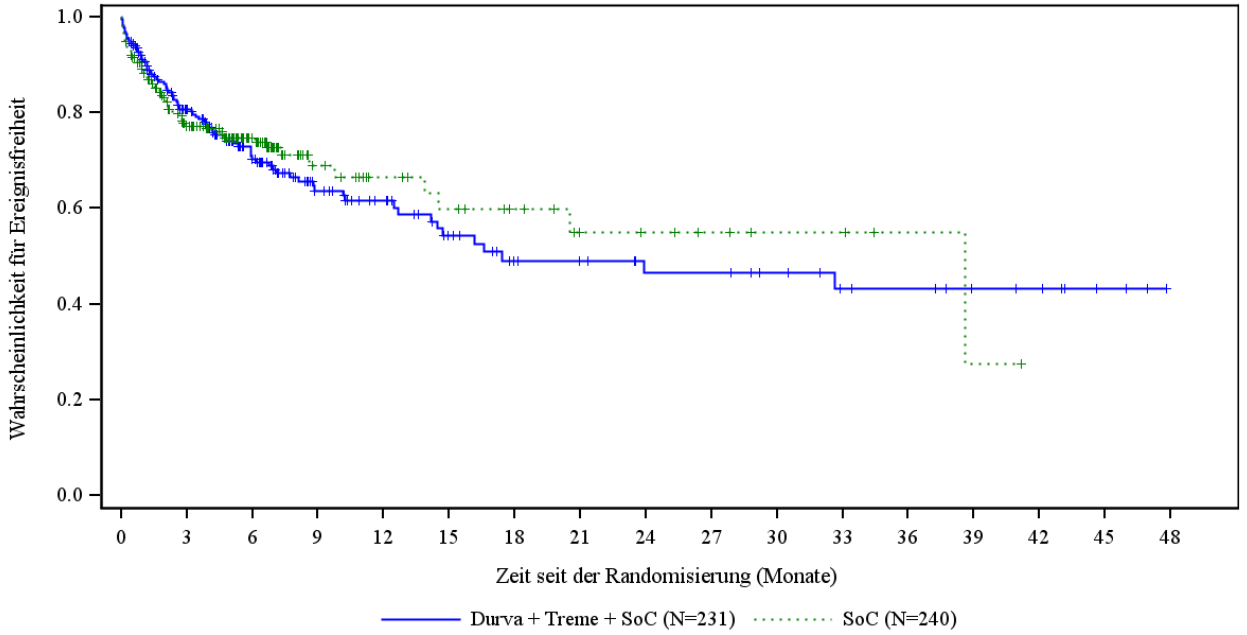


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen des Nervensystems



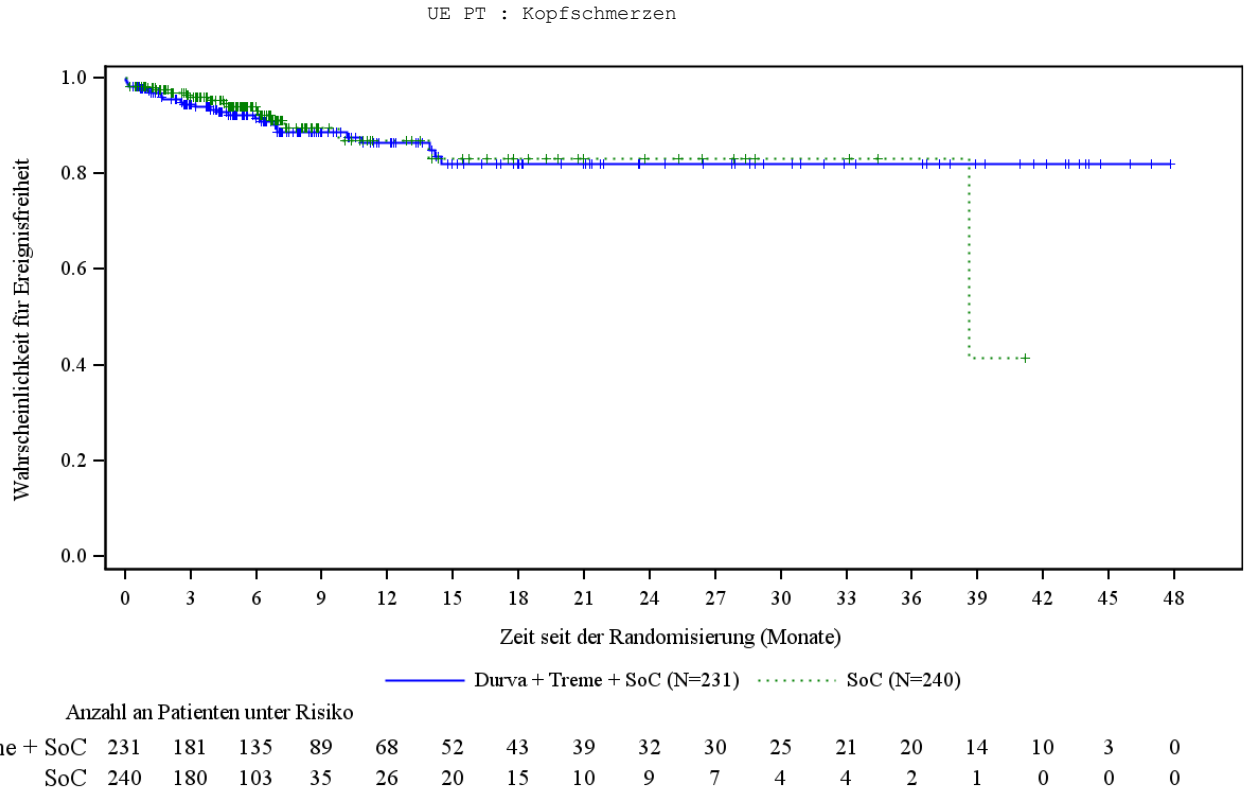
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	155	106	65	48	34	25	23	19	19	16	12	11	8	7	3	0
SoC	240	143	81	30	22	18	14	9	8	6	4	4	2	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

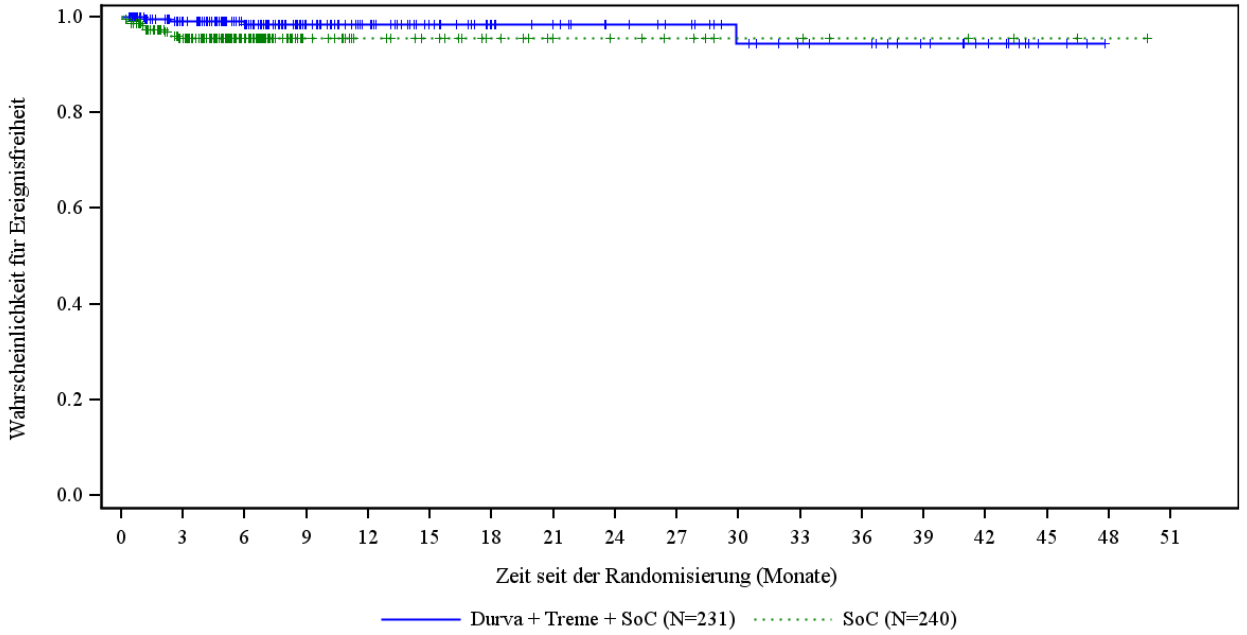
Durva + Treme + SoC	231	181	135	89	68	52	43	39	32	30	25	21	20	14	10	3	0
SoC	240	180	103	35	26	20	15	10	9	7	4	4	2	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Periphere Neuropathie



Anzahl an Patienten unter Risiko

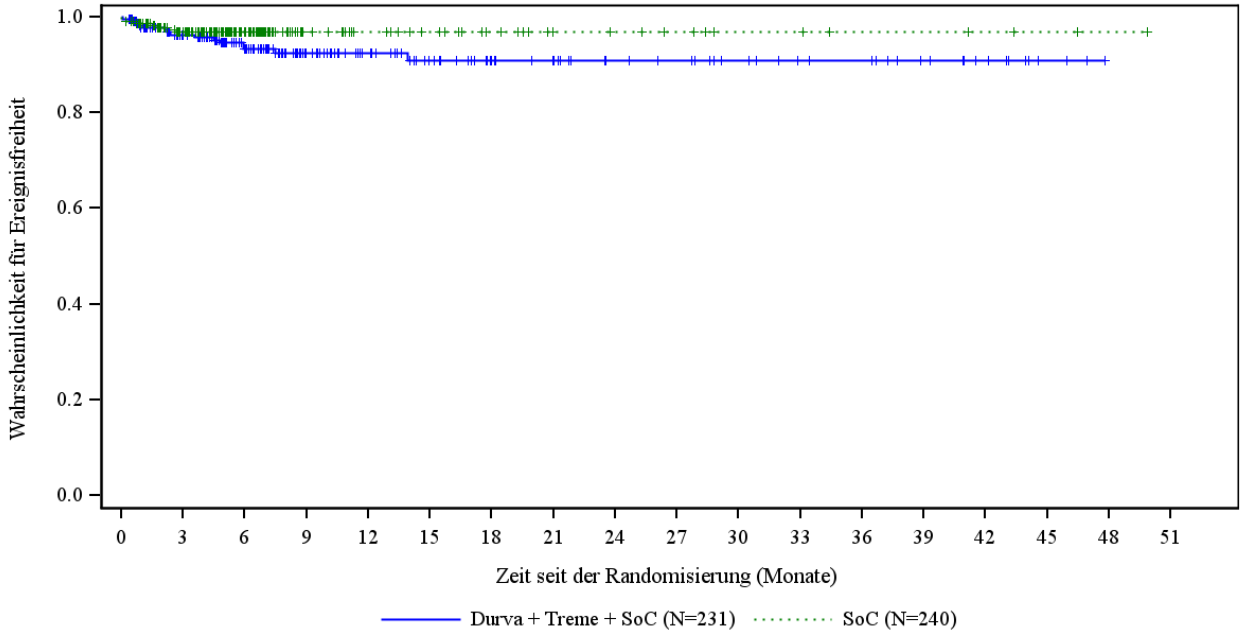
Durva + Treme + SoC	231	190	142	94	70	54	42	38	33	30	24	20	19	14	10	3	0	0
SoC	240	179	105	36	27	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Schwindelgefuehl



Anzahl an Patienten unter Risiko

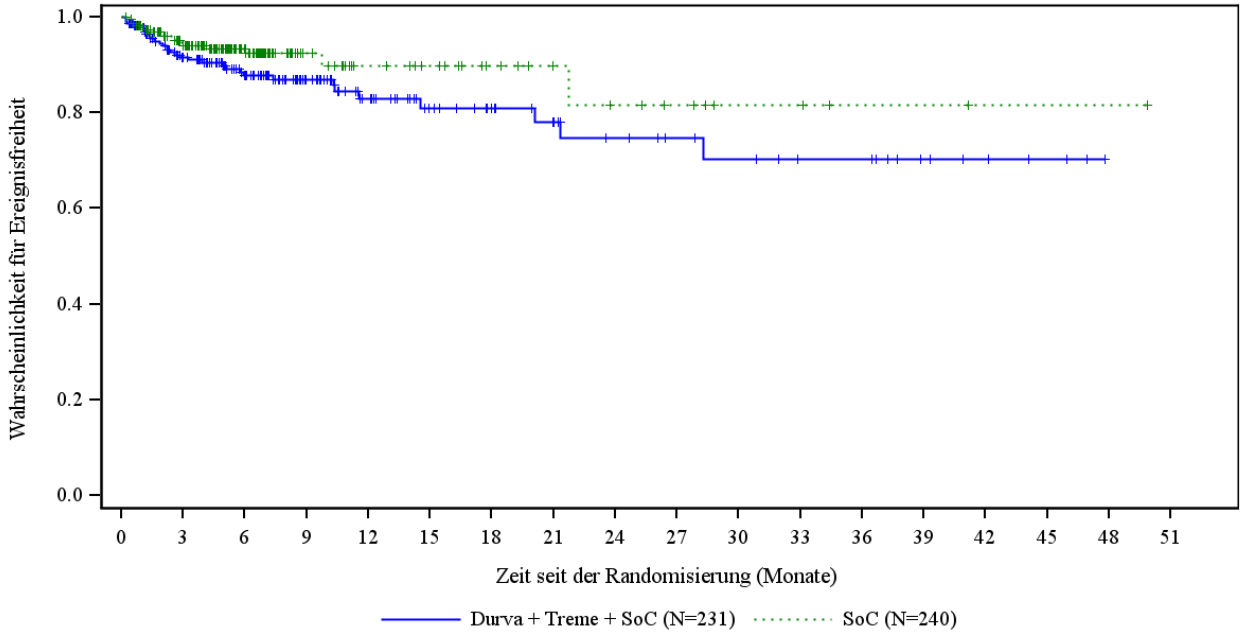
Durva + Treme + SoC	231	185	136	91	69	54	42	38	31	29	24	20	19	13	9	3	0	0
SoC	240	182	106	37	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Augenerkrankungen



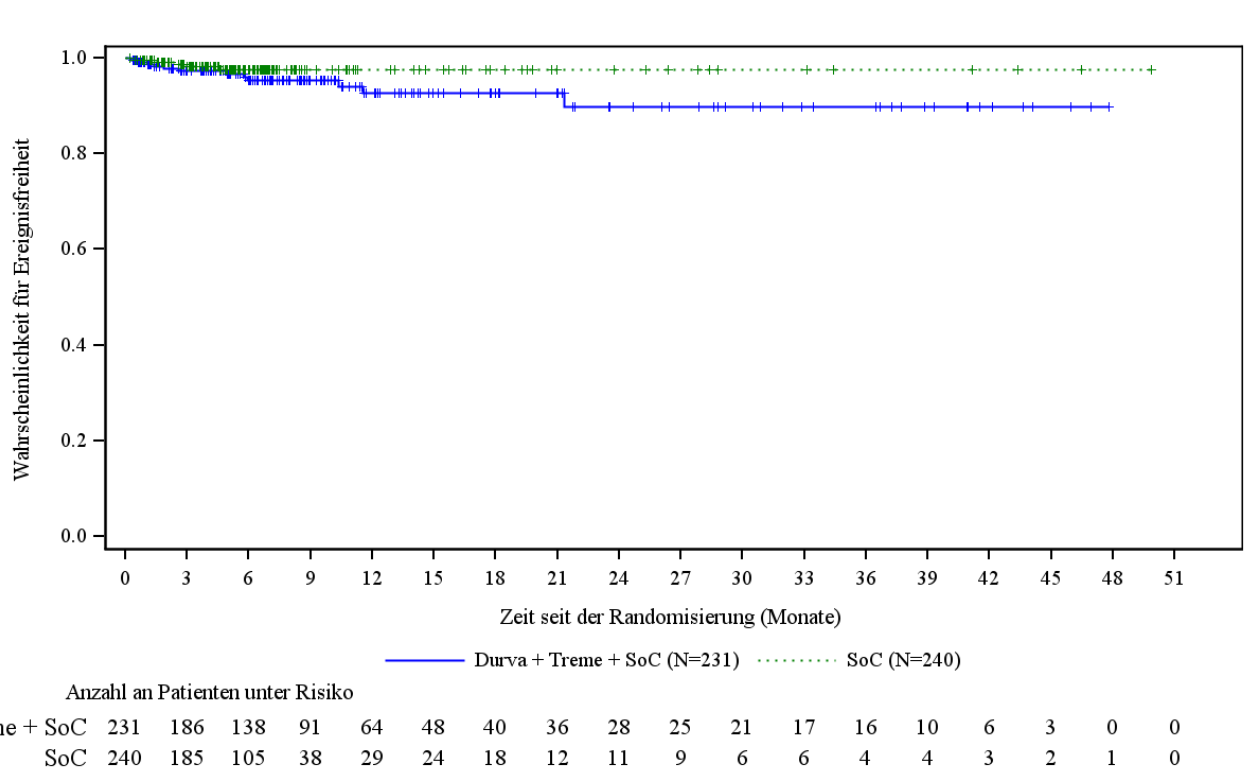
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	174	127	81	55	39	31	26	21	18	16	13	13	7	5	3	0	0
SoC	240	177	99	35	25	21	15	11	9	7	4	4	2	2	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

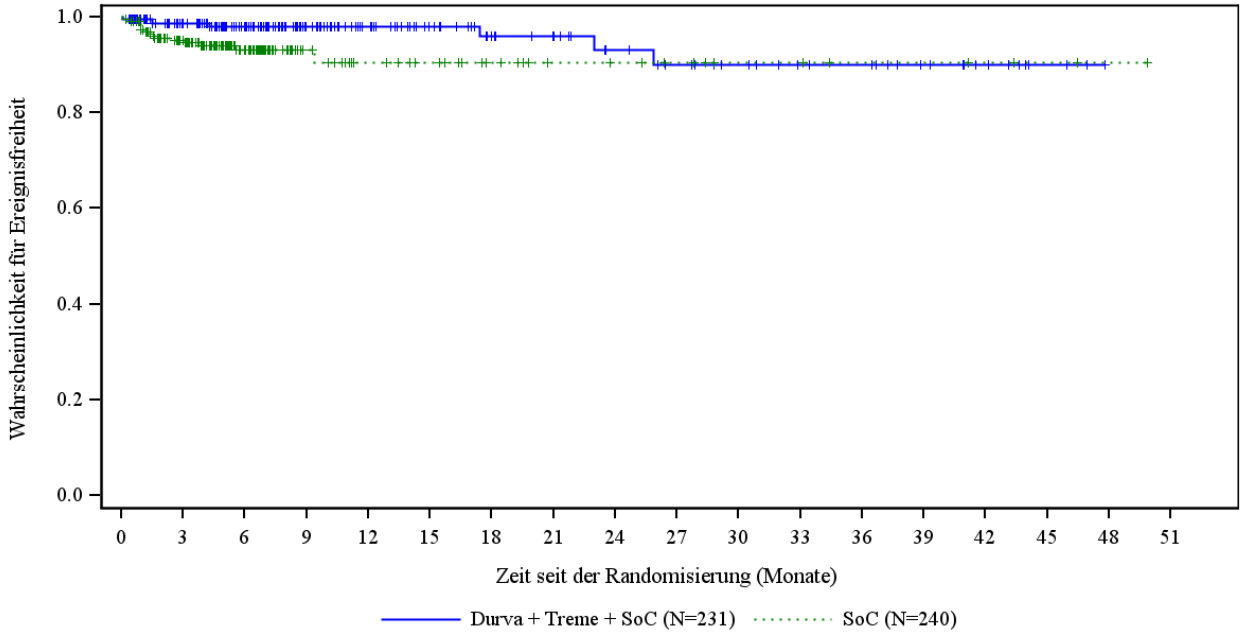
Durva + Treme + SoC	231	186	138	91	64	48	40	36	28	25	21	17	16	10	6	3	0	0
SoC	240	185	105	38	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen des Ohrs und des Labyrinths



Anzahl an Patienten unter Risiko

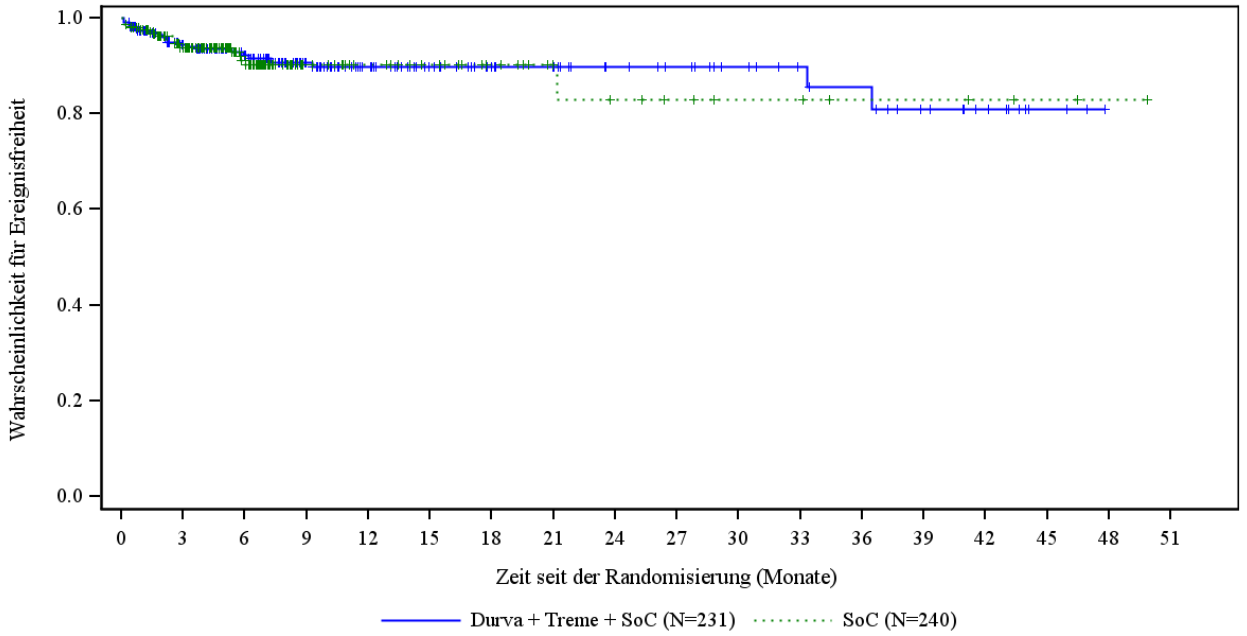
Durva + Treme + SoC	231	189	142	95	70	54	42	38	31	27	23	19	18	12	8	3	0	0
SoC	240	178	102	36	27	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Herzerkrankungen



Anzahl an Patienten unter Risiko

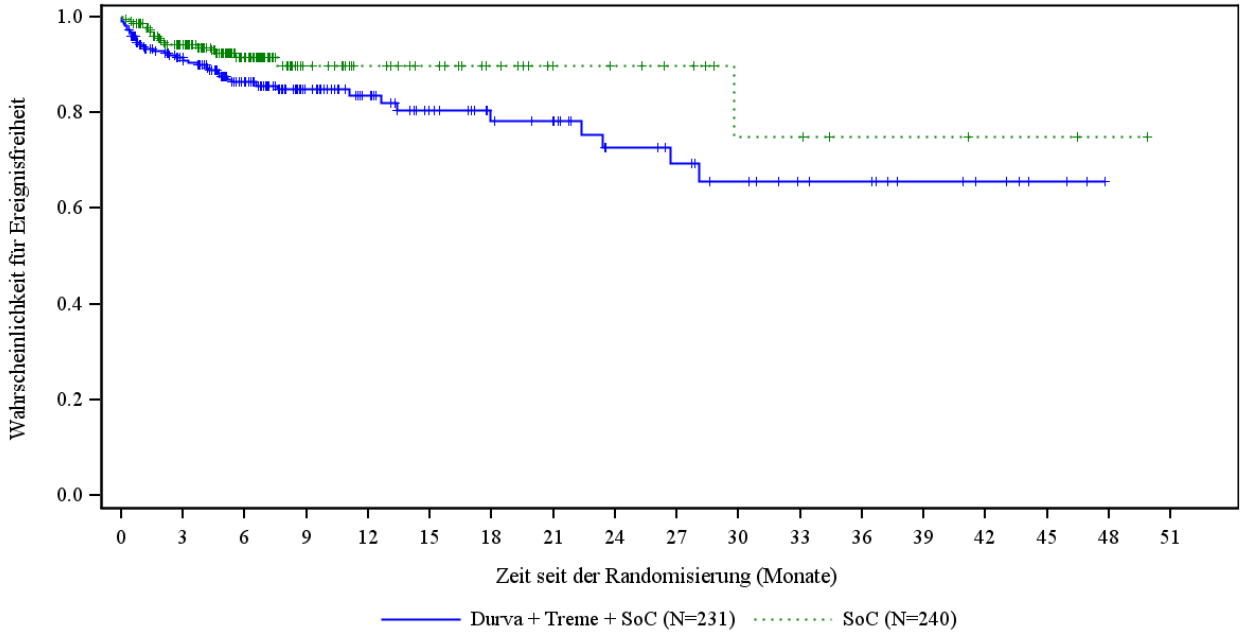
Durva + Treme + SoC	231	183	139	95	69	54	43	40	33	30	25	21	19	13	9	3	0	0
SoC	240	181	106	37	29	24	18	12	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Gefaesserkrankungen



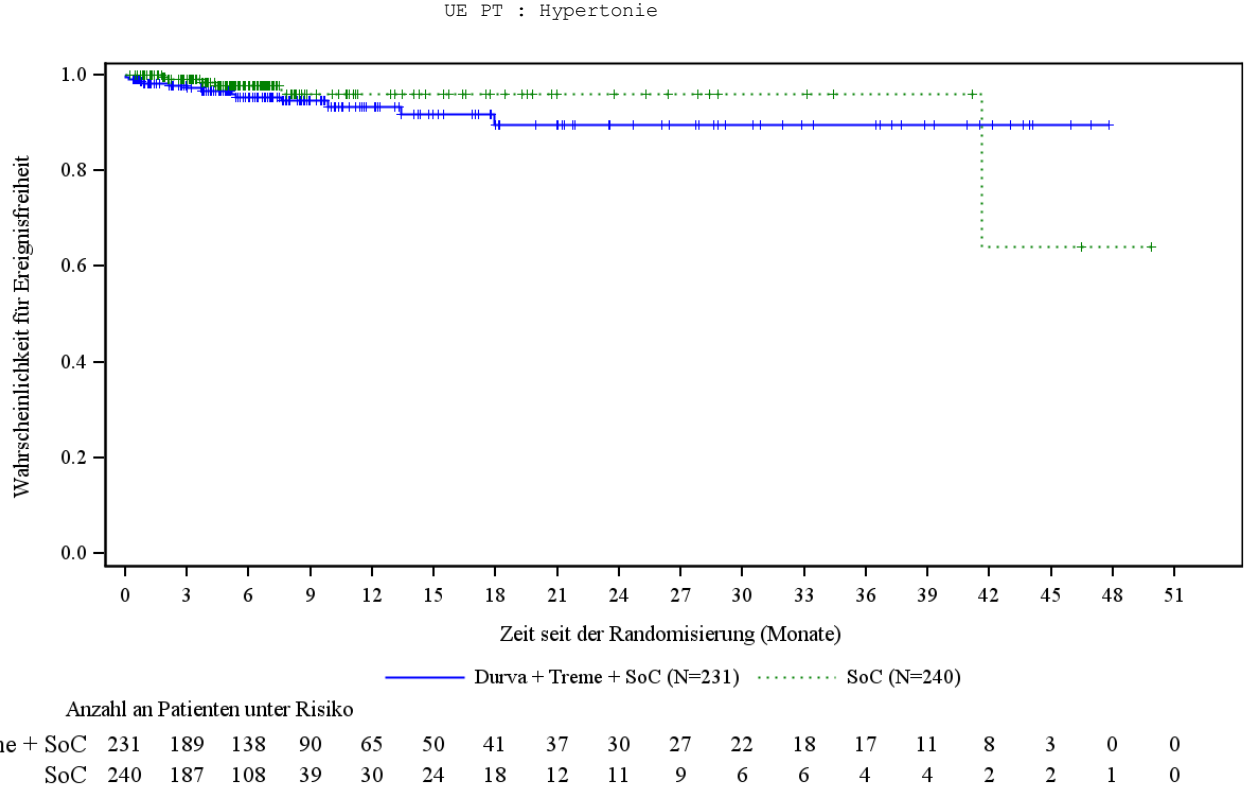
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	179	127	82	60	44	36	33	24	21	17	13	12	8	6	3	0	0
SoC	240	179	104	38	29	24	18	12	11	9	5	5	3	3	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



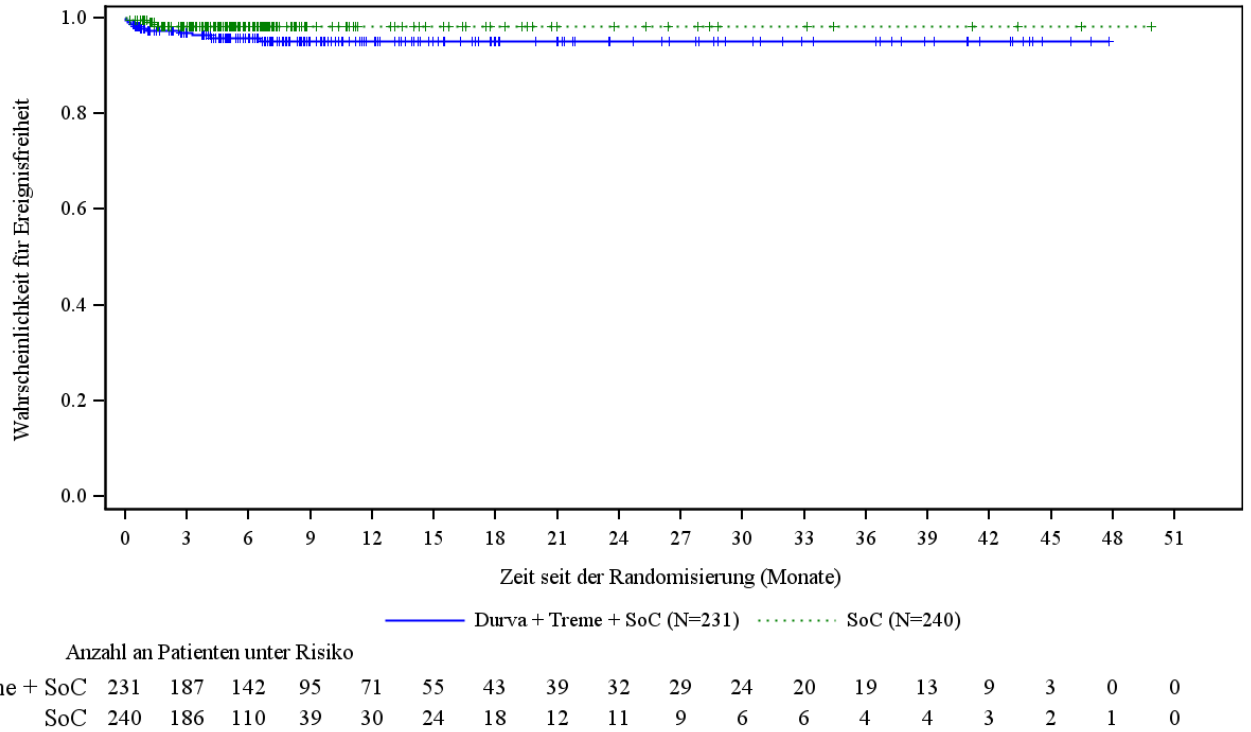
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	138	90	65	50	41	37	30	27	22	18	17	11	8	3	0	0
SoC	240	187	108	39	30	24	18	12	11	9	6	6	4	4	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

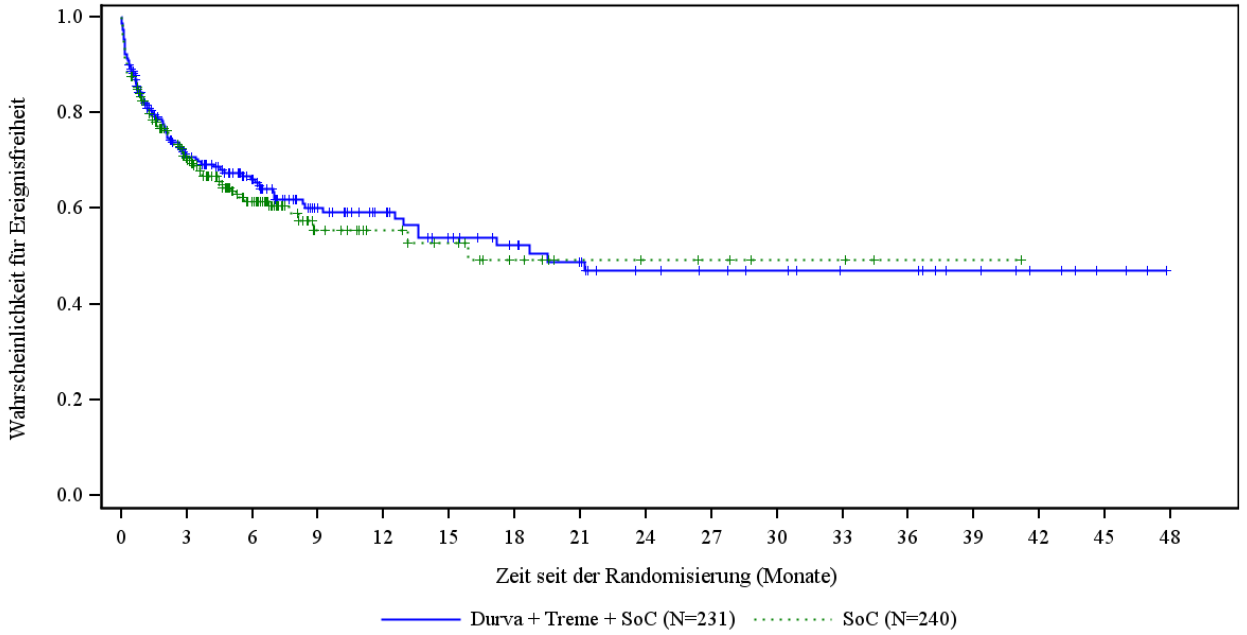
Durva + Treme + SoC	231	187	142	95	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	186	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen der Atemwege, des Brustraums und Mediastinums



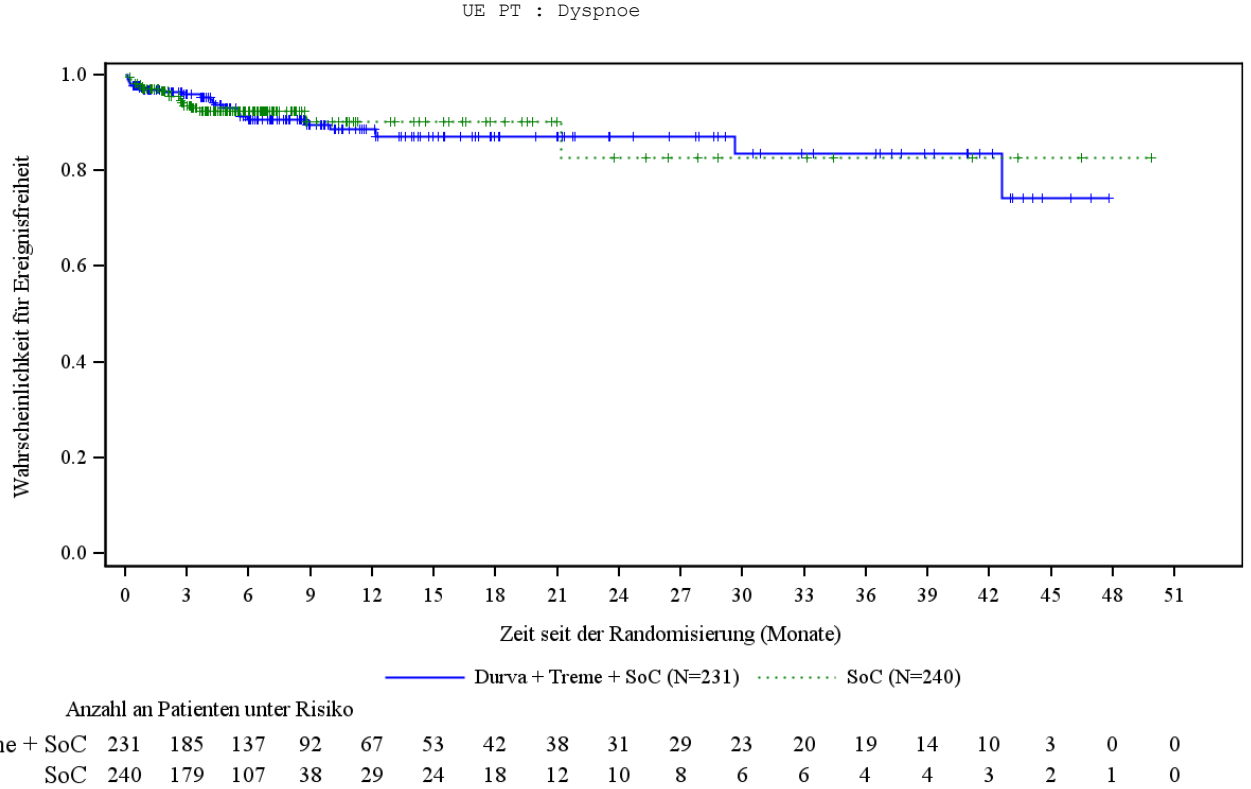
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	134	100	62	48	38	32	27	21	19	17	14	14	10	6	3	0
SoC	240	140	76	28	21	17	11	7	6	5	3	3	1	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

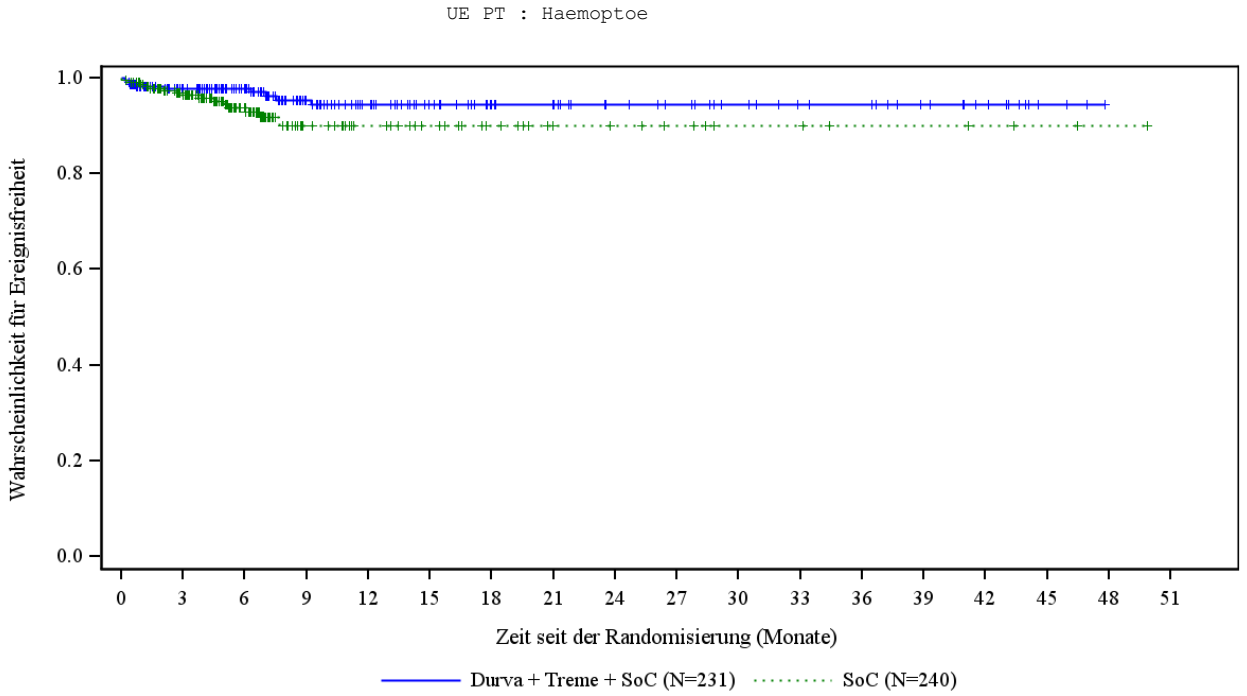
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



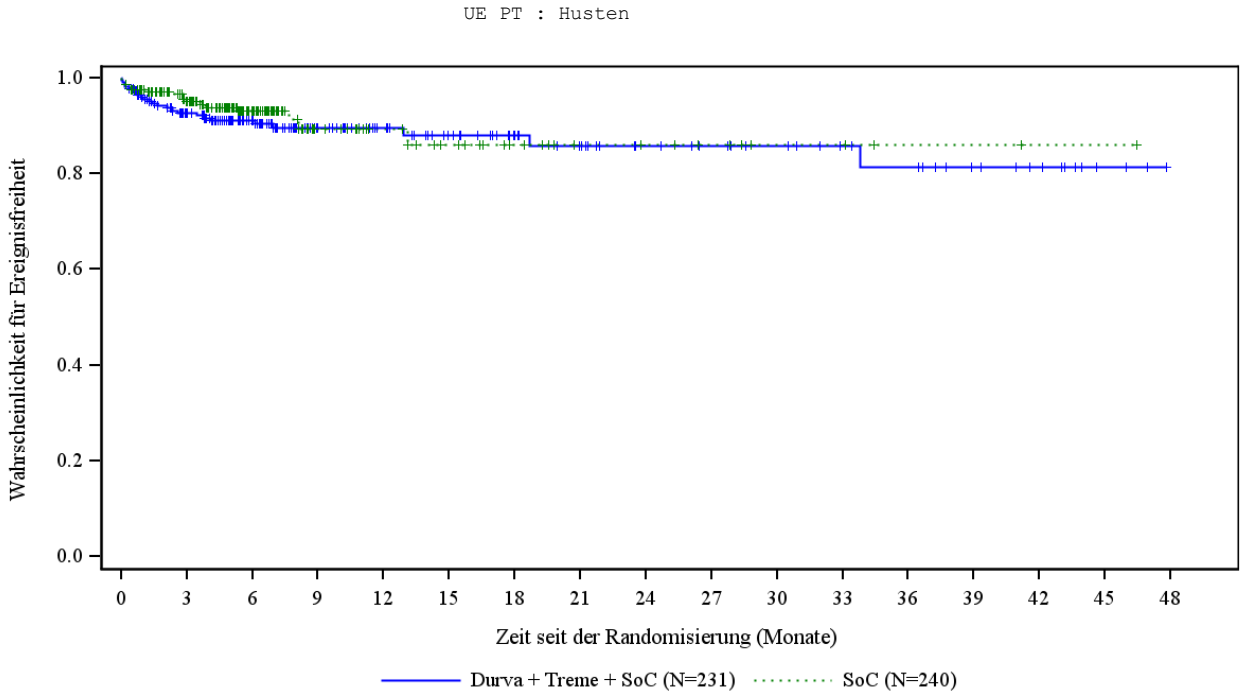
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	187	142	94	71	55	43	40	33	30	25	21	20	14	10	3	0	0
SoC	240	183	106	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



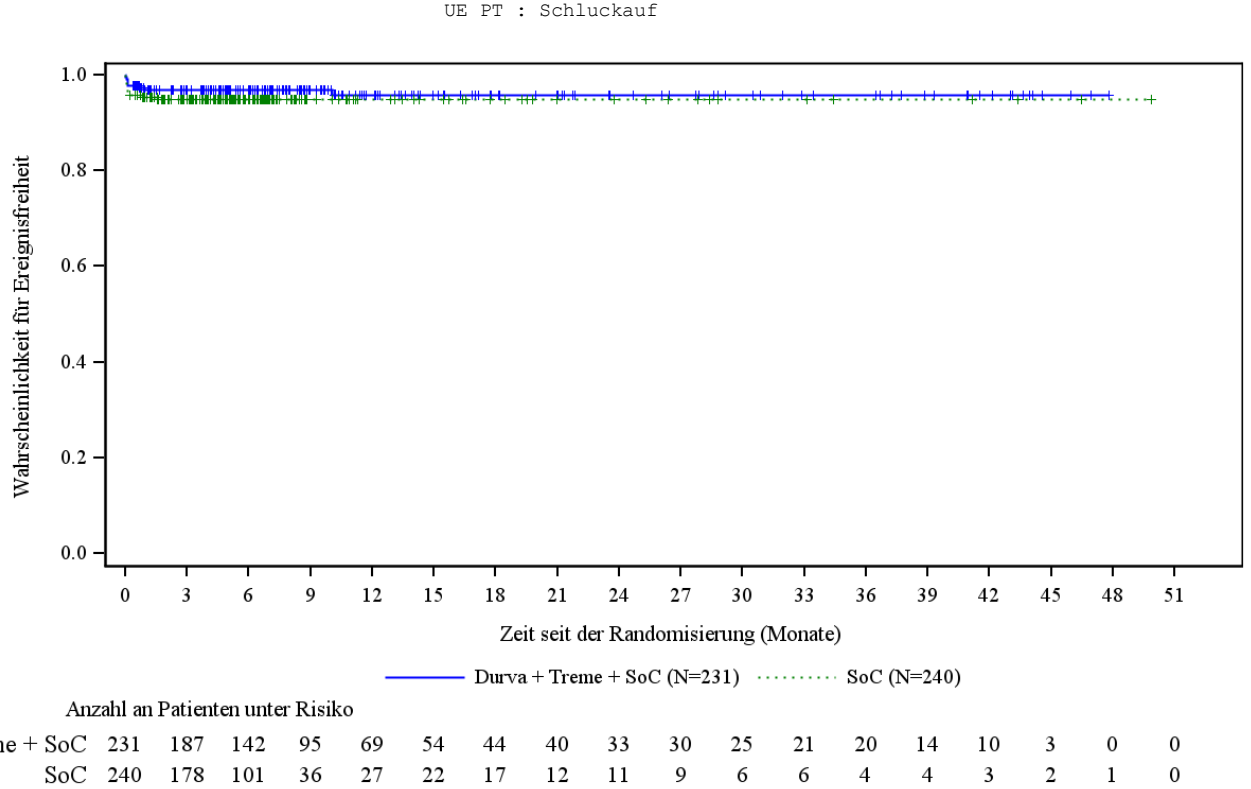
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	177	132	86	66	54	42	37	30	27	24	20	18	13	9	3	0
SoC	240	180	101	36	27	21	15	10	9	7	4	4	2	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

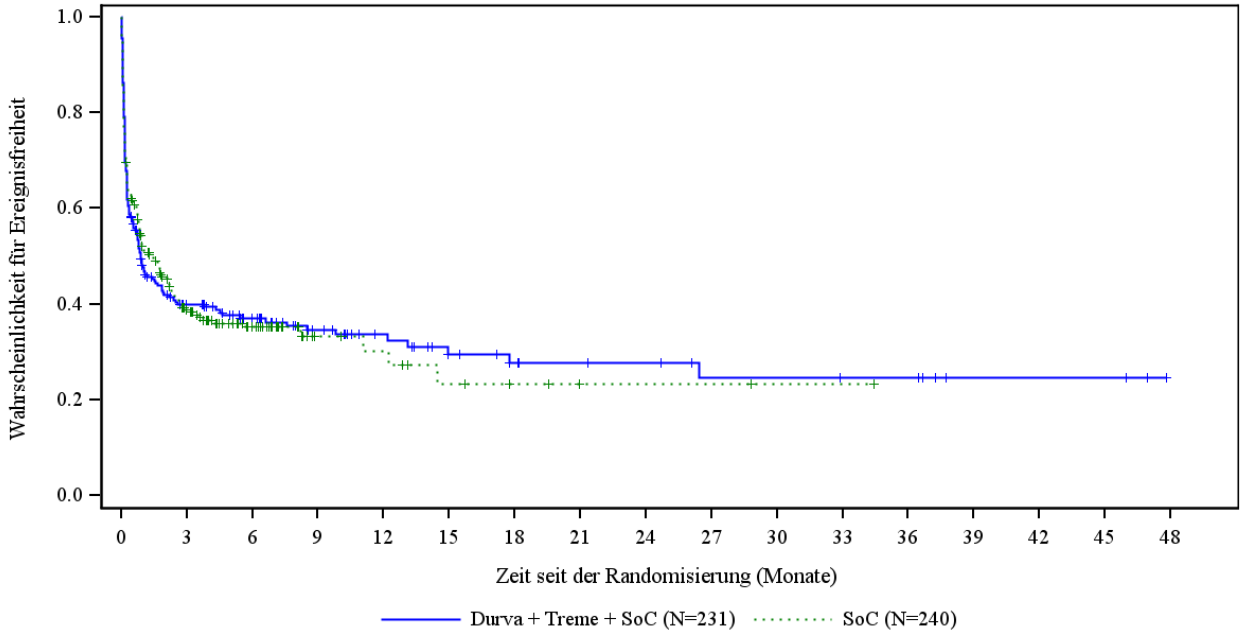


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen des Gastrointestinaltrakts



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	74	55	38	26	18	14	12	11	8	8	7	7	3	3	3	0
SoC	240	74	39	12	10	6	4	2	2	2	1	1	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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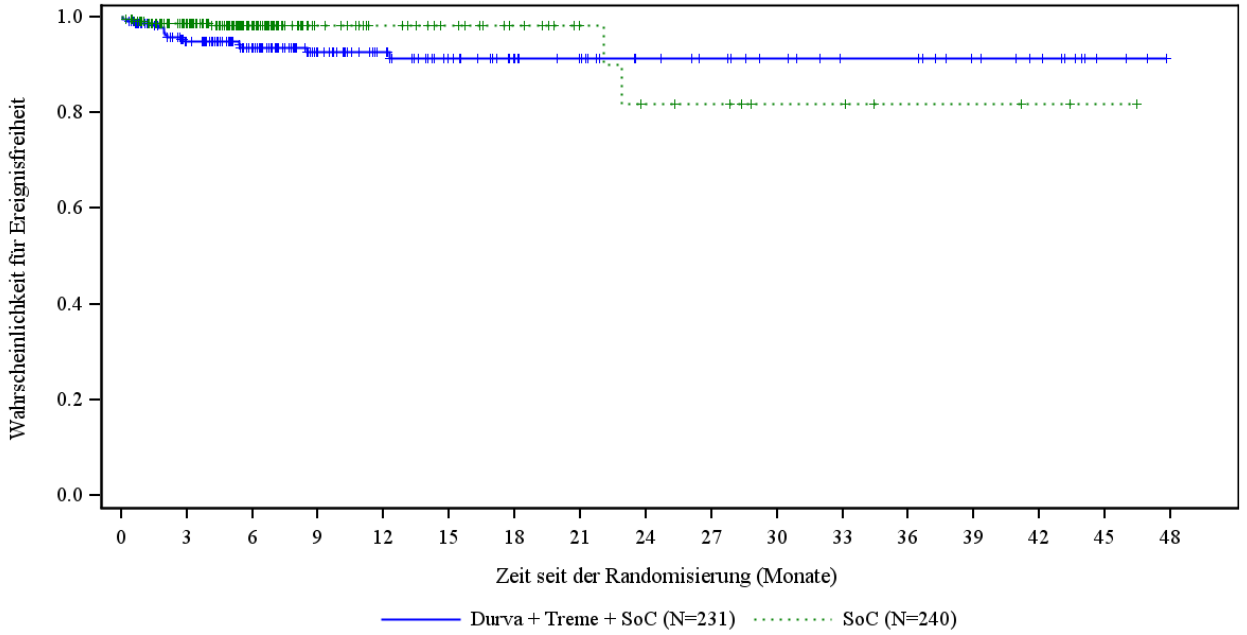
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Abdominalschmerz



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	183	140	92	69	54	42	38	31	28	24	20	20	14	10	3	0
SoC	240	186	107	38	30	24	18	12	9	8	5	5	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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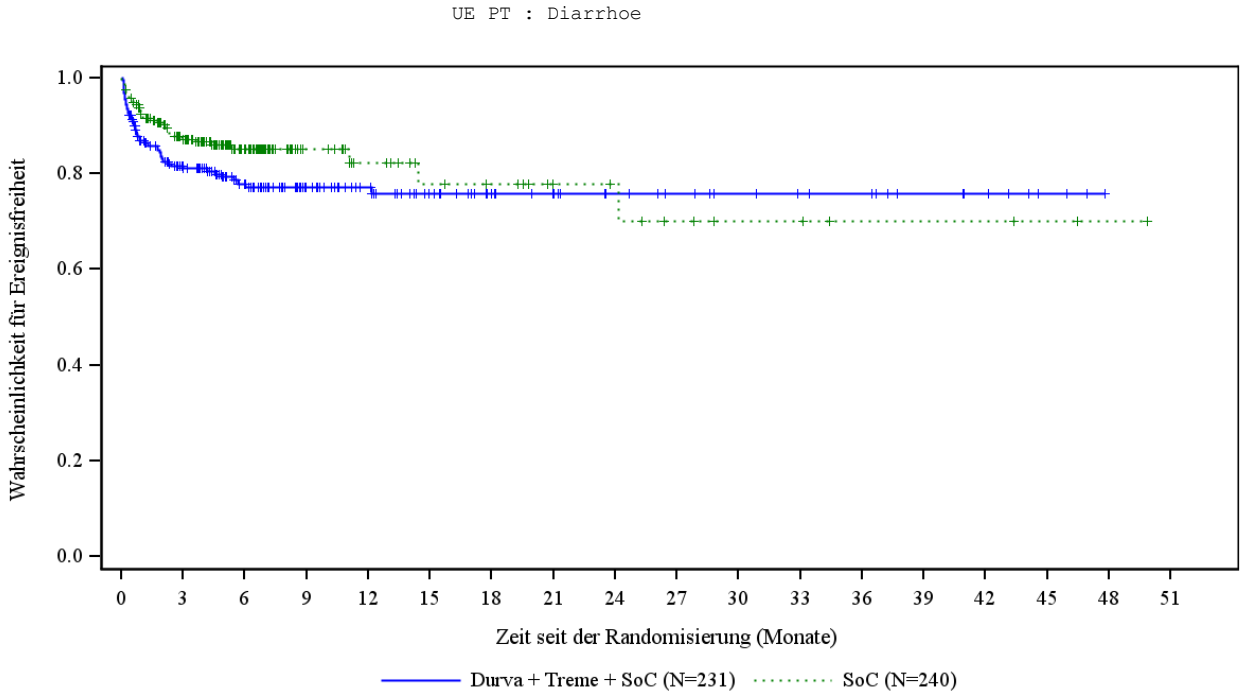
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



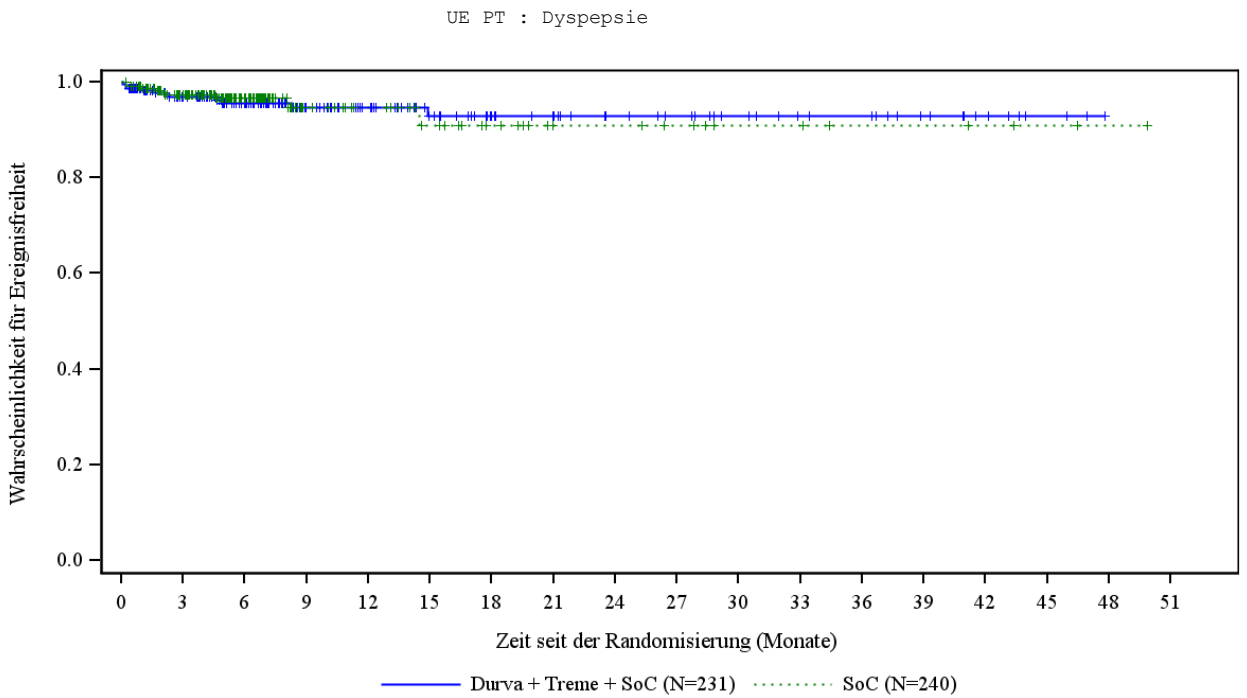
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	156	111	76	56	42	32	28	23	20	17	15	14	9	7	3	0	0
SoC	240	165	93	33	24	18	16	11	10	7	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

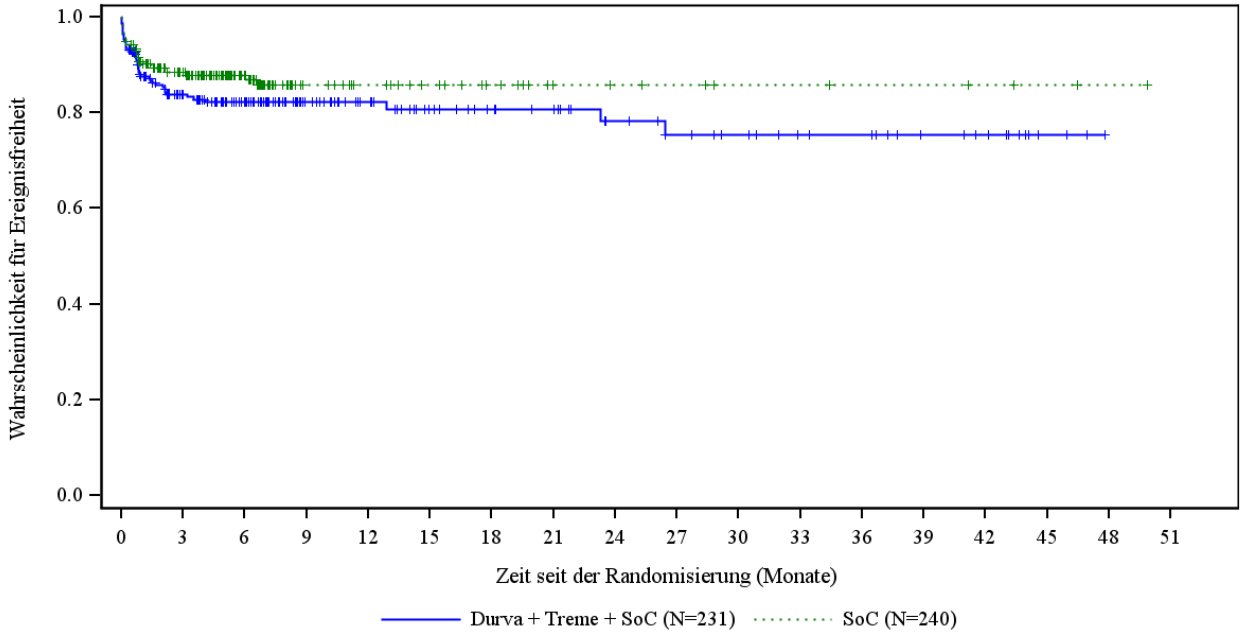


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Erbrechen



Anzahl an Patienten unter Risiko

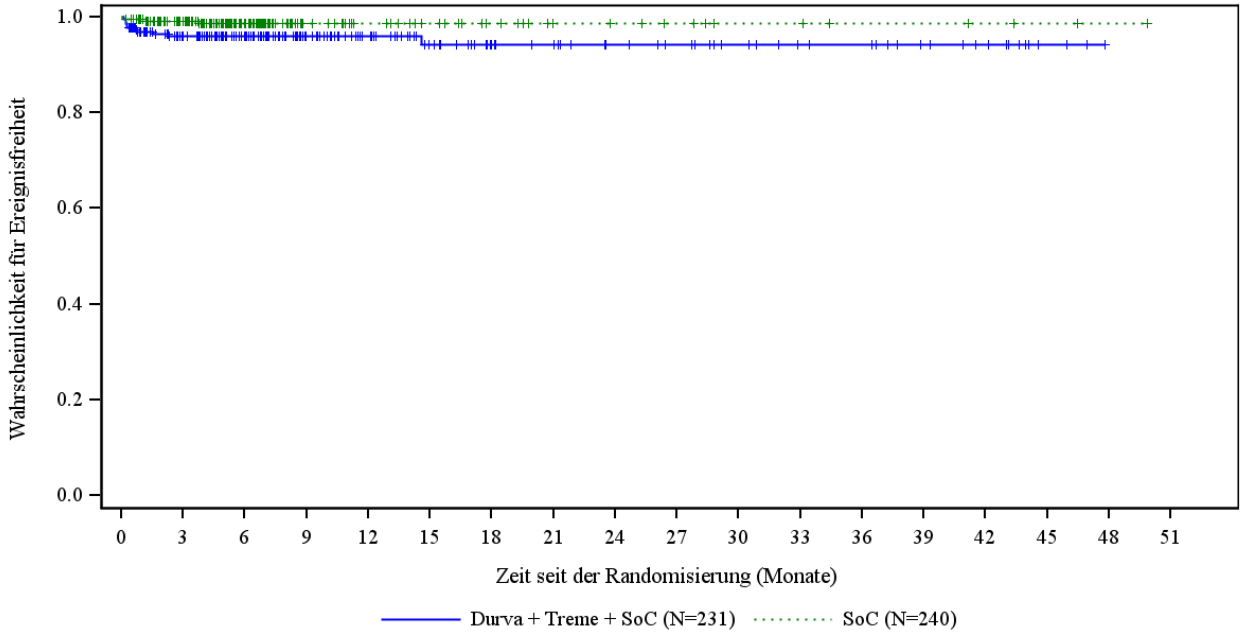
Durva + Treme + SoC	231	159	124	80	61	47	40	37	29	25	22	18	17	12	10	3	0	0
SoC	240	167	91	31	25	20	15	9	8	7	5	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Gastrooesophageale Refluxerkrankung



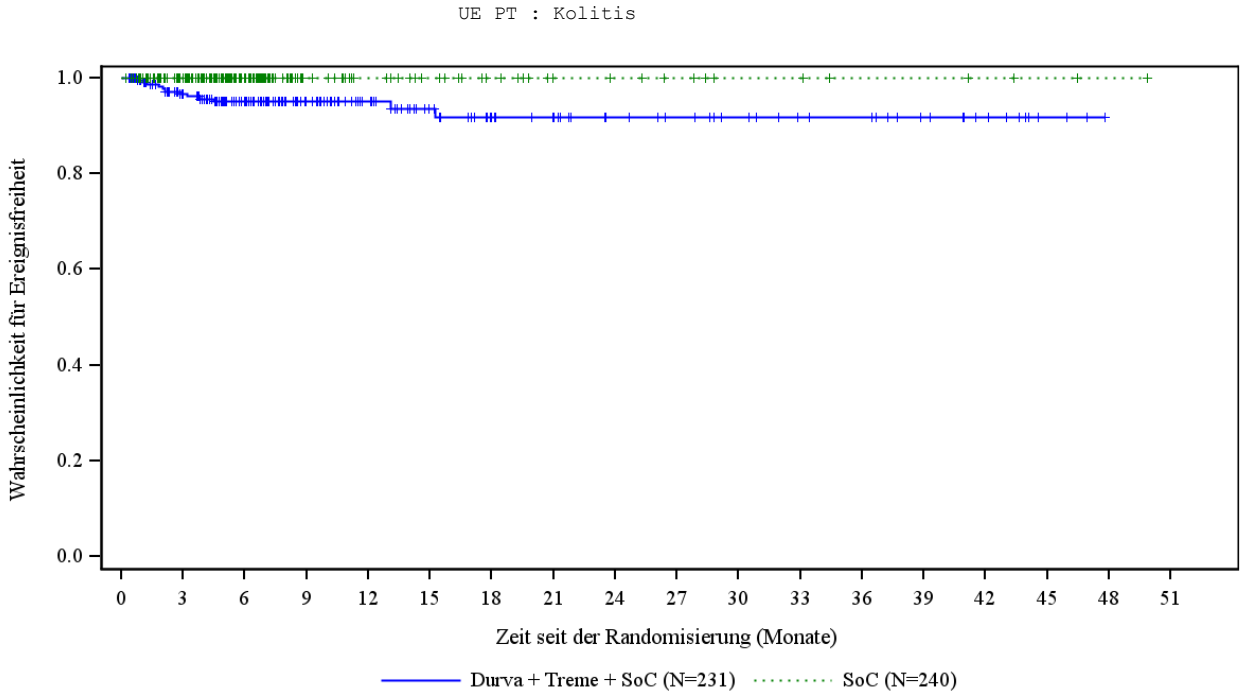
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	183	140	93	69	52	41	38	32	29	24	20	19	13	10	3	0	0
SoC	240	187	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

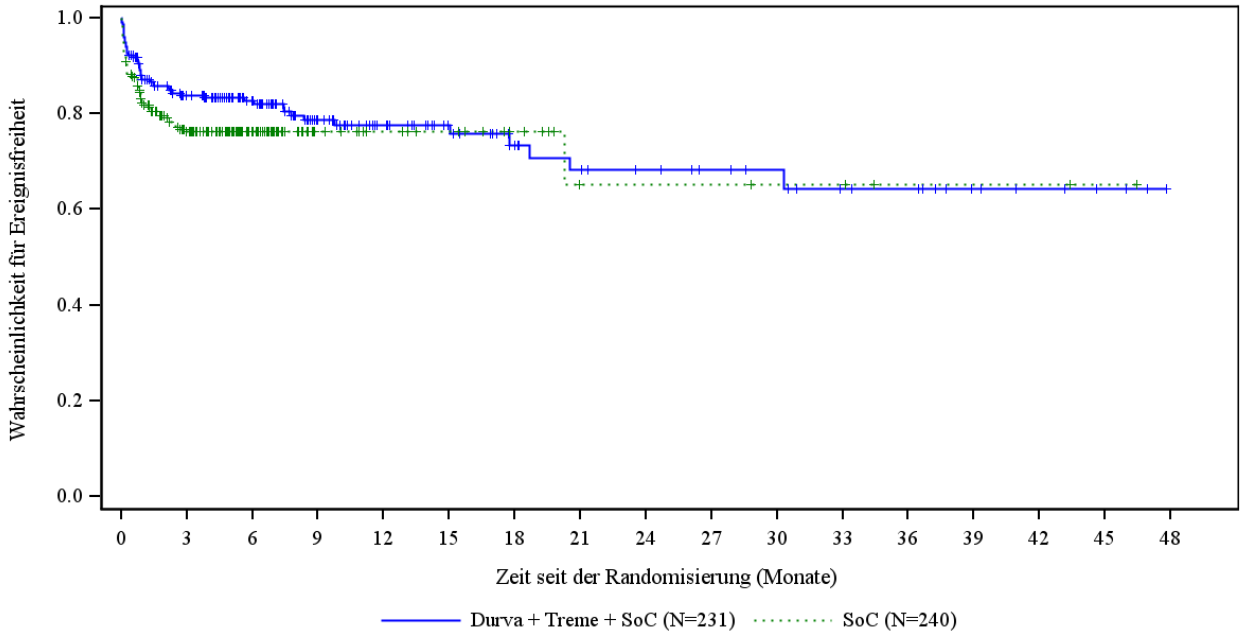
Durva + Treme + SoC	231	186	140	96	71	54	42	38	31	28	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Obstipation



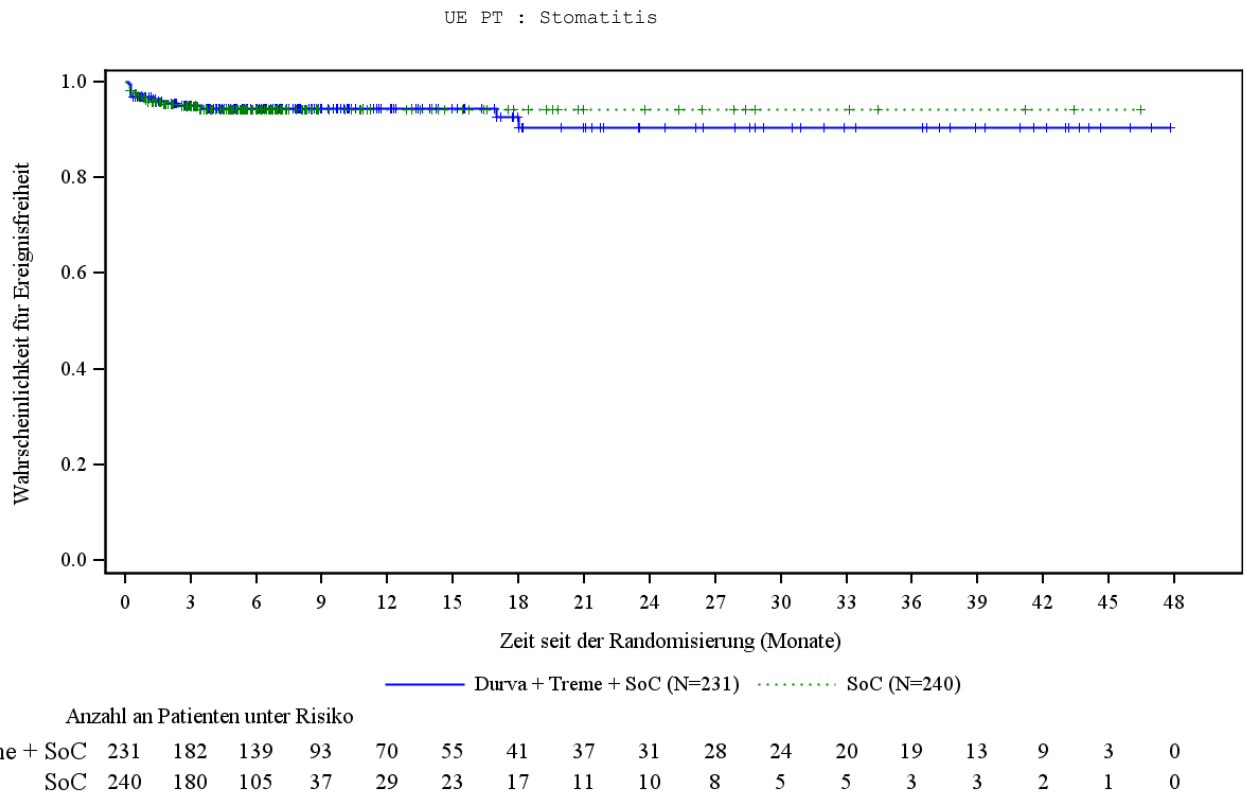
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	160	124	79	55	41	30	26	23	20	18	14	13	7	5	3	0
SoC	240	141	80	25	19	16	11	5	5	5	4	4	2	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

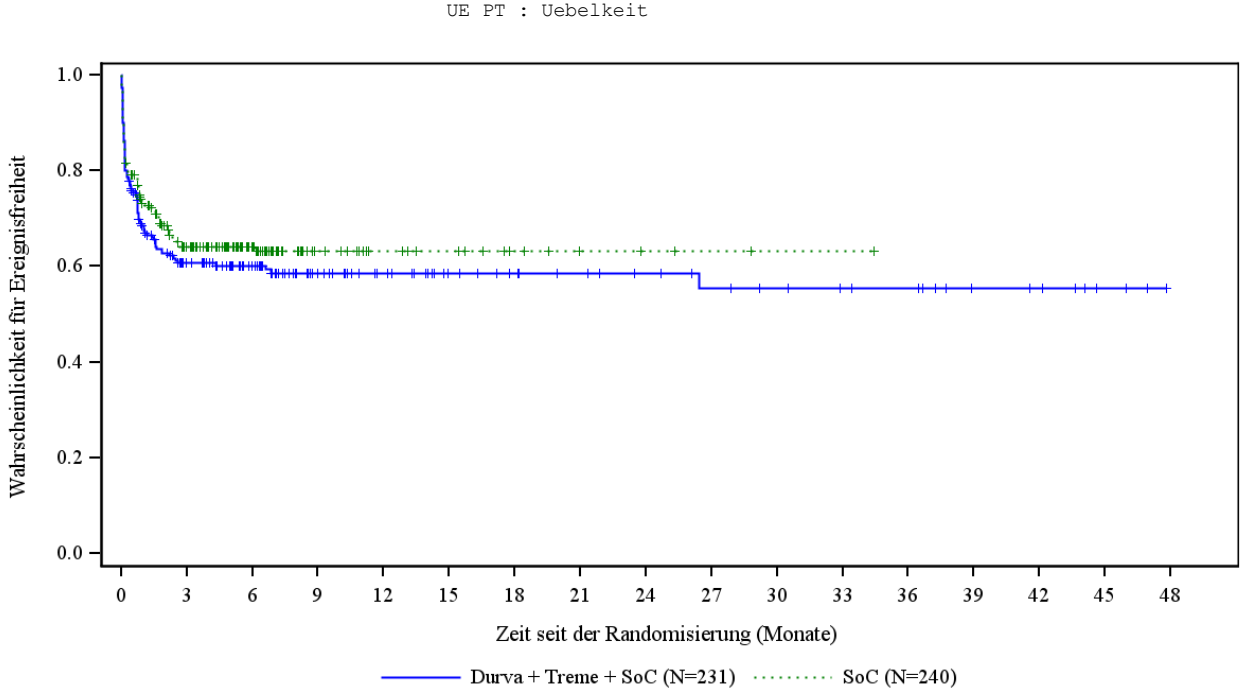
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

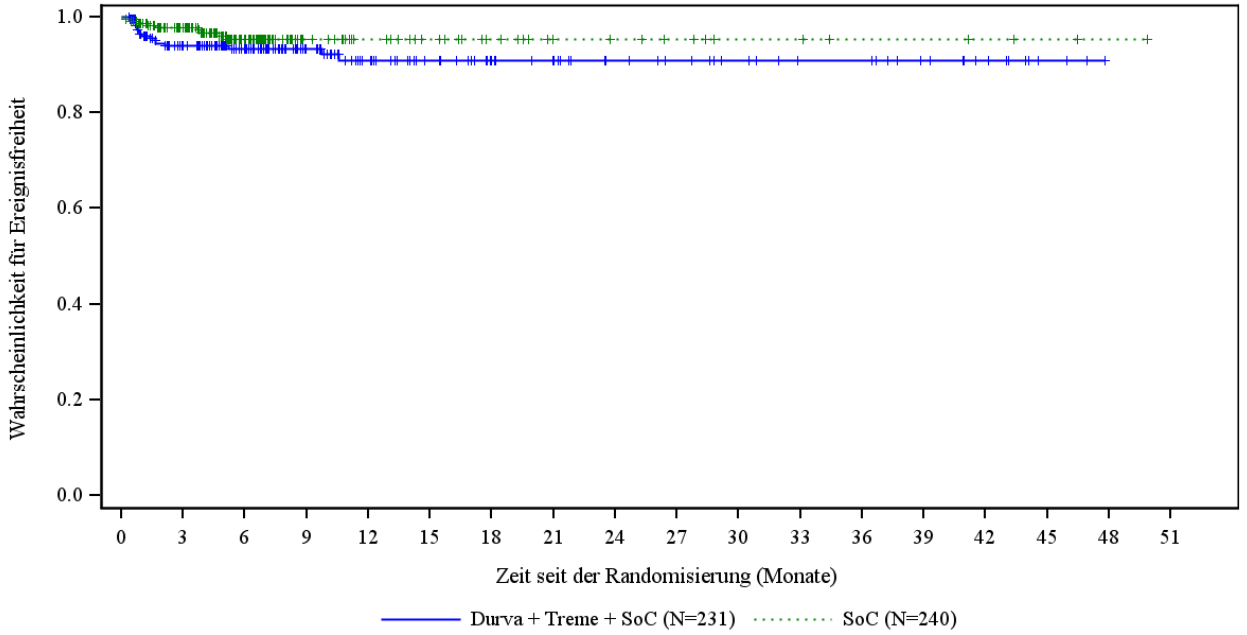


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Leber- und Gallenerkrankungen



Anzahl an Patienten unter Risiko

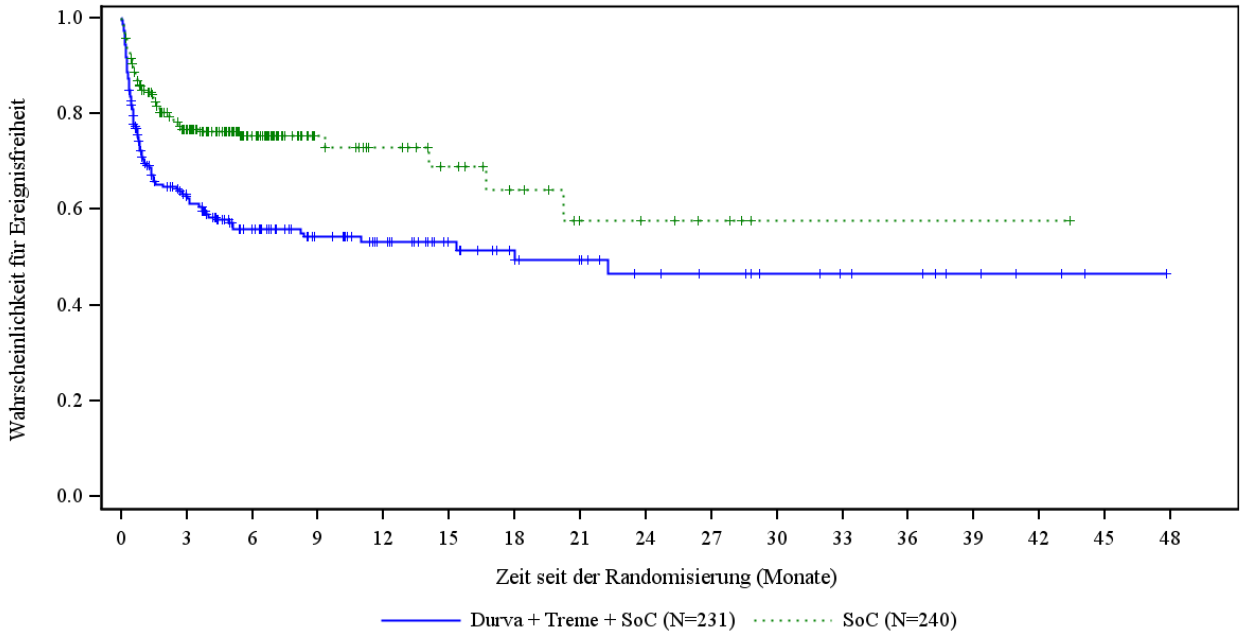
Durva + Treme + SoC	231	182	135	89	65	52	41	37	30	27	23	19	19	13	9	3	0	0
SoC	240	184	104	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen der Haut und des Unterhautgewebes



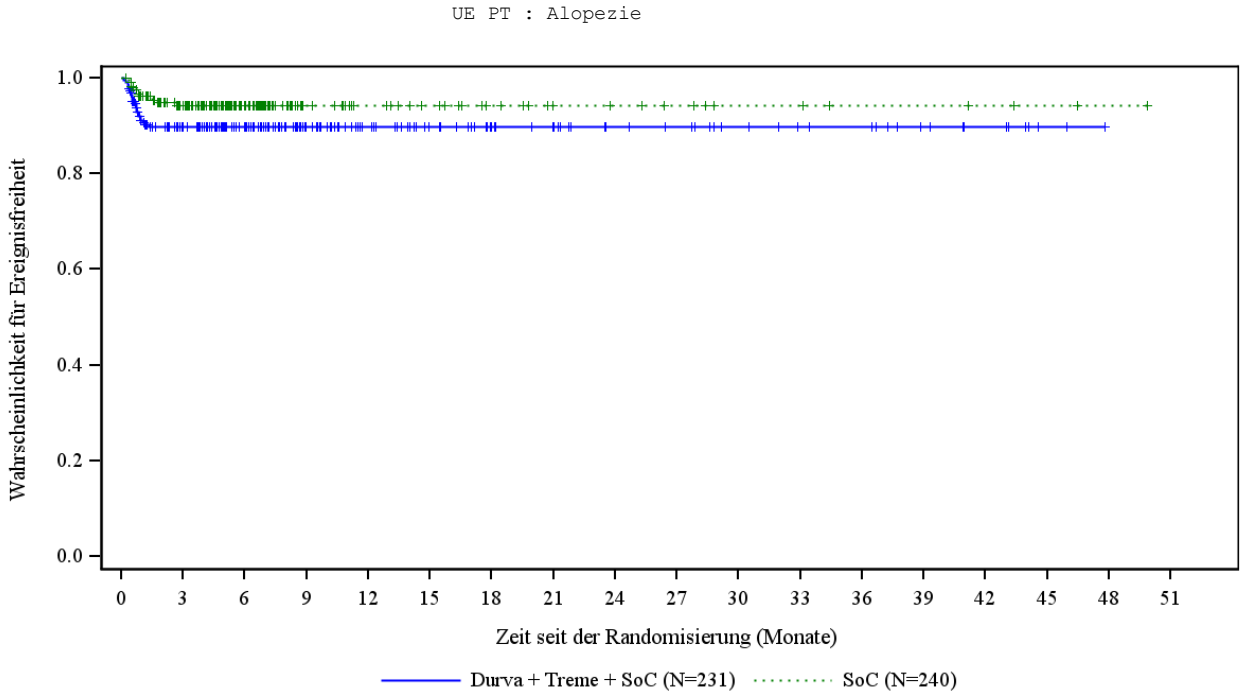
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	118	82	59	44	32	23	21	16	14	11	9	8	5	3	1	0
SoC	240	141	78	30	23	17	12	7	6	4	1	1	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

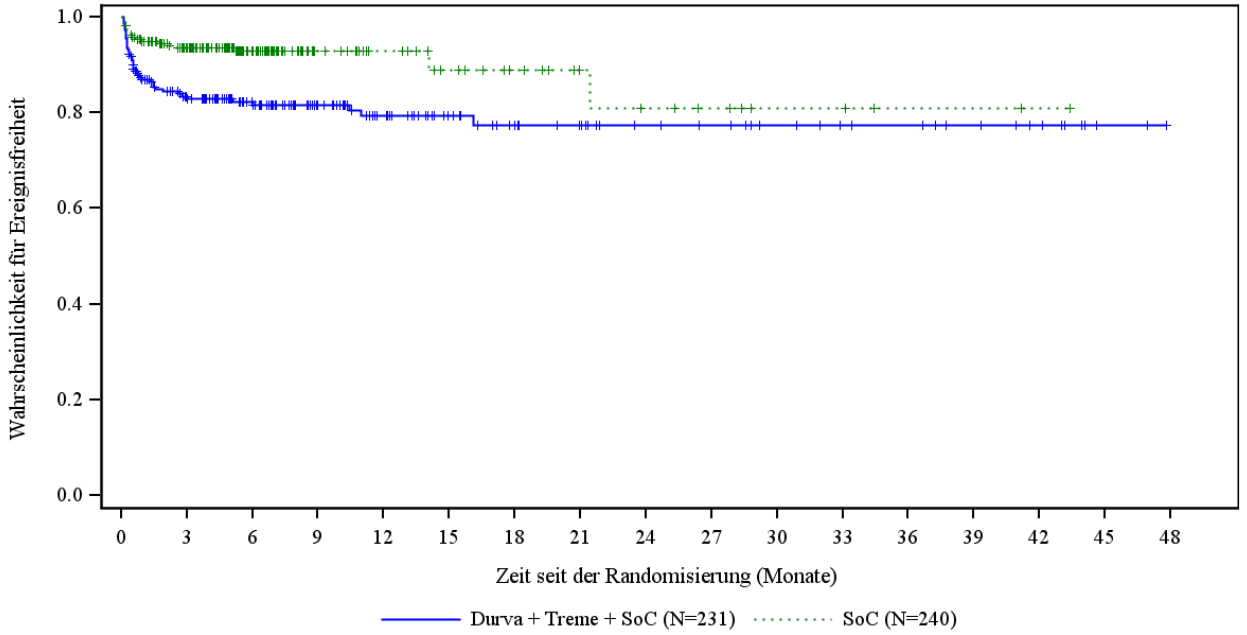
Durva + Treme + SoC	231	170	128	85	62	48	38	34	27	25	20	17	16	10	7	2	0	0
SoC	240	176	99	36	28	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Ausschlag



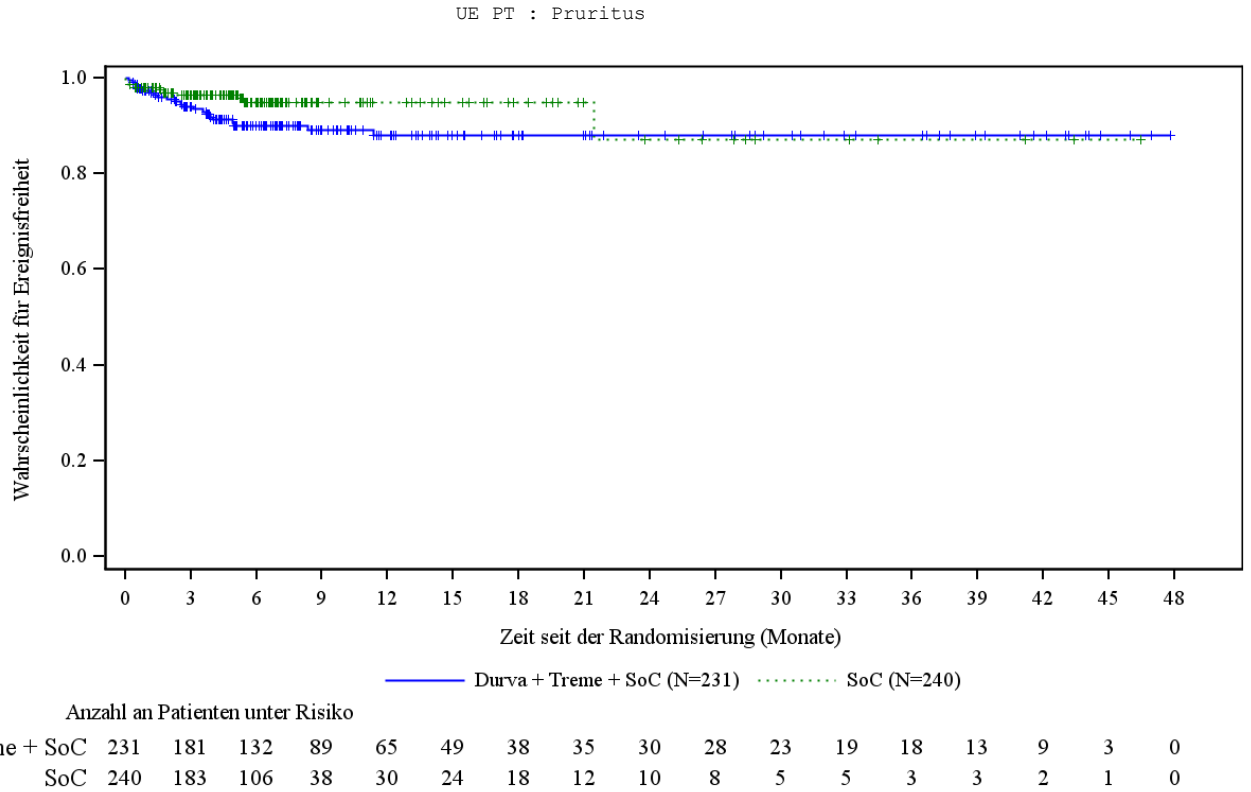
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	160	122	84	61	46	36	32	26	24	20	17	16	12	8	2	0
SoC	240	178	104	37	28	21	16	11	9	7	4	4	2	2	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

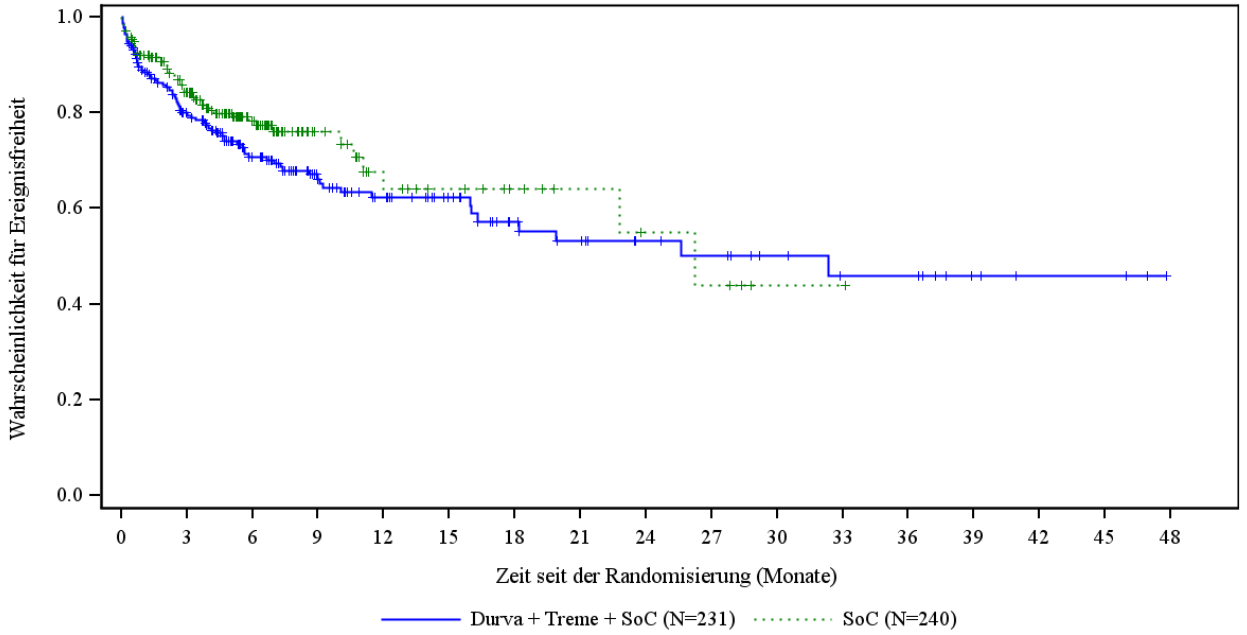


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen



Anzahl an Patienten unter Risiko

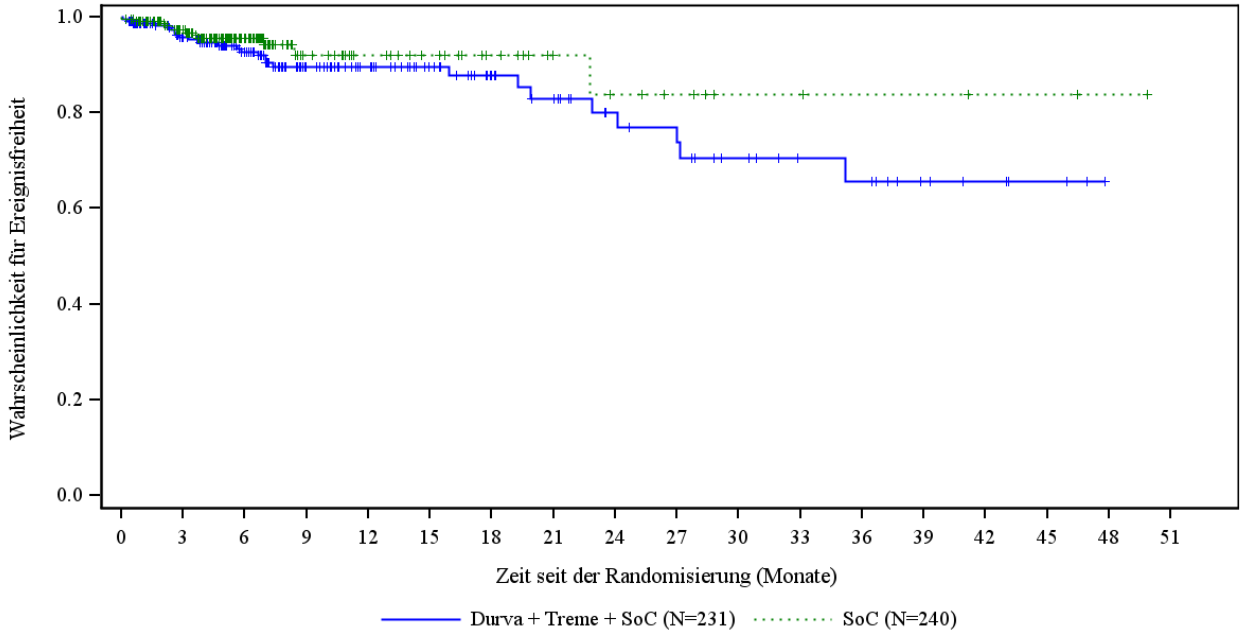
Durva + Treme + SoC	231	157	108	72	53	41	29	24	19	17	13	10	10	5	3	3	0
SoC	240	162	87	31	18	14	10	7	5	4	1	1	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Arthralgie



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	185	135	87	66	52	39	34	26	24	18	14	13	7	5	3	0	0
SoC	240	184	105	37	28	23	17	11	9	7	4	4	3	3	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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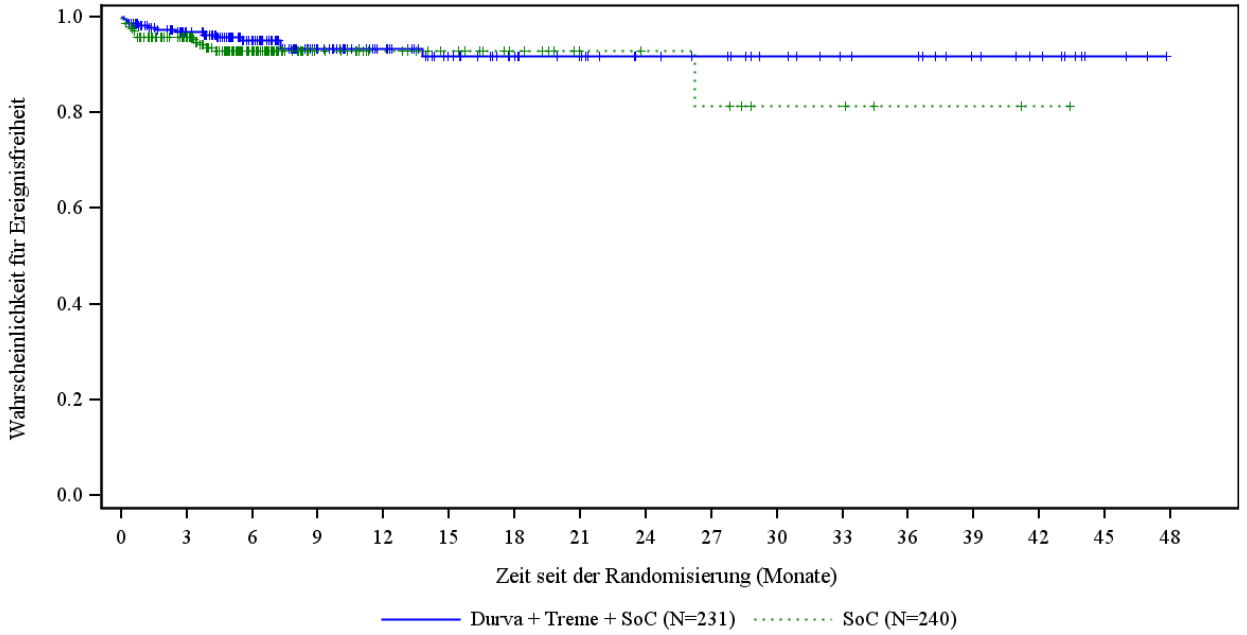
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Brustschmerzen die Skelettmuskulatur betreffend



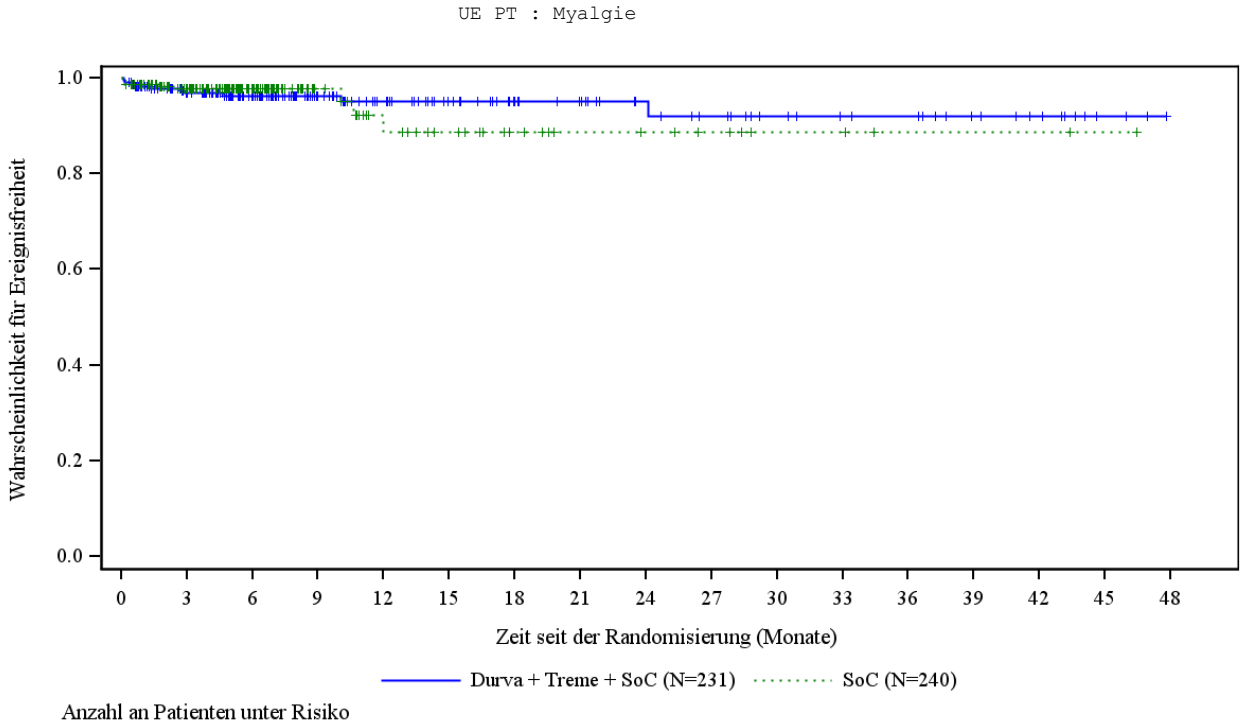
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	141	94	69	52	41	37	31	29	24	20	19	13	9	3	0
SoC	240	183	102	35	26	21	15	9	8	7	4	4	2	2	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

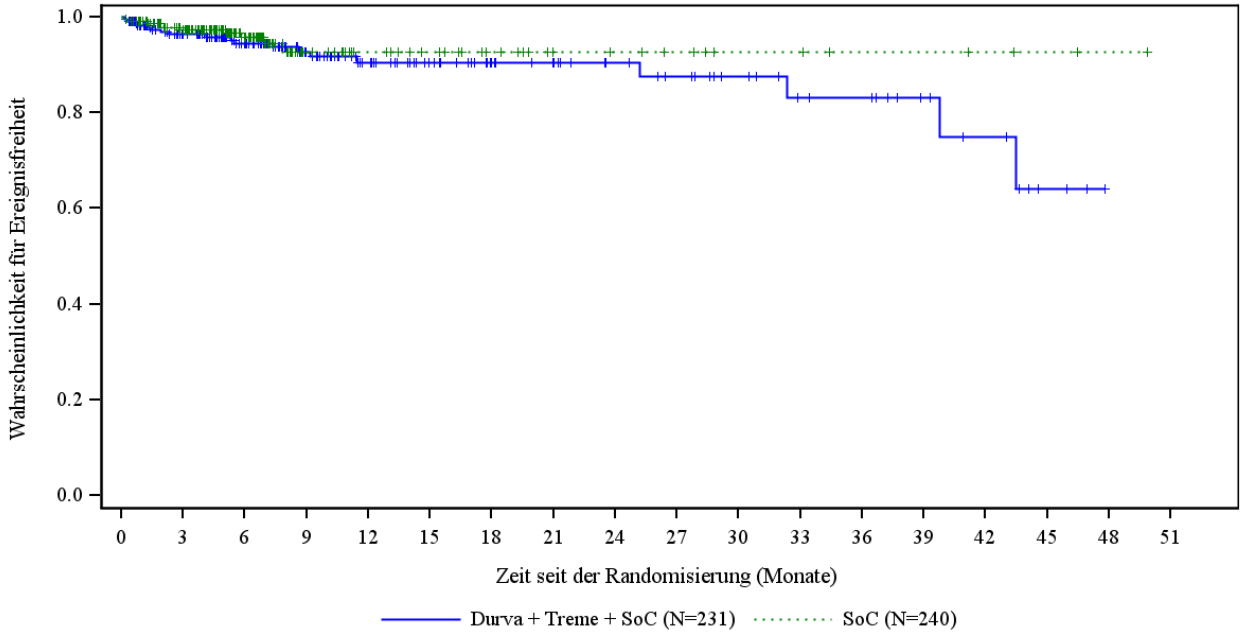
Durva + Treme + SoC	231	187	141	94	70	55	43	39	32	28	23	20	19	13	9	3	0
SoC	240	185	107	37	25	20	14	10	9	7	4	4	2	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Rueckenschmerzen



Anzahl an Patienten unter Risiko

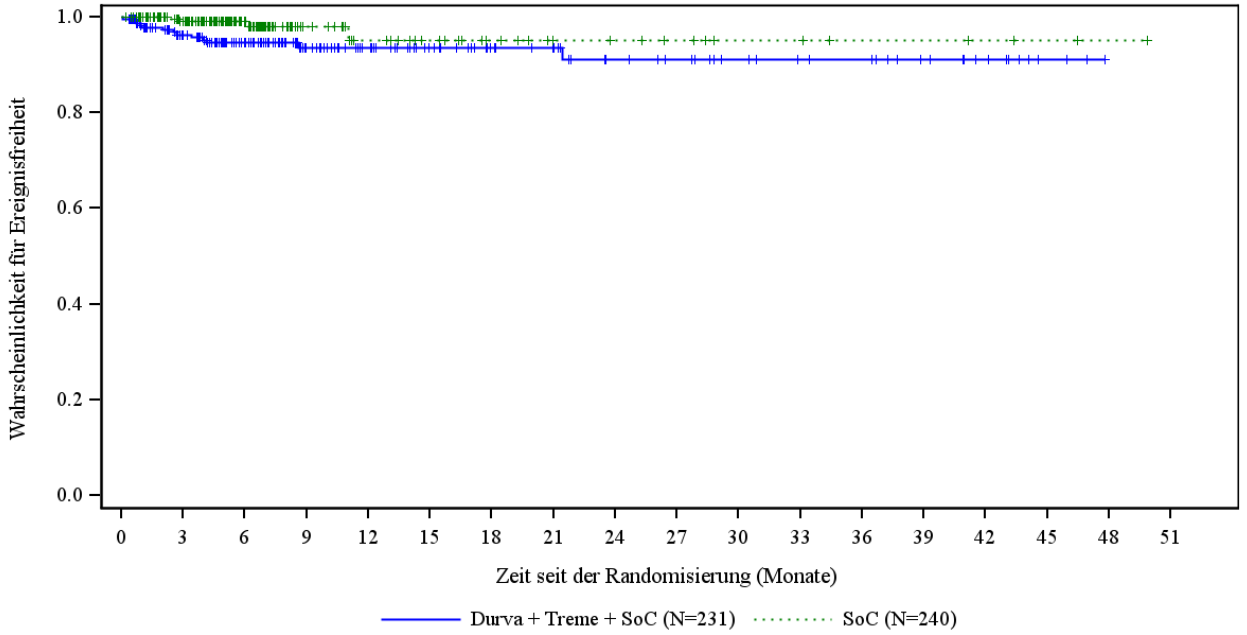
Durva + Treme + SoC	231	187	139	94	69	54	42	38	32	28	23	18	17	11	8	3	0	0
SoC	240	185	106	38	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Schmerz in einer Extremitaet



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	184	137	91	69	54	43	39	31	28	23	20	19	13	9	3	0	0
SoC	240	187	109	39	29	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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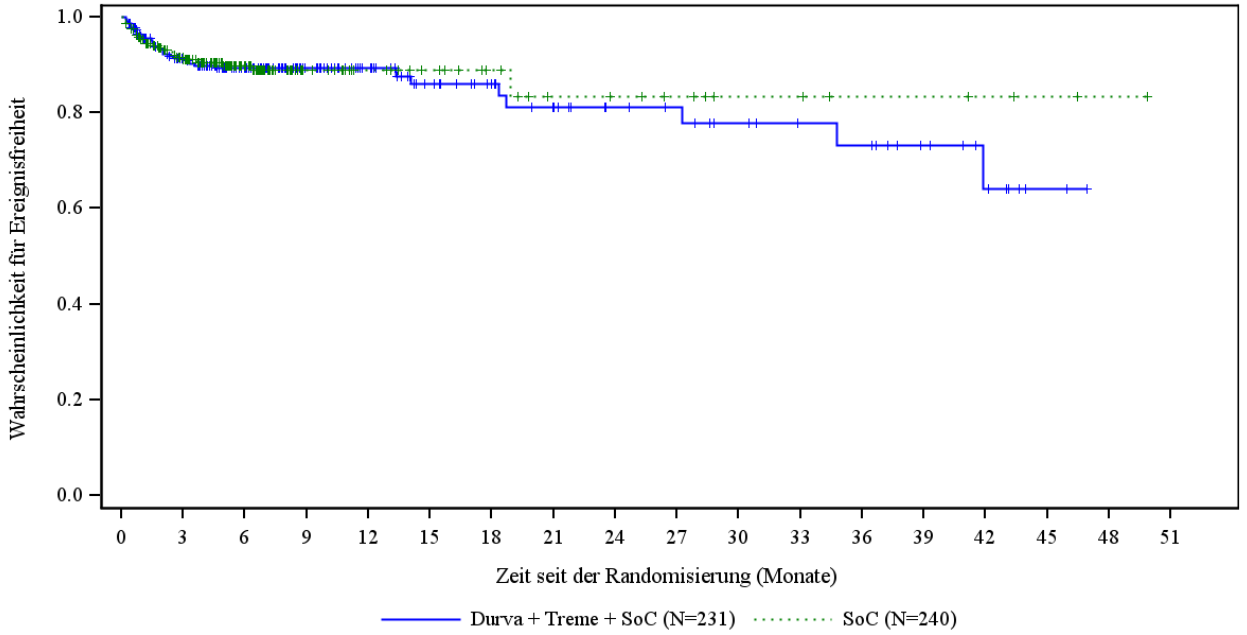
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Erkrankungen der Nieren und Harnwege



Anzahl an Patienten unter Risiko

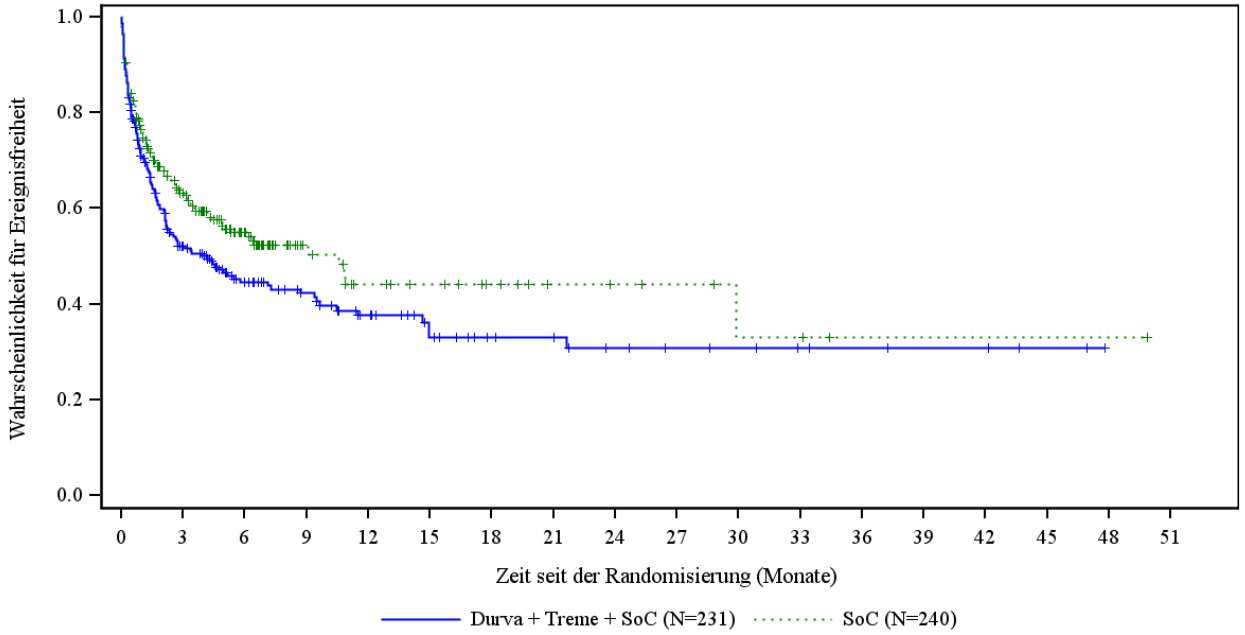
Durva + Treme + SoC	231	181	133	87	64	47	38	32	26	24	20	17	16	11	7	2	0	0
SoC	240	174	101	36	27	22	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Allgemeine Erkrankungen und Beschwerden am Verabreichungsort



Anzahl an Patienten unter Risiko

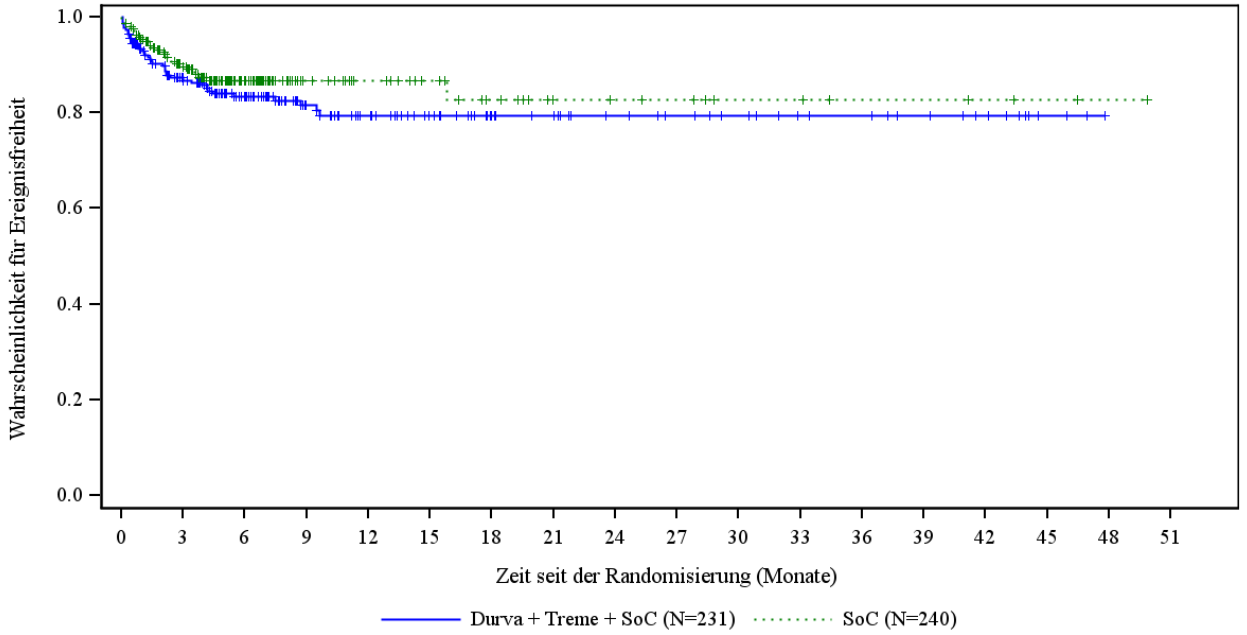
Durva + Treme + SoC	231	101	66	49	33	22	16	15	11	9	8	6	5	4	4	2	0	0
SoC	240	119	65	27	18	15	11	7	6	5	3	3	1	1	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Asthenie



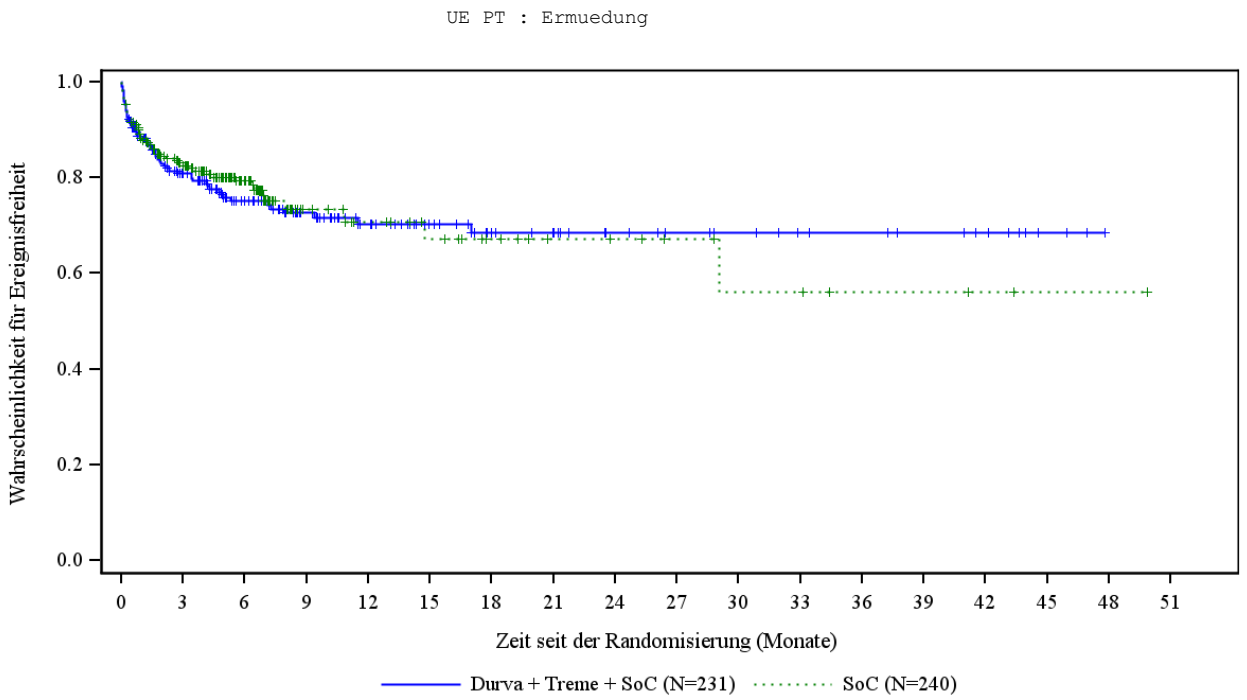
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	170	120	76	59	46	35	32	26	23	20	16	15	12	9	3	0	0
SoC	240	167	98	37	29	23	17	11	10	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



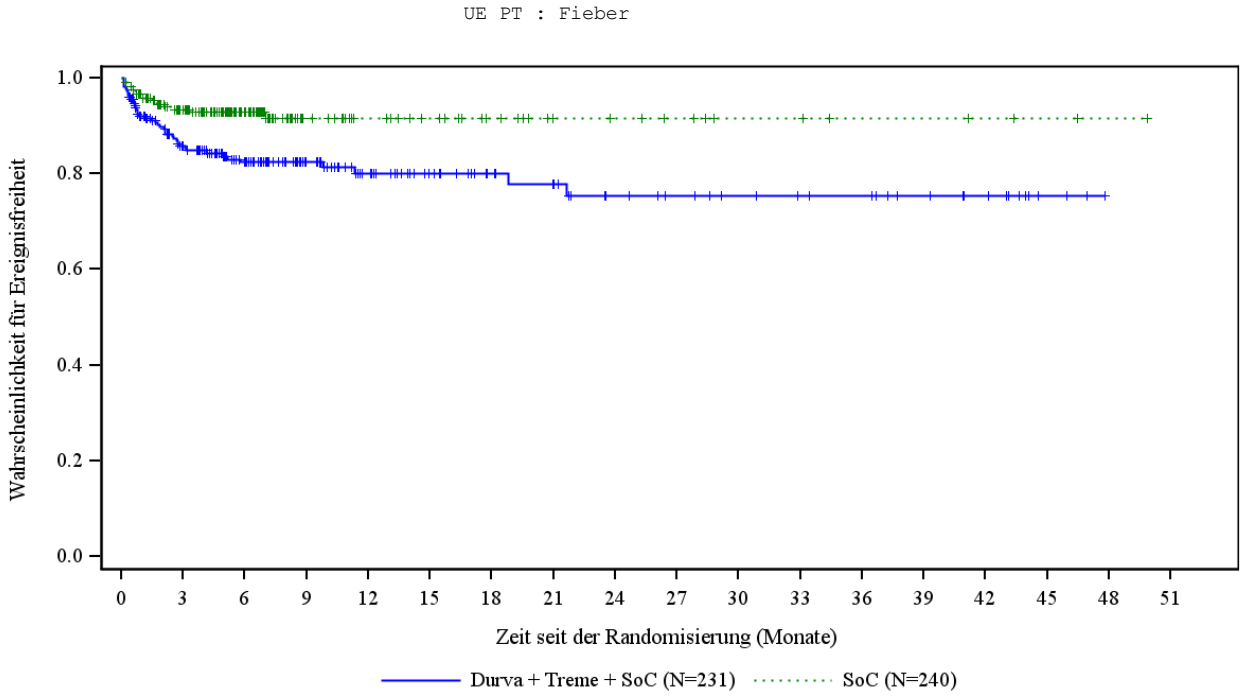
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	153	108	74	54	41	30	27	21	18	16	13	12	10	8	3	0	0
SoC	240	153	91	31	24	19	14	10	9	7	5	5	3	3	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



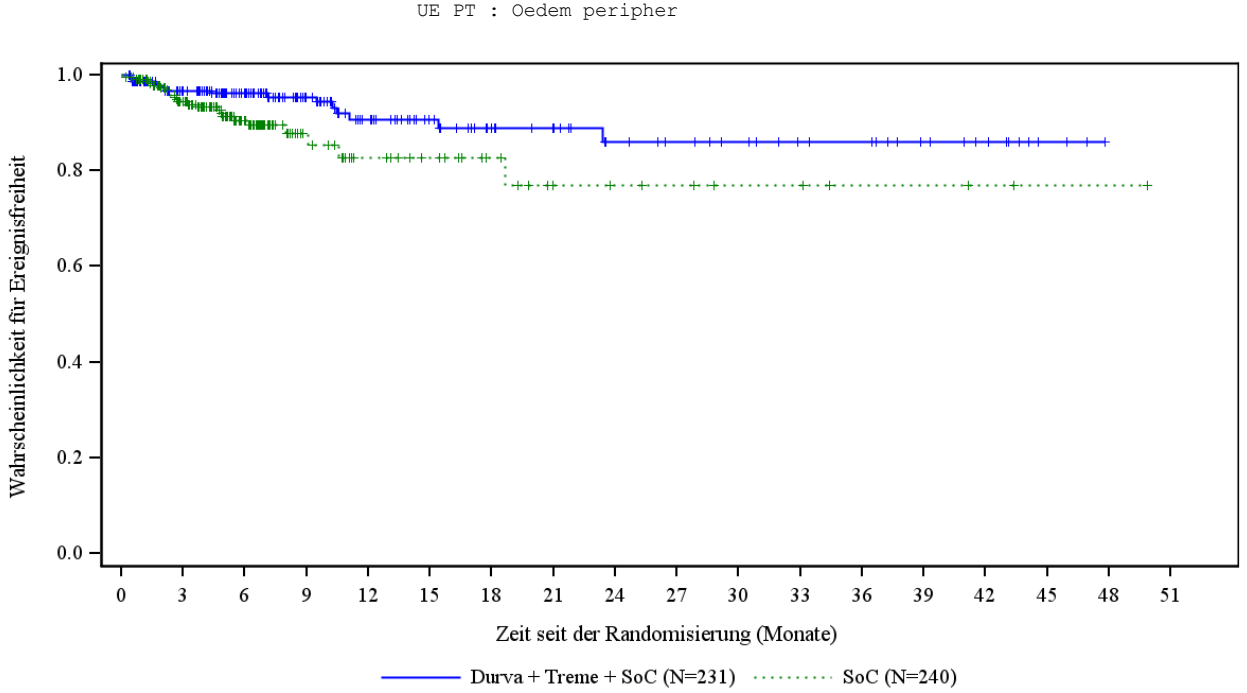
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	168	124	87	62	48	38	34	27	24	21	19	18	13	10	3	0	0
SoC	240	176	107	38	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



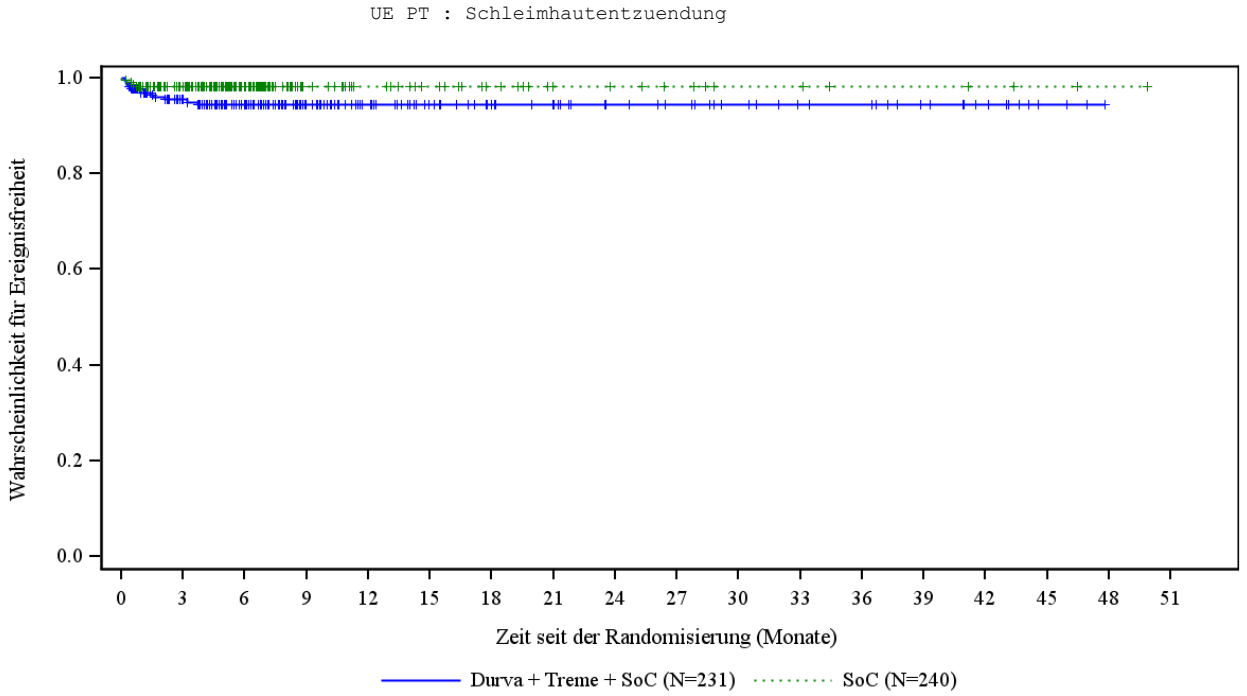
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	140	95	67	51	39	35	28	25	22	18	17	12	9	3	0	0
SoC	240	178	100	37	26	21	15	9	8	7	5	5	3	3	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

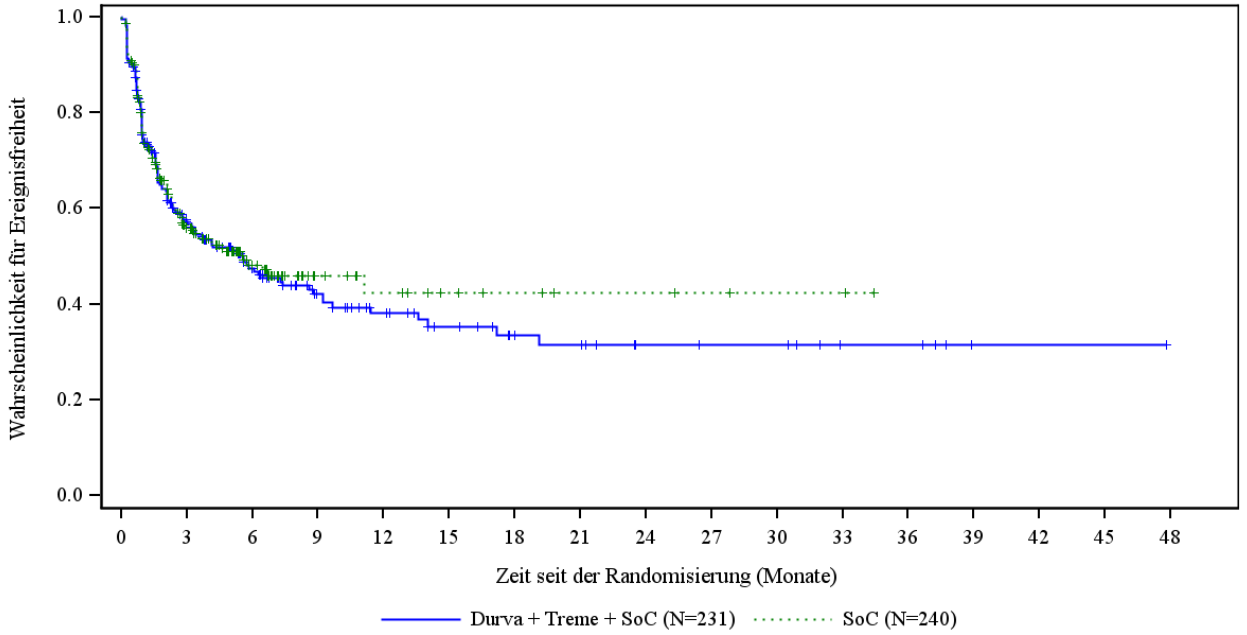


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Untersuchungen



Anzahl an Patienten unter Risiko

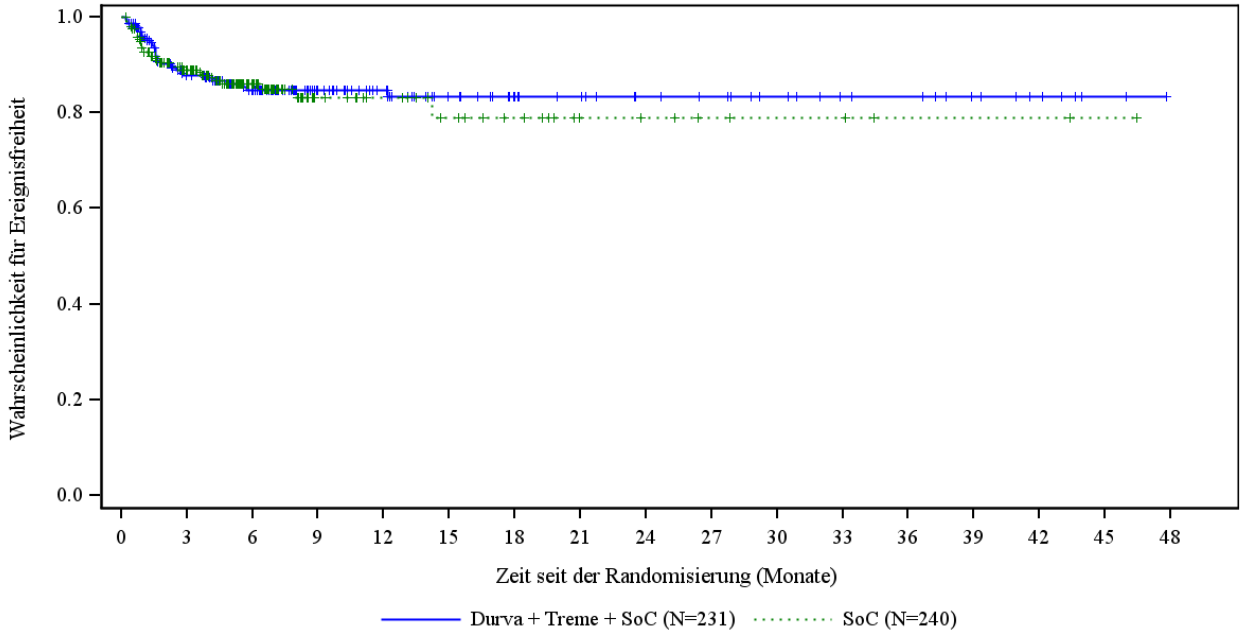
Durva + Treme + SoC	231	110	72	46	31	23	16	15	10	9	9	5	5	1	1	1	0
SoC	240	102	48	17	12	8	6	4	4	3	2	2	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Alaninaminotransferase erhoeht



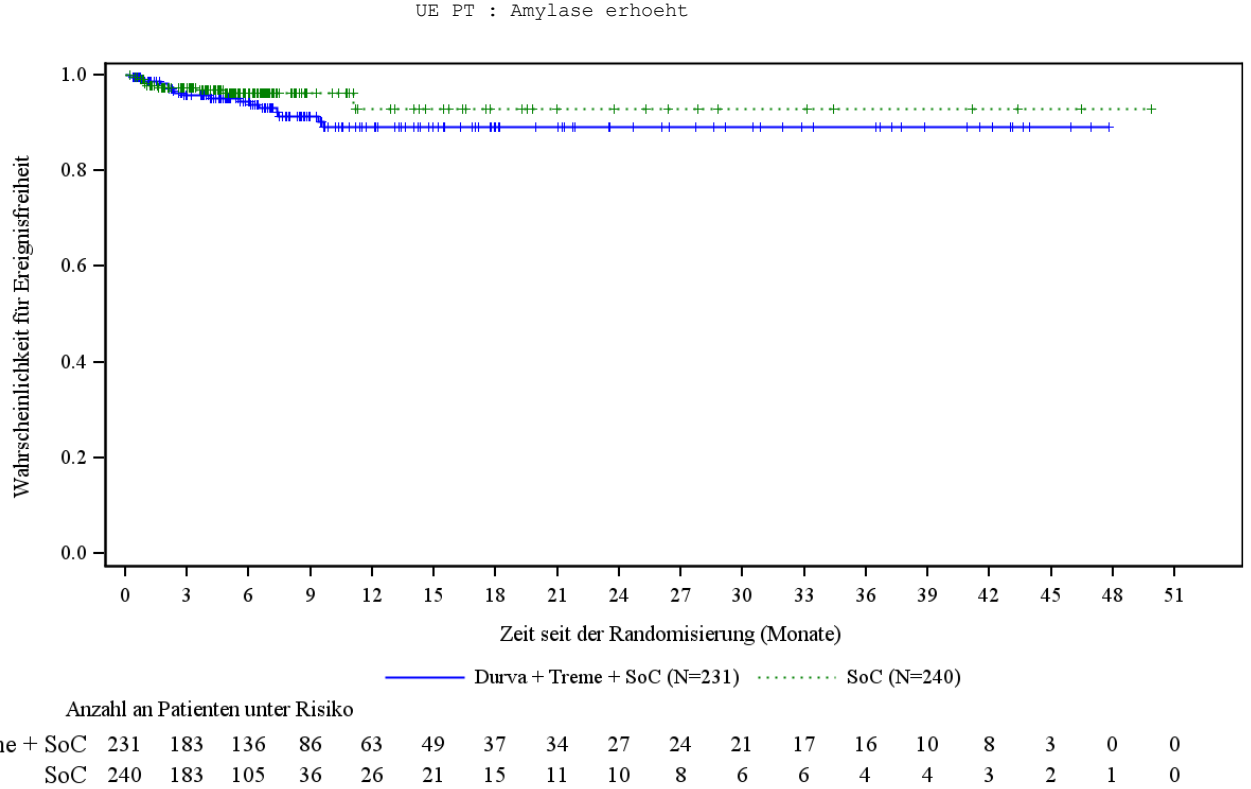
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	168	123	79	59	44	34	31	26	24	20	16	15	10	6	2	0
SoC	240	169	91	30	24	18	14	8	7	5	4	4	2	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

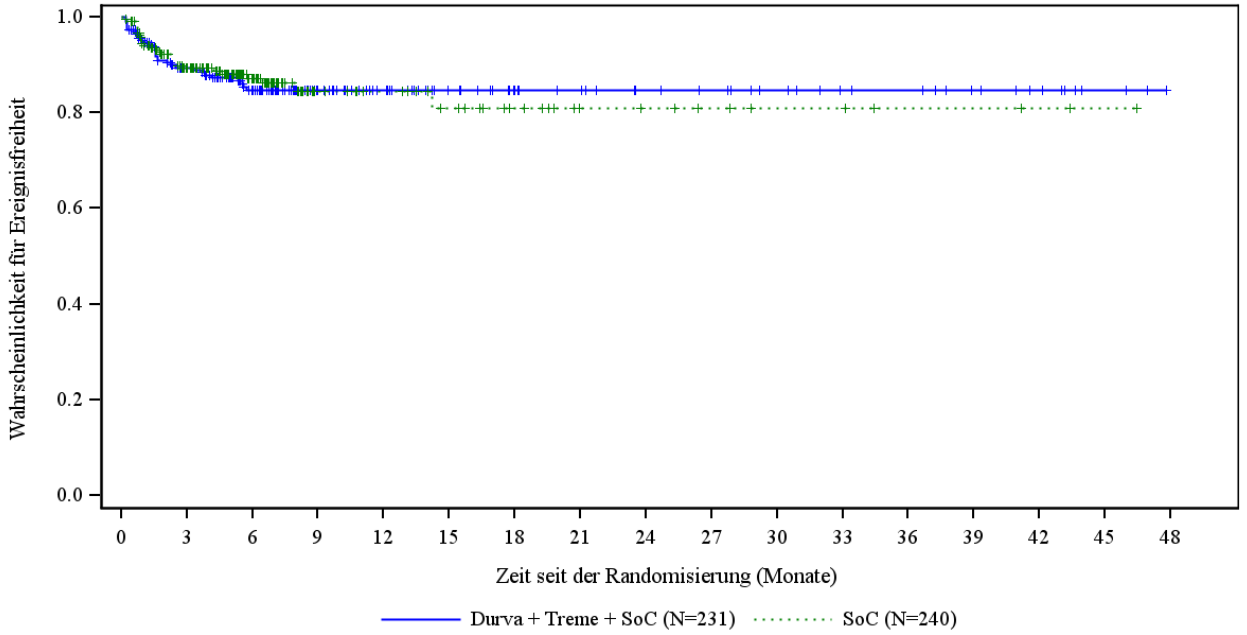


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Aspartataminotransferase erhoeht



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	172	125	81	60	46	36	33	28	26	22	18	17	12	8	3	0
SoC	240	172	94	33	28	22	16	10	9	7	5	5	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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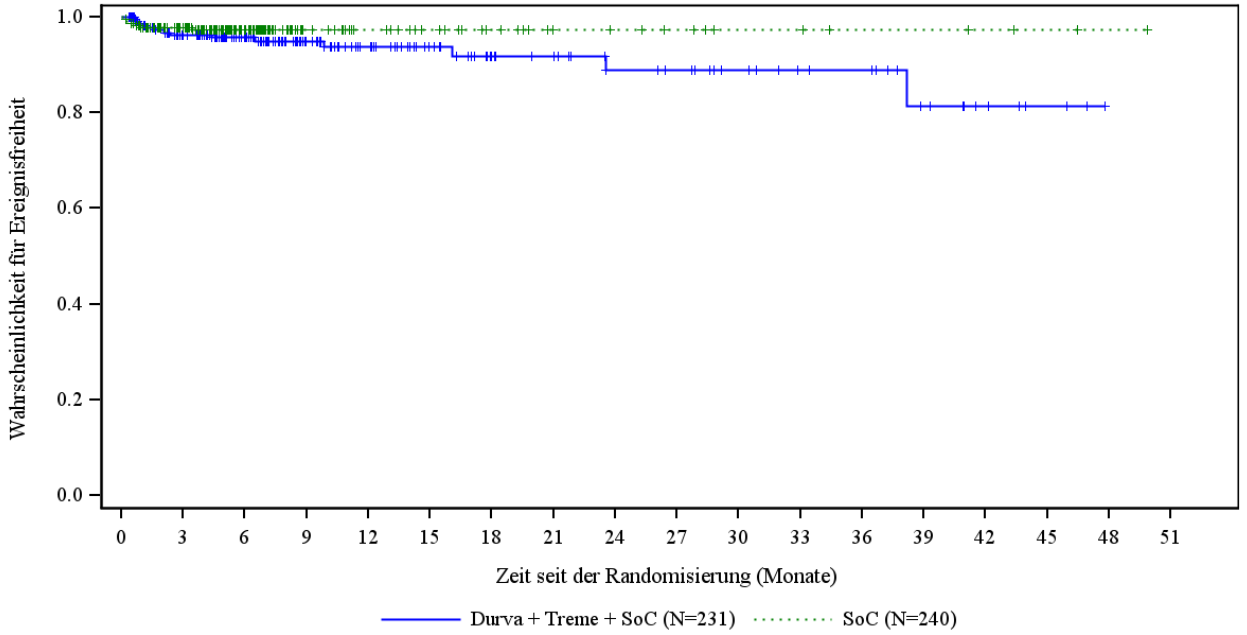
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Gamma-Glutamyltransferase erhoeht



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	185	137	90	67	52	39	36	29	27	22	18	17	10	6	3	0	0
SoC	240	186	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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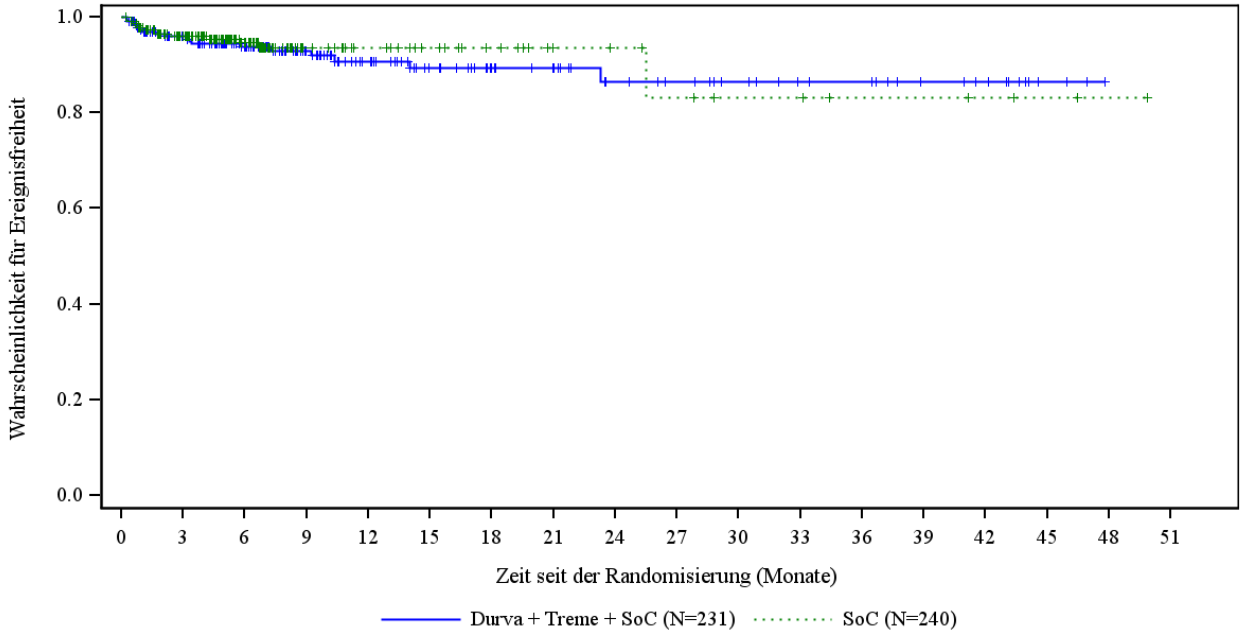
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Gewicht erniedrigt



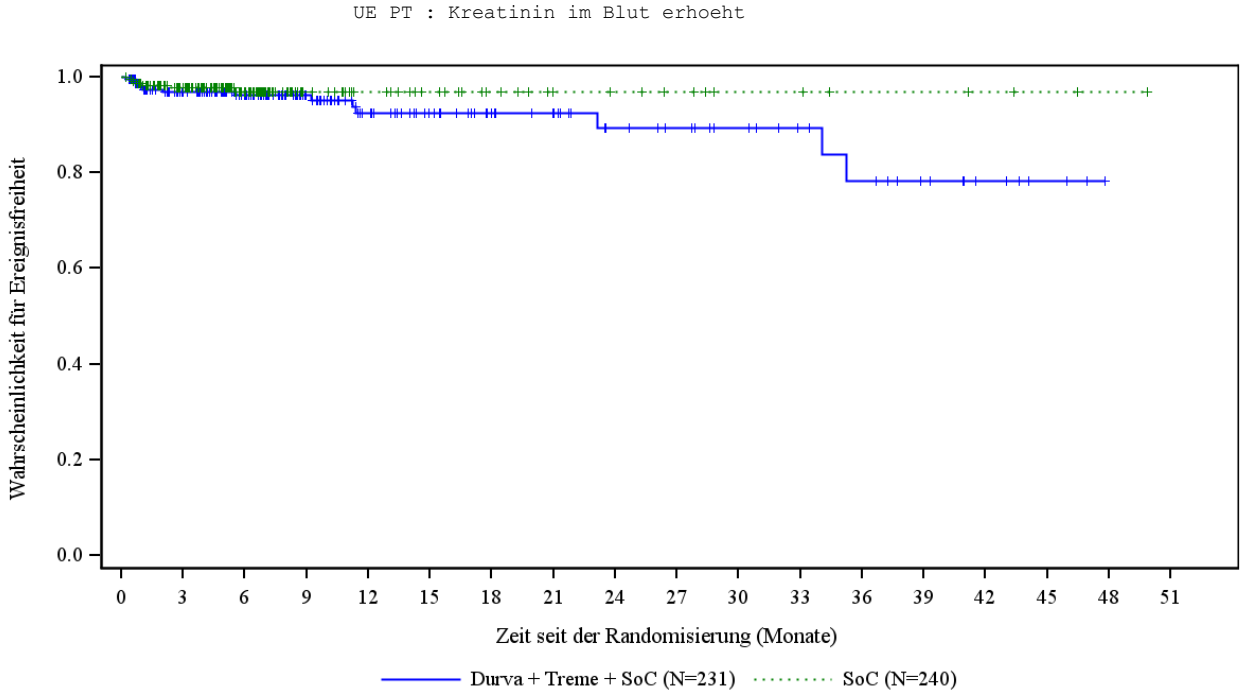
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	184	139	95	70	53	42	38	30	27	23	19	18	12	10	3	0	0
SoC	240	184	104	36	28	22	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	139	93	65	51	40	36	28	25	21	17	14	10	6	3	0	0
SoC	240	184	108	38	29	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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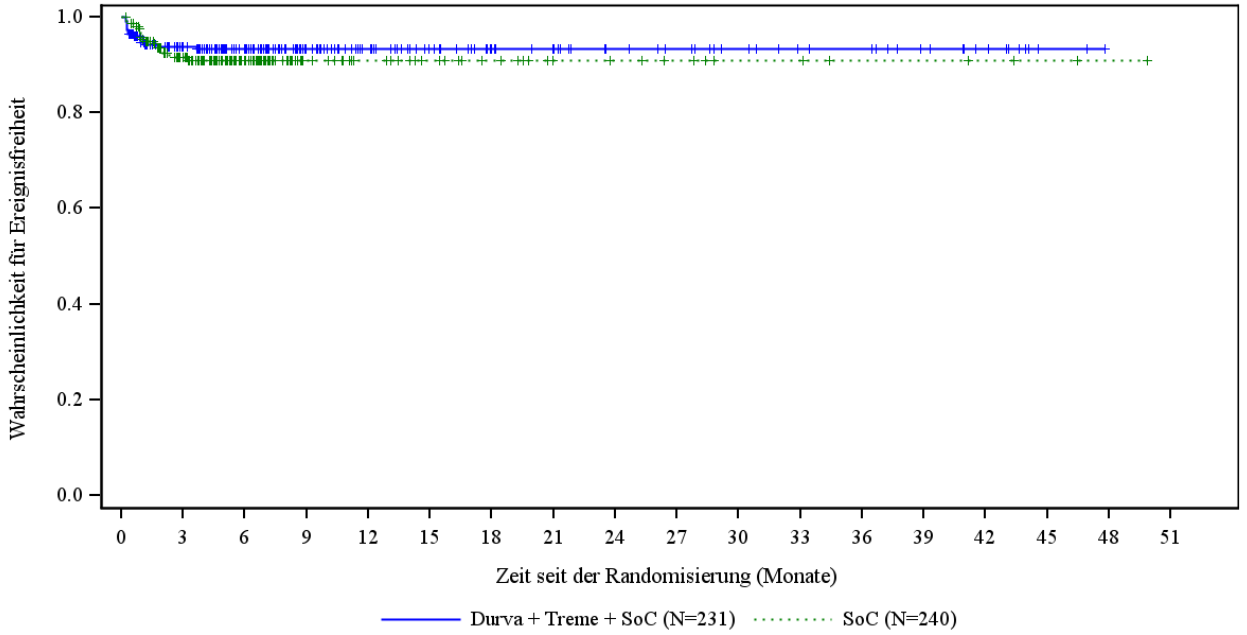
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Leukozytenzahl erniedrigt



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	180	136	92	70	55	43	39	32	29	24	20	19	13	9	2	0	0
SoC	240	172	99	37	29	23	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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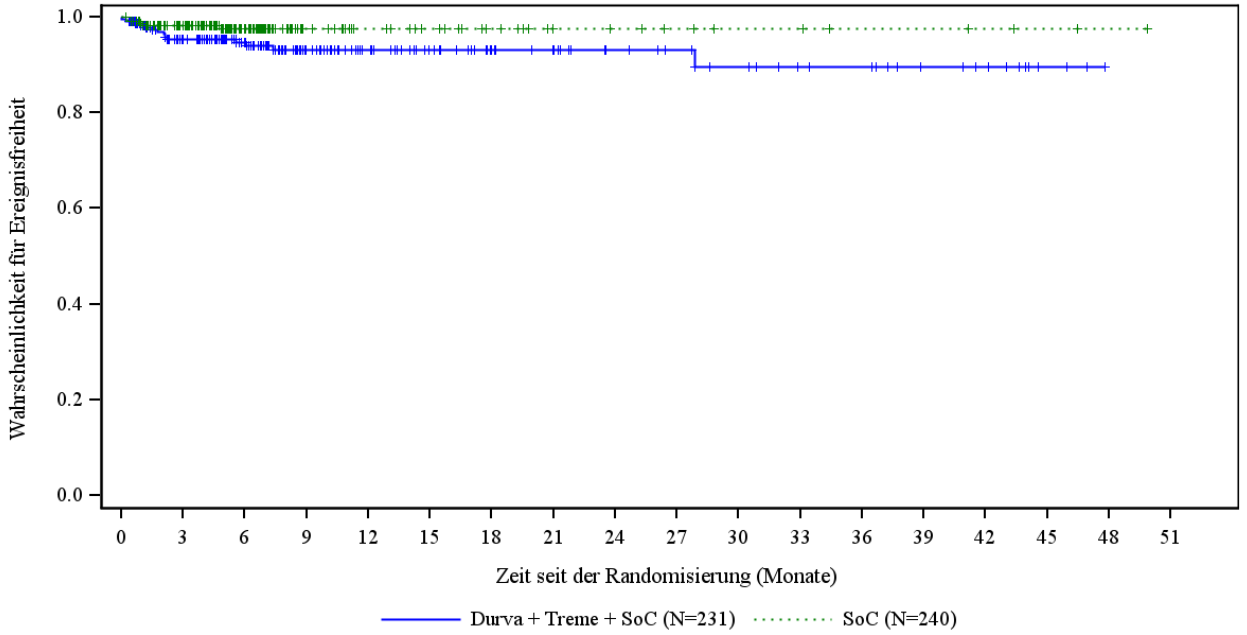
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE PT : Lipase erhoeht



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	183	138	89	65	51	40	36	29	26	22	18	17	11	9	3	0	0
SoC	240	186	107	37	28	23	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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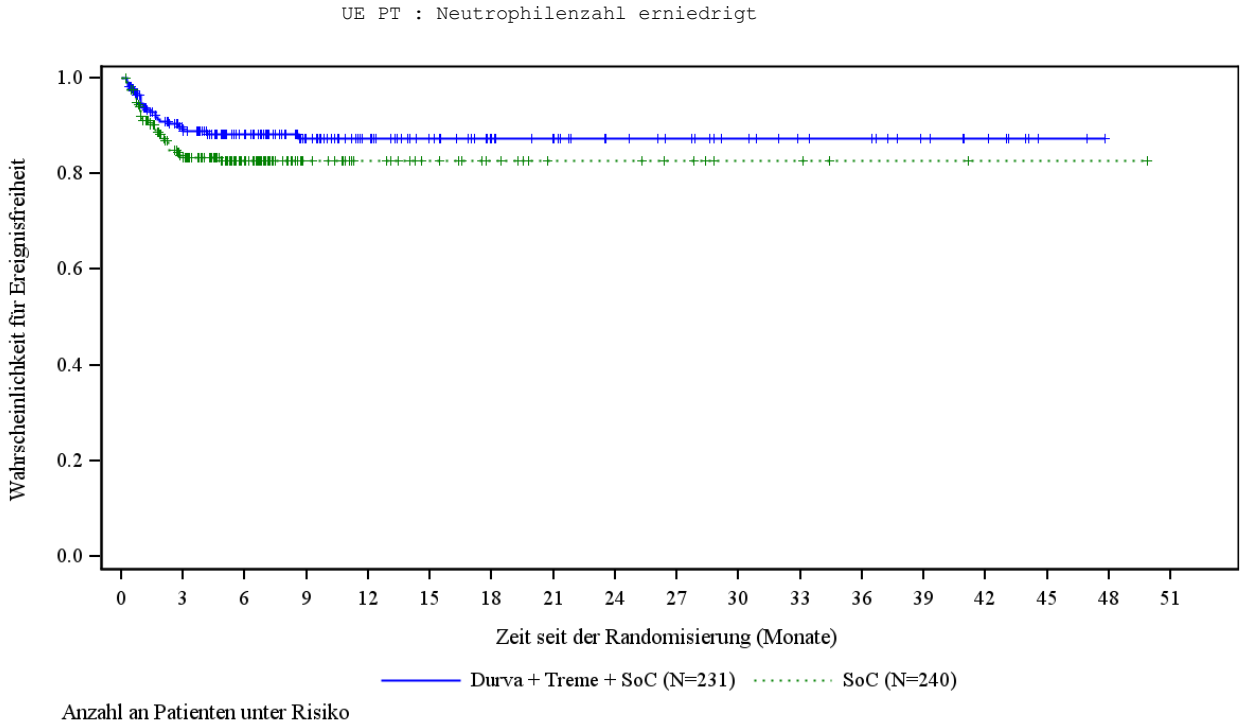
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



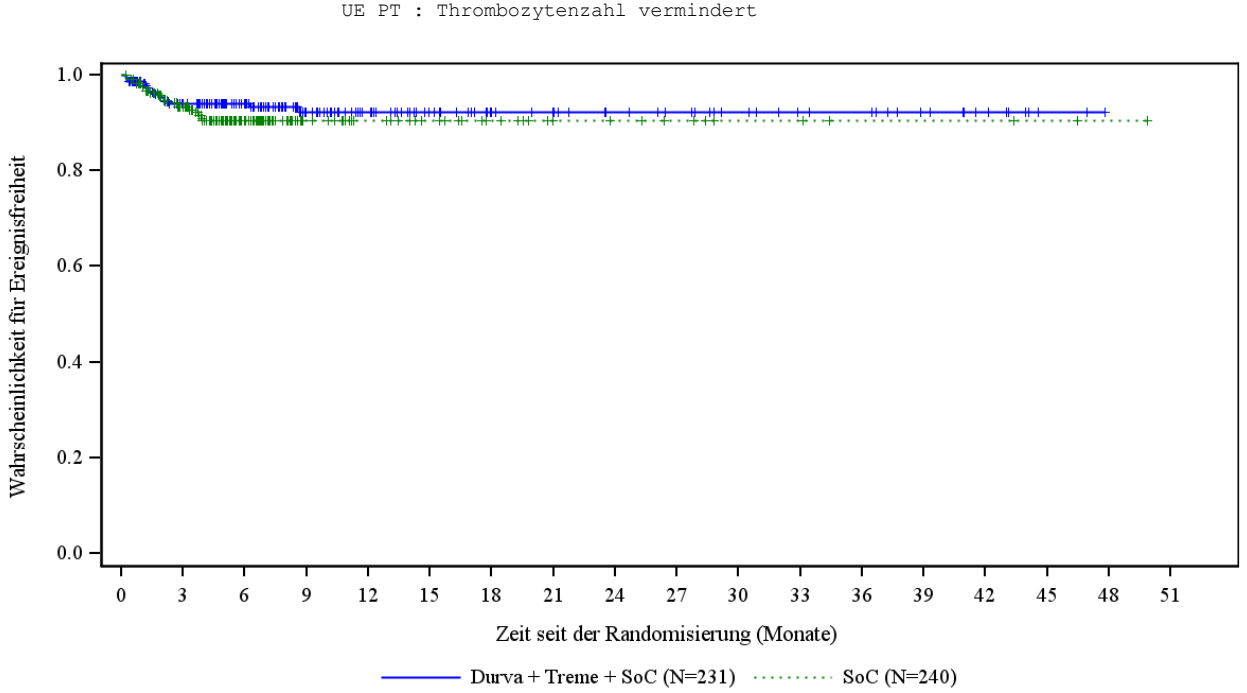
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	170	129	88	66	53	41	37	30	27	22	18	17	11	8	2	0	0
SoC	240	155	91	34	25	19	14	9	9	7	4	4	2	2	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	181	136	90	66	51	39	36	31	28	23	19	18	12	8	2	0	0
SoC	240	177	104	38	29	23	17	11	10	8	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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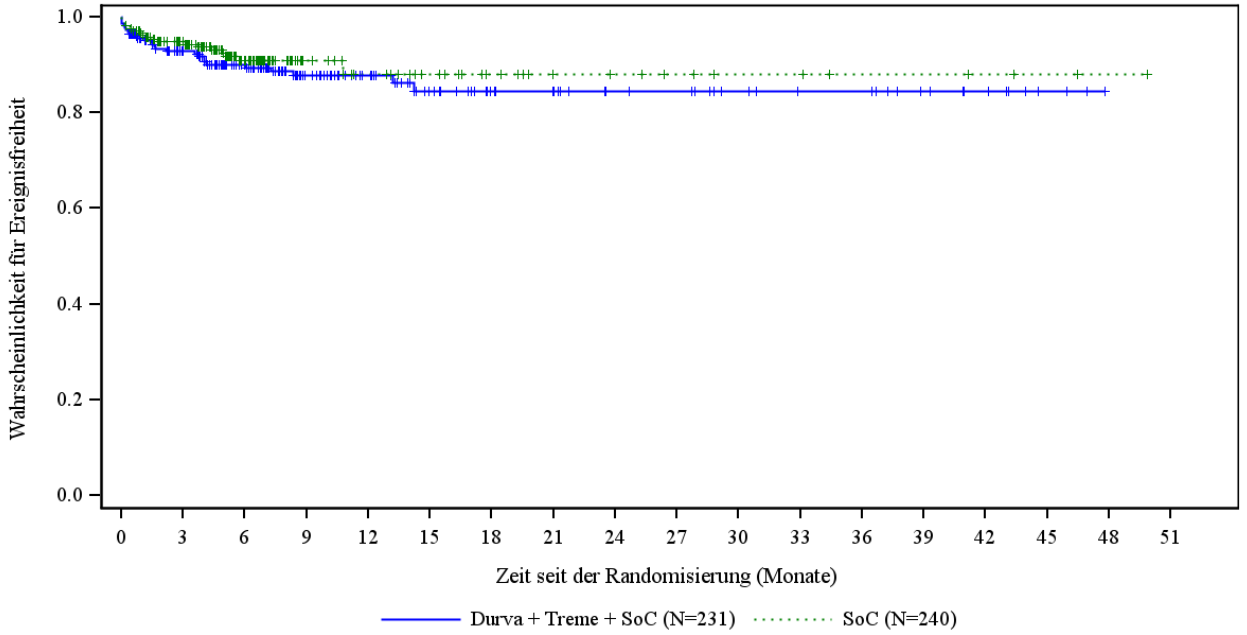
Figure 4.2.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE SOC : Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	180	133	86	63	46	35	32	26	25	20	17	17	11	8	3	0	0
SoC	240	179	100	36	28	22	16	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. N Number of patients in treatment group.
AE Adverse event. PT Preferred term. SOC System organ class.
Time to event analysis for AE is defined as the time from the date of first dose until the date of the first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae306g.sas Executed : 2022-11-22T124956

Anhang 4-G 1.2.1.2: Behandlungsabbruch aufgrund unerwünschter Ereignisse nach SOC und PT

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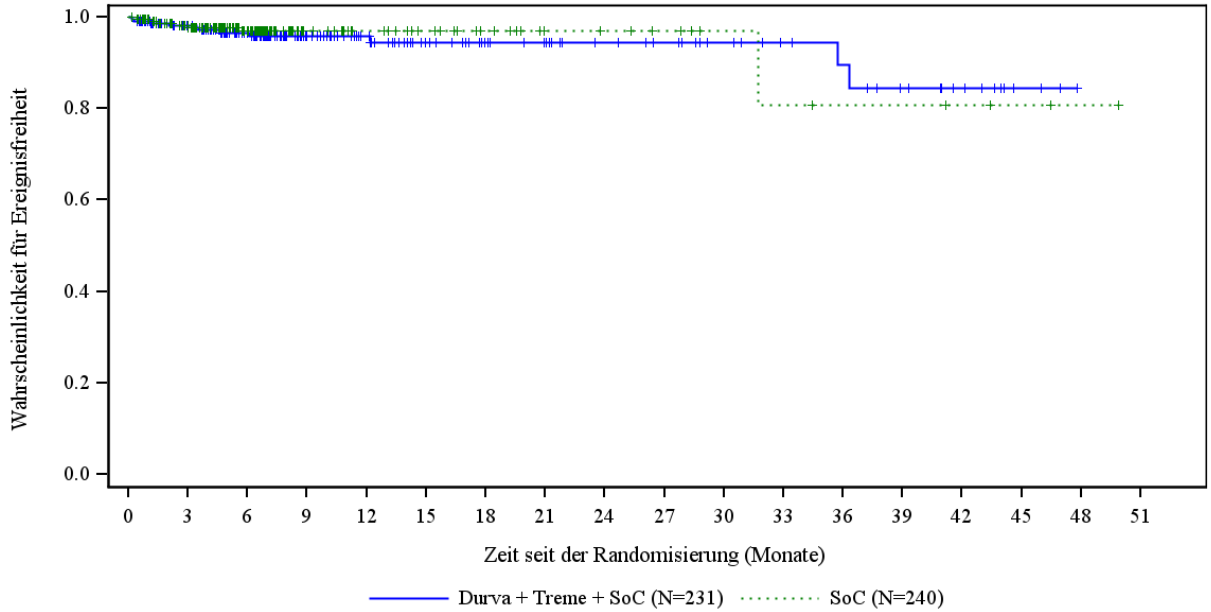
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Infektionen und parasitaere Erkrankungen



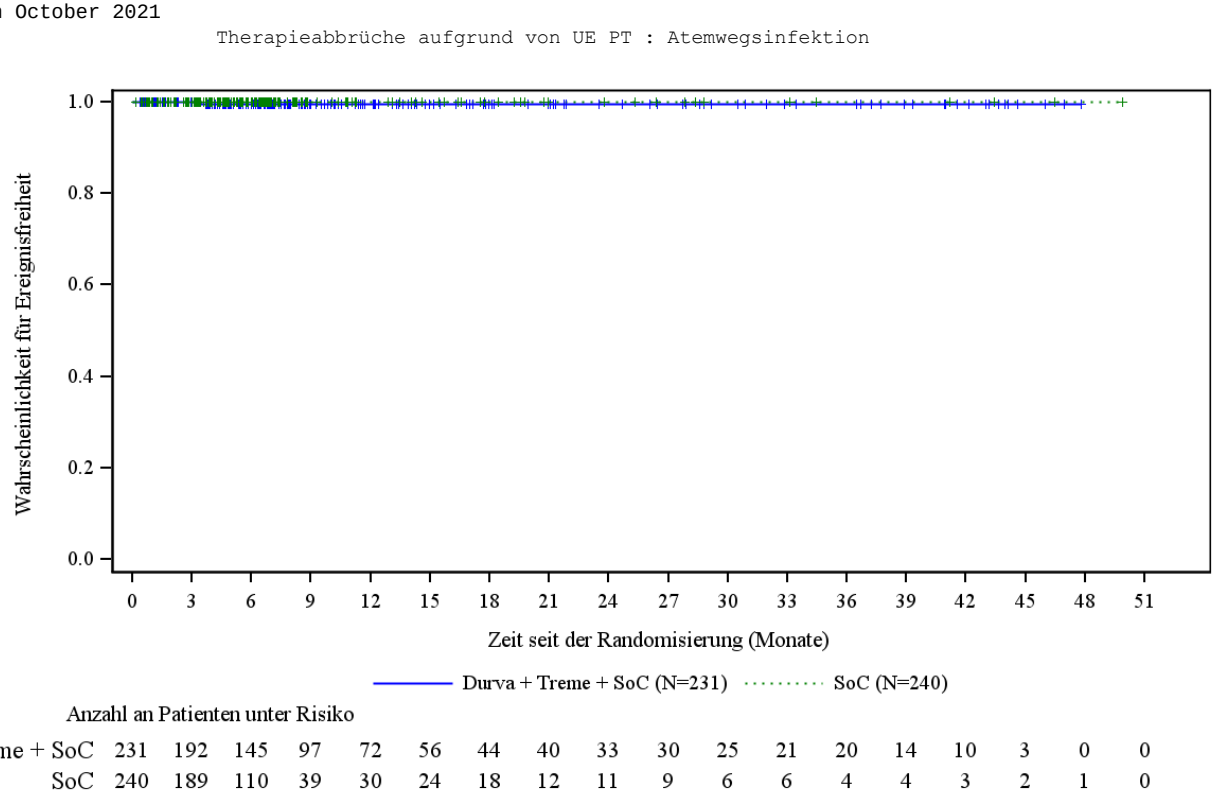
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	71	55	43	39	32	29	24	20	18	13	9	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

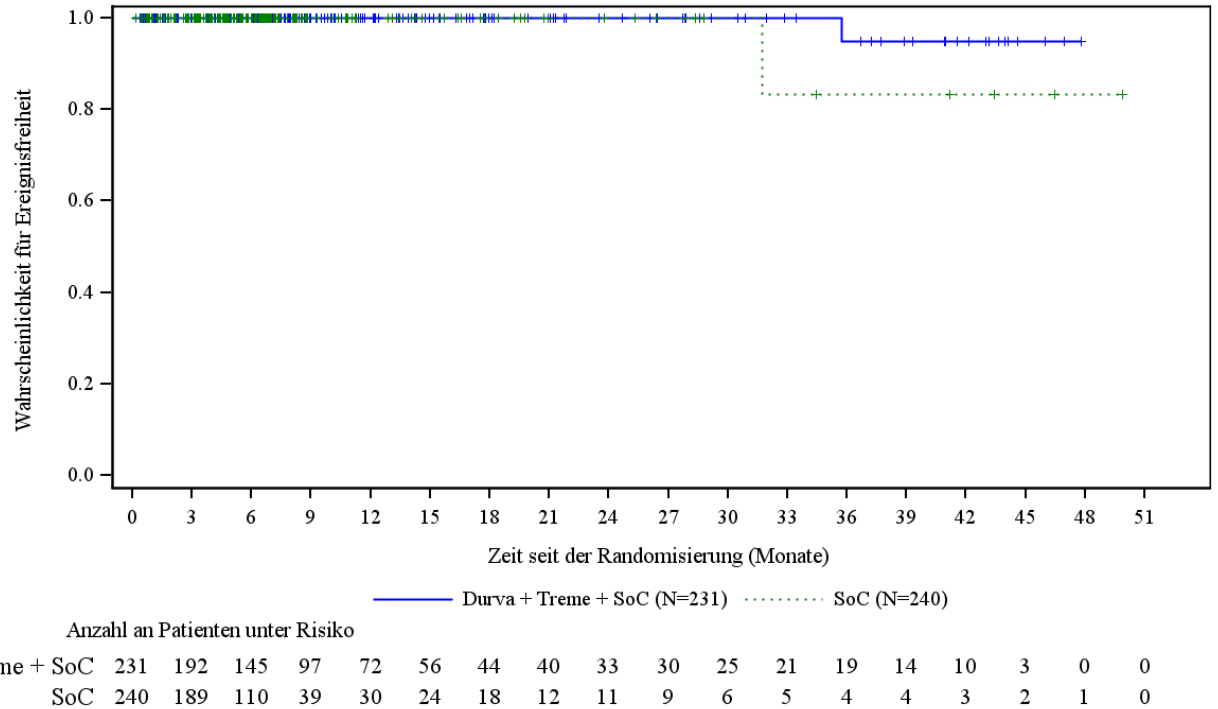


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : COVID-19-Lungenentzuendung



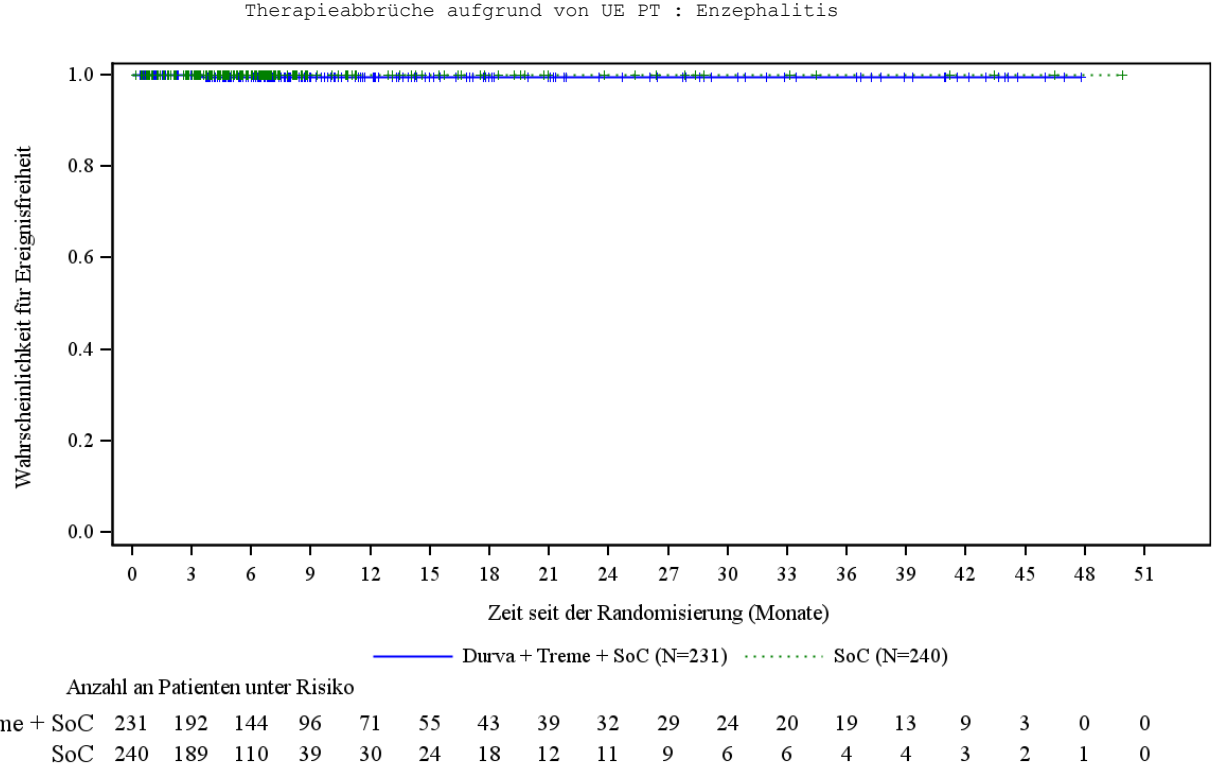
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	19	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



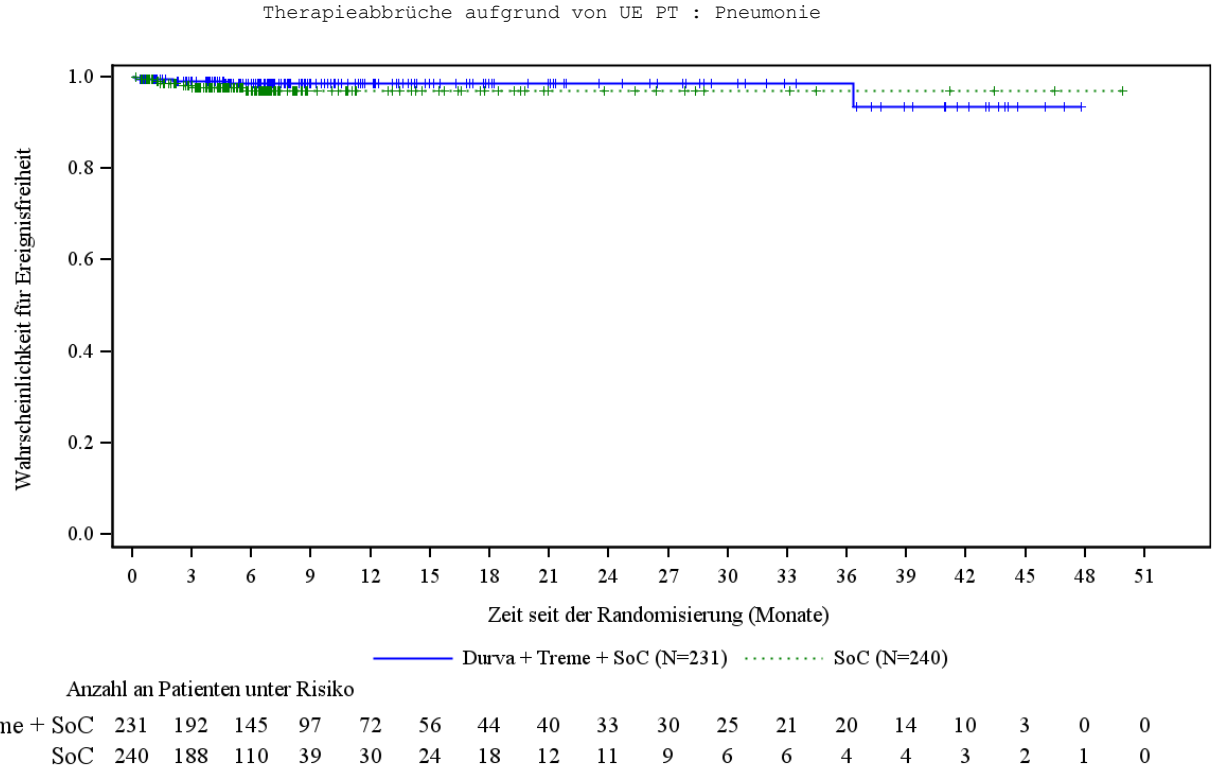
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

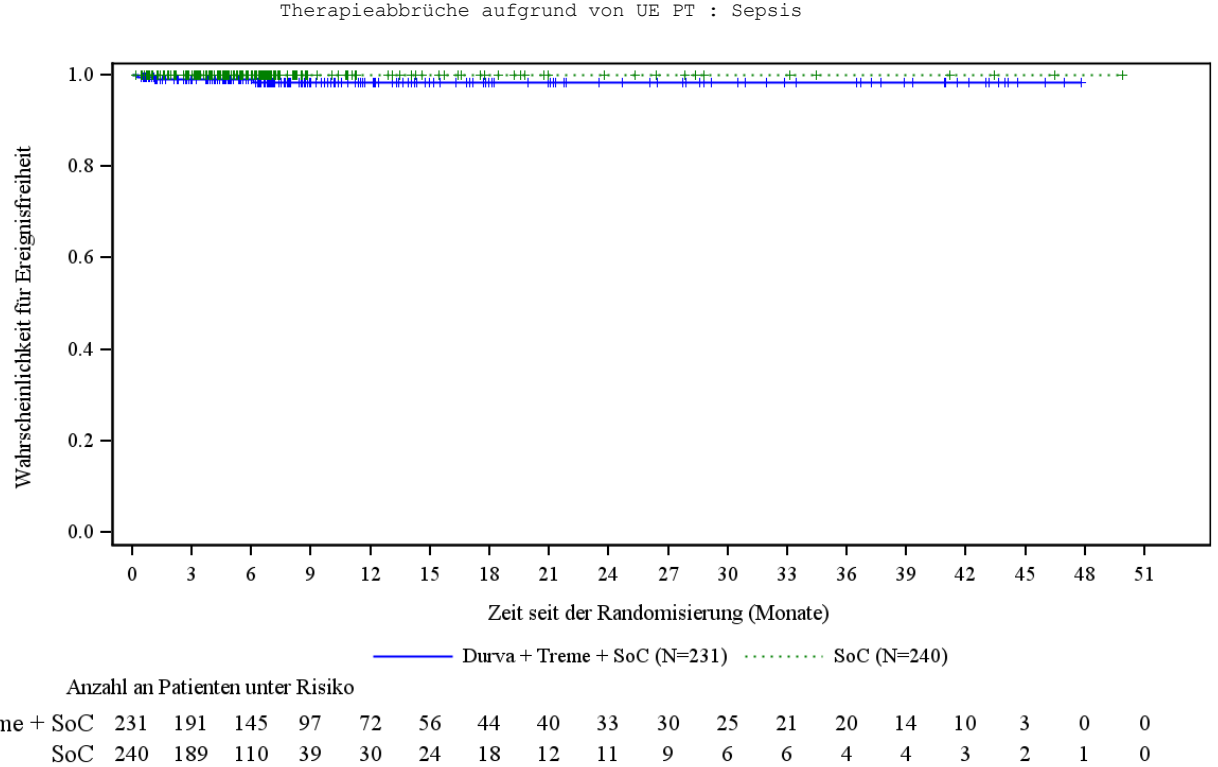
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

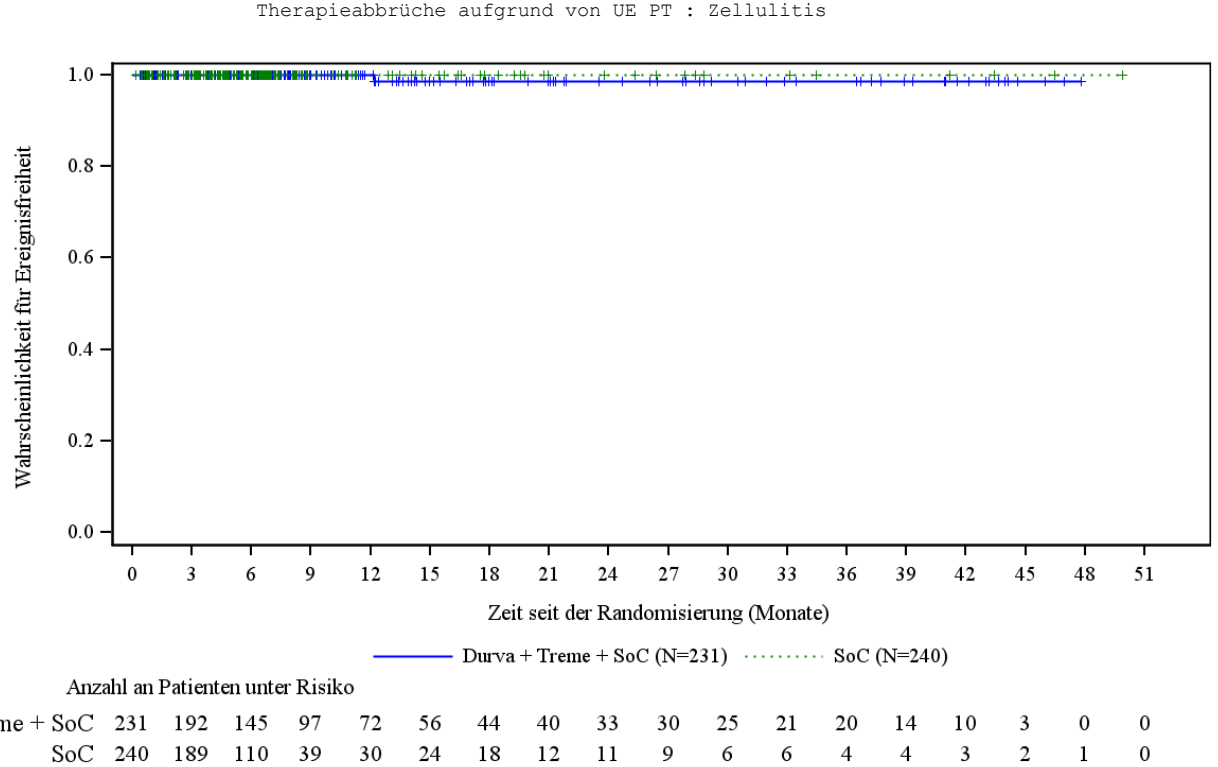
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

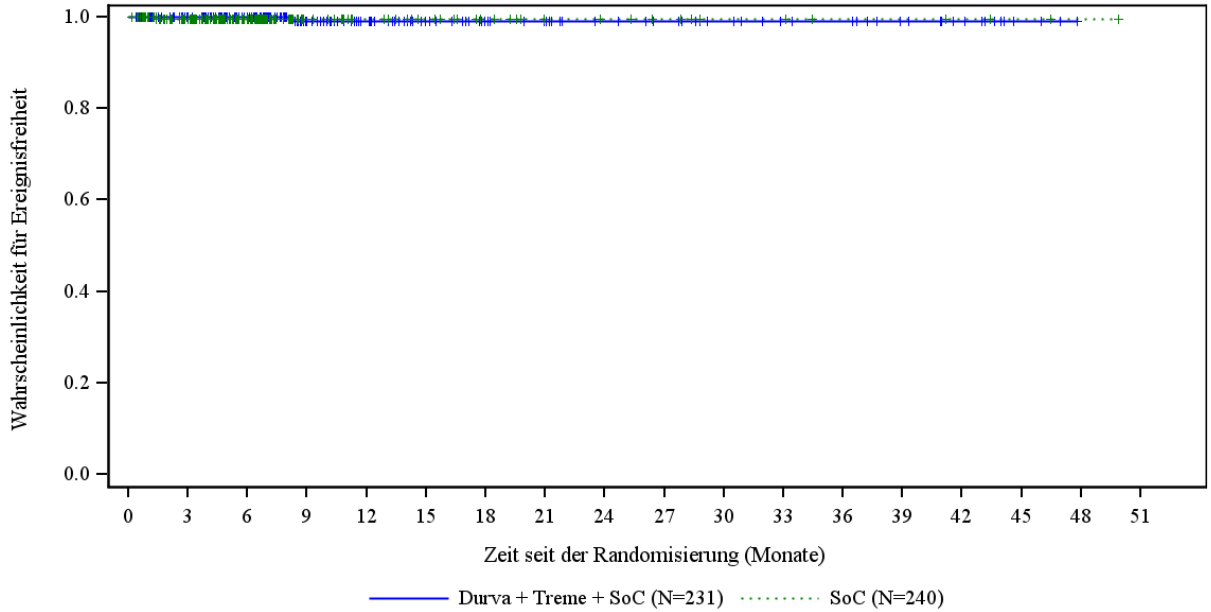
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021
Therapieabbrüche aufgrund von UE SOC : Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)



Anzahl an Patienten unter Risiko

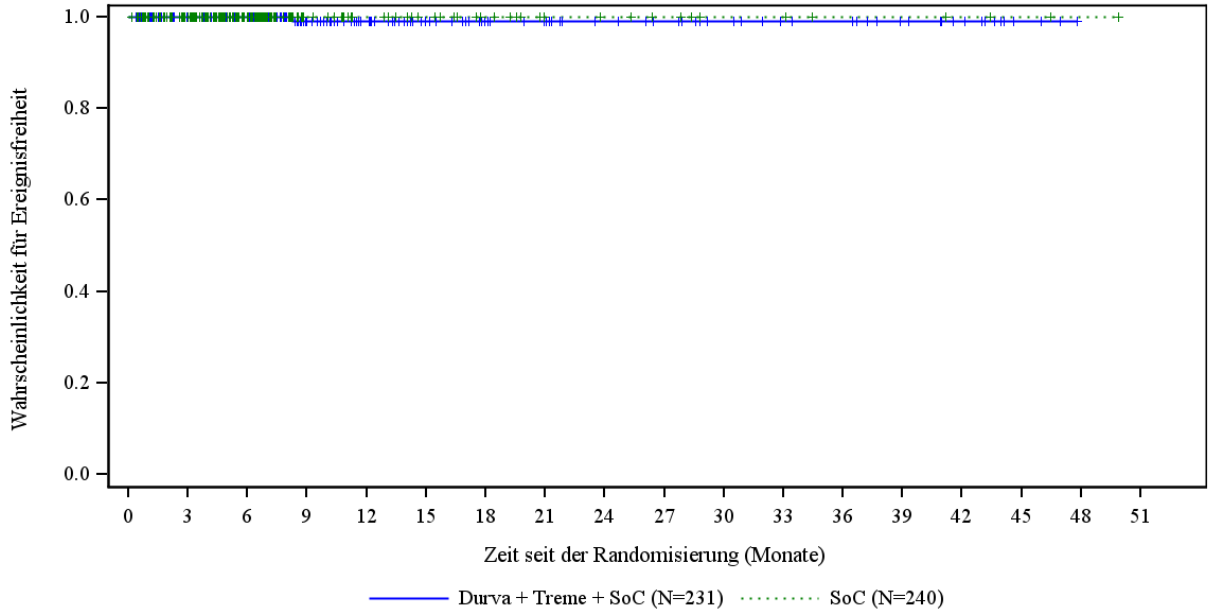
Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	109	38	29	23	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Neuroendokrines Karzinom metastatisch



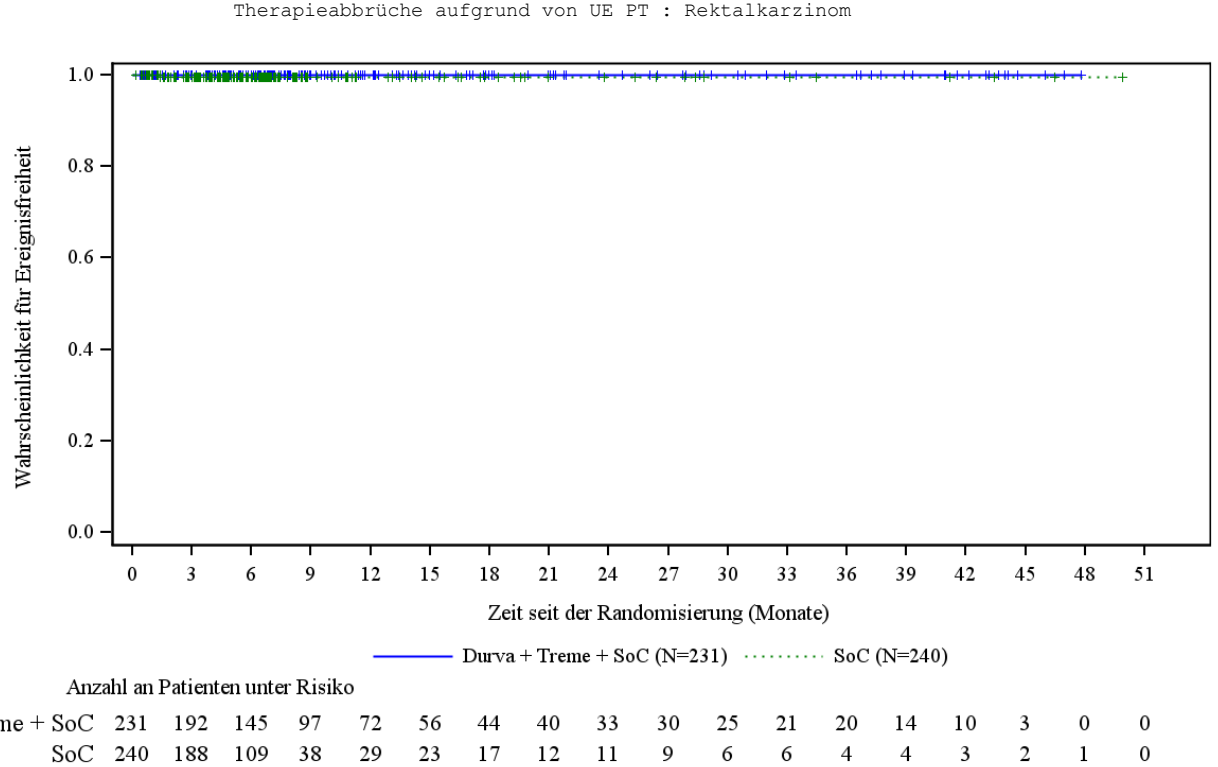
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

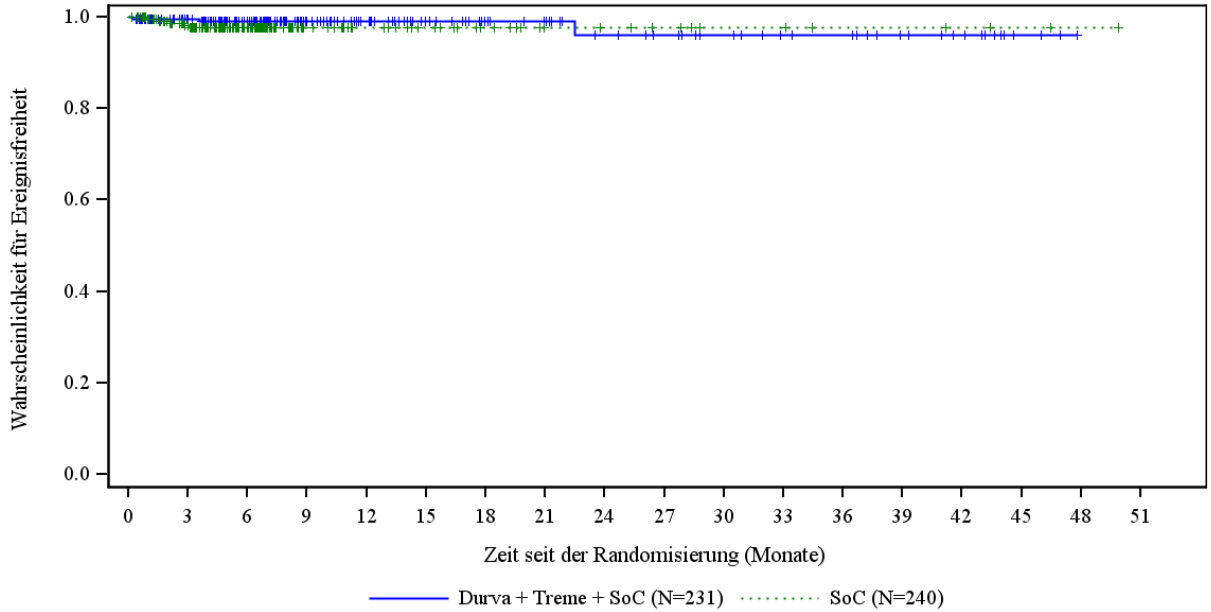


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen des Blutes und des Lymphsystems



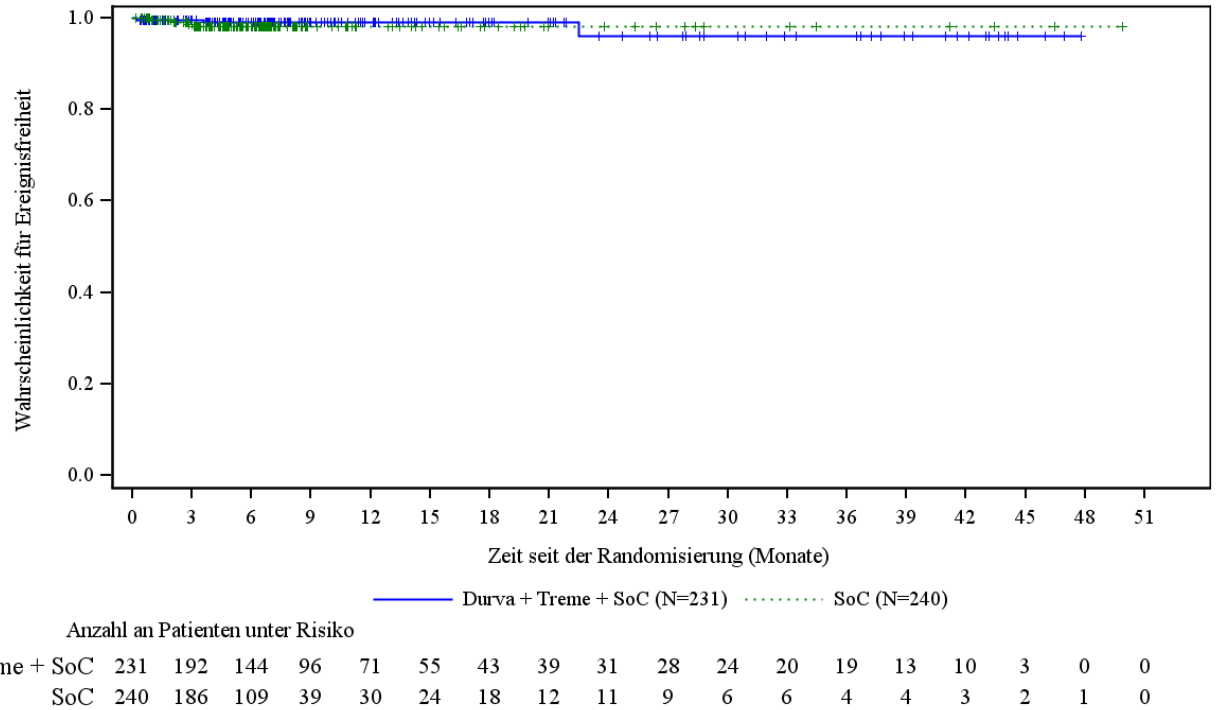
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	71	55	43	39	31	28	24	20	19	13	10	3	0	0
SoC	240	186	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

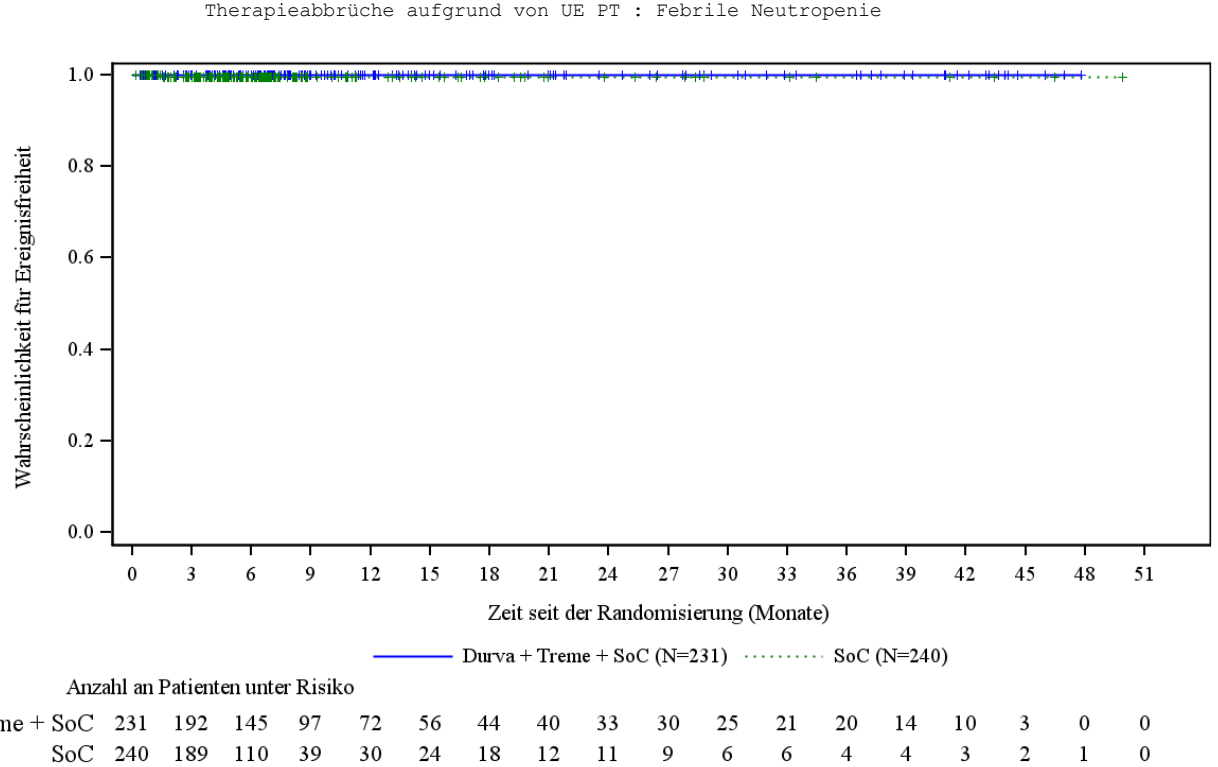
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

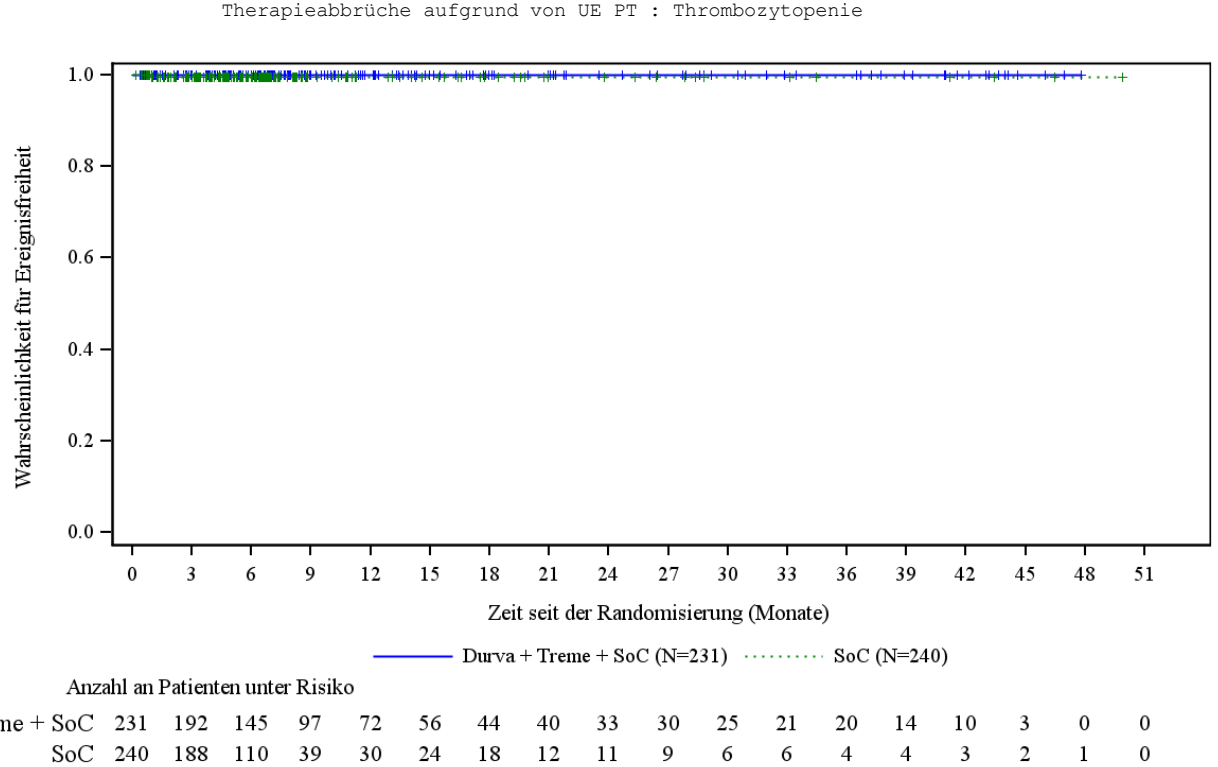
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

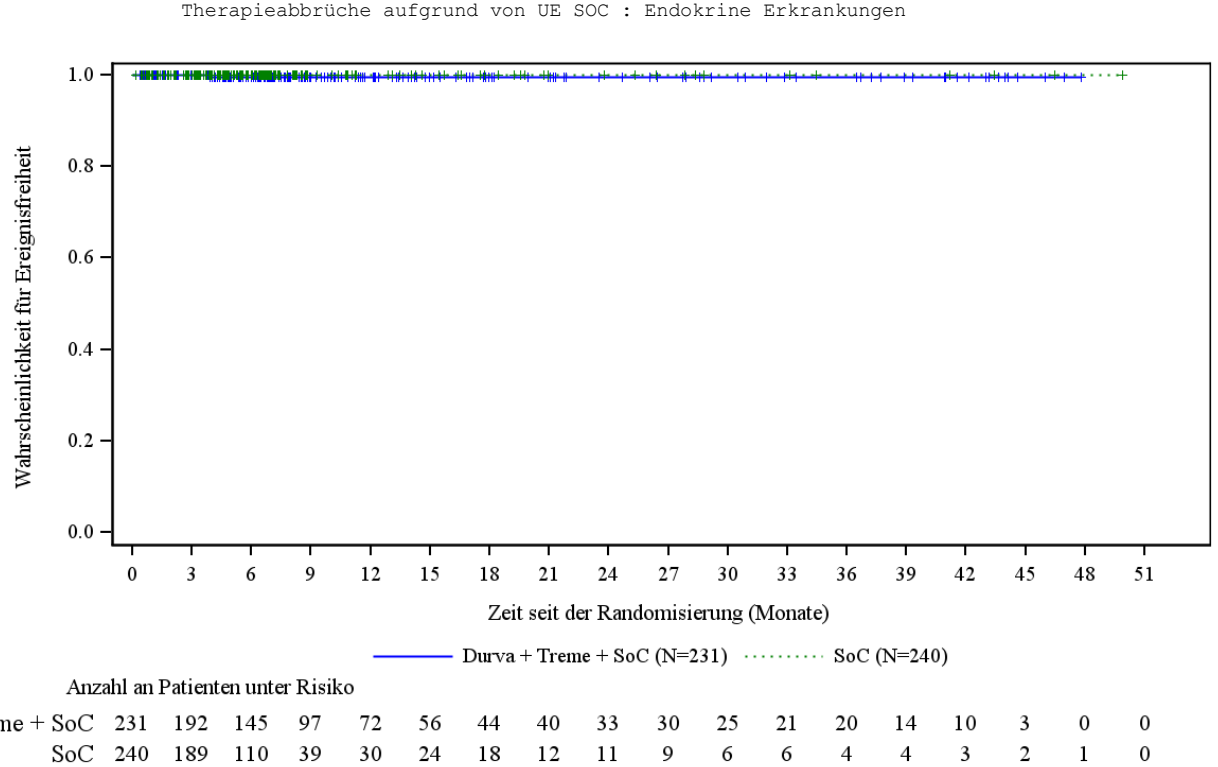
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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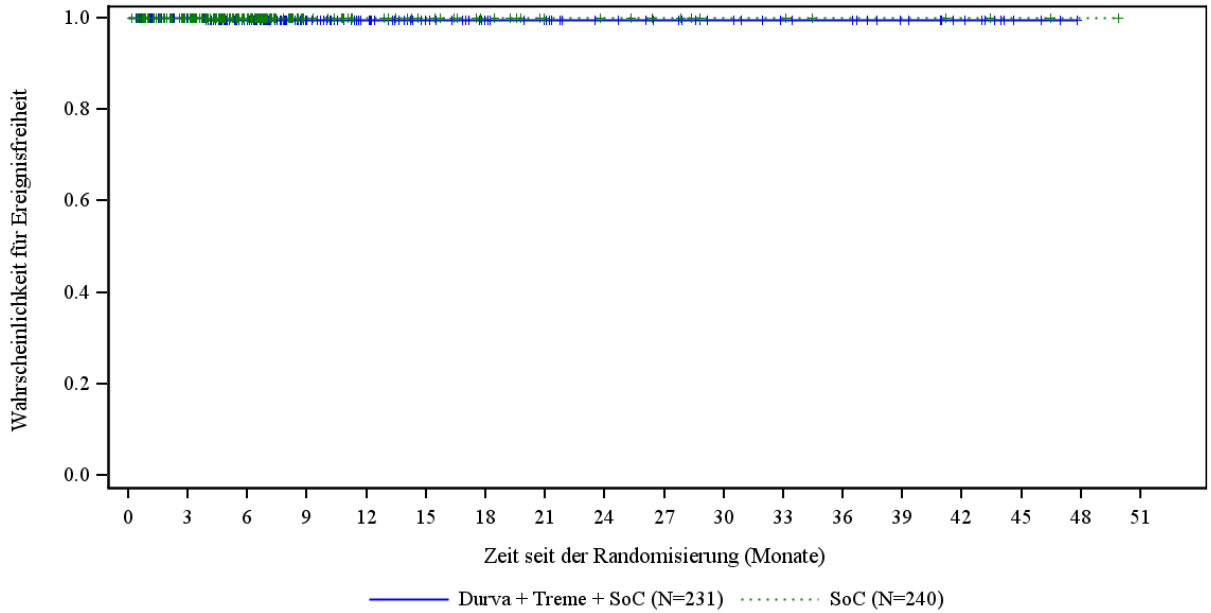
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Immunthyreoiditis



Anzahl an Patienten unter Risiko

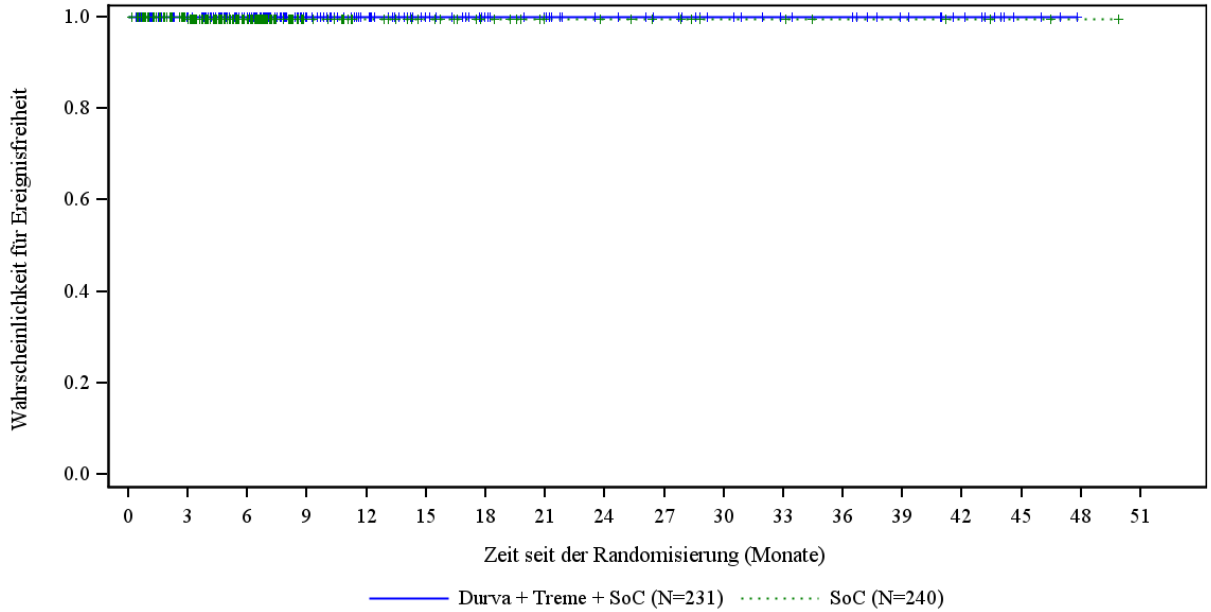
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Stoffwechsel- und Ernaehrungsstoerungen



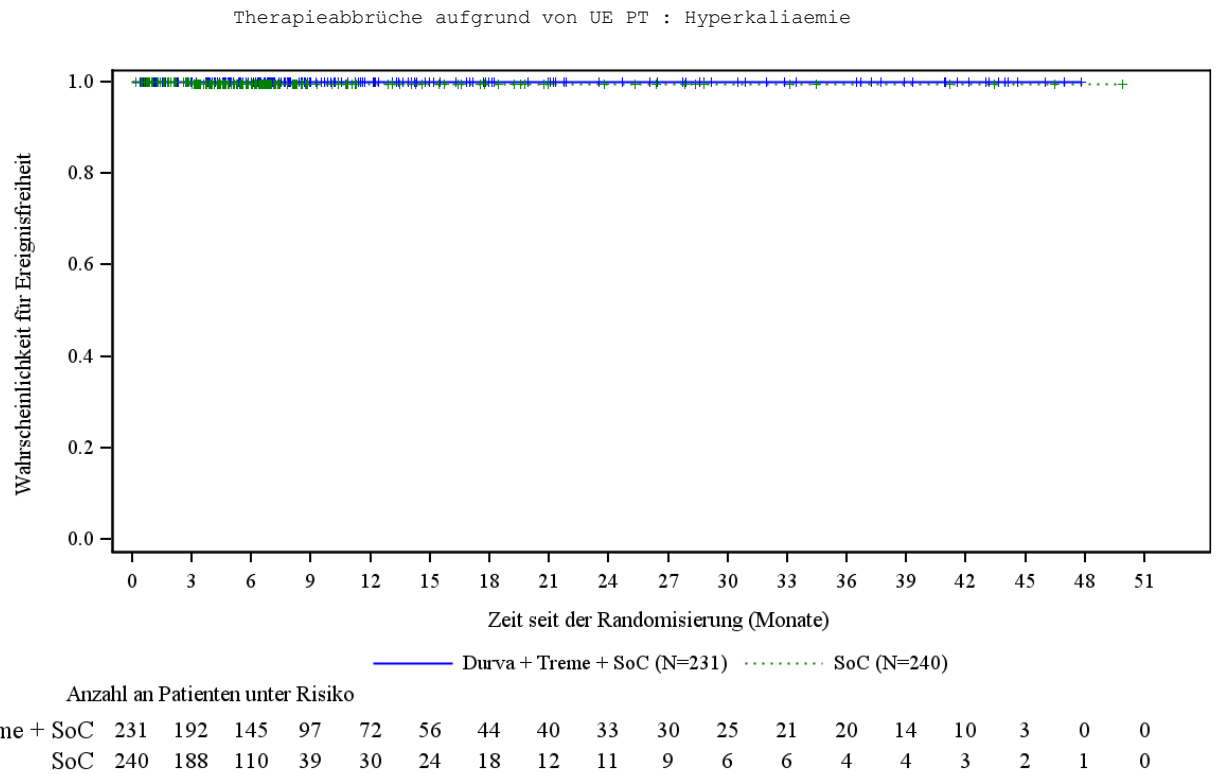
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

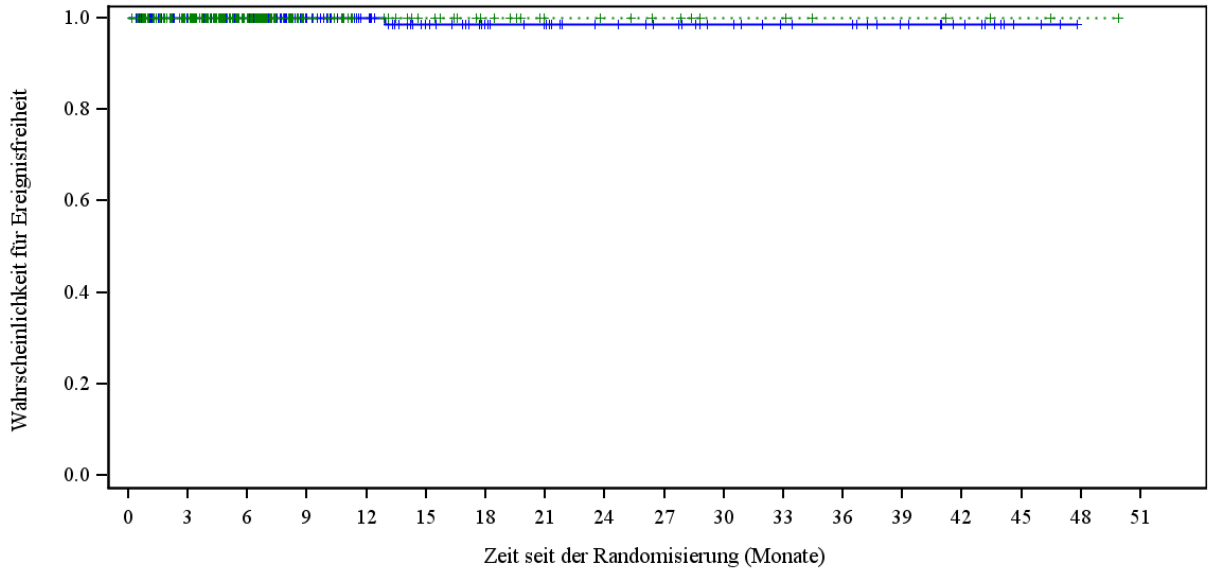


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Psychiatrische Erkrankungen



Anzahl an Patienten unter Risiko

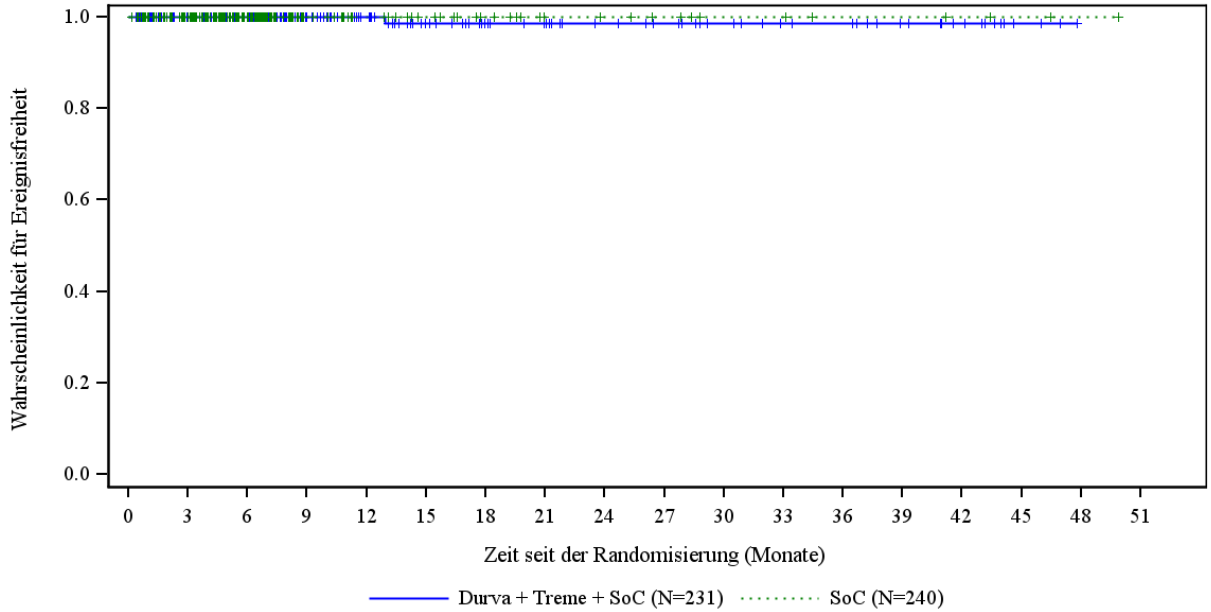
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Suizidversuch



Anzahl an Patienten unter Risiko

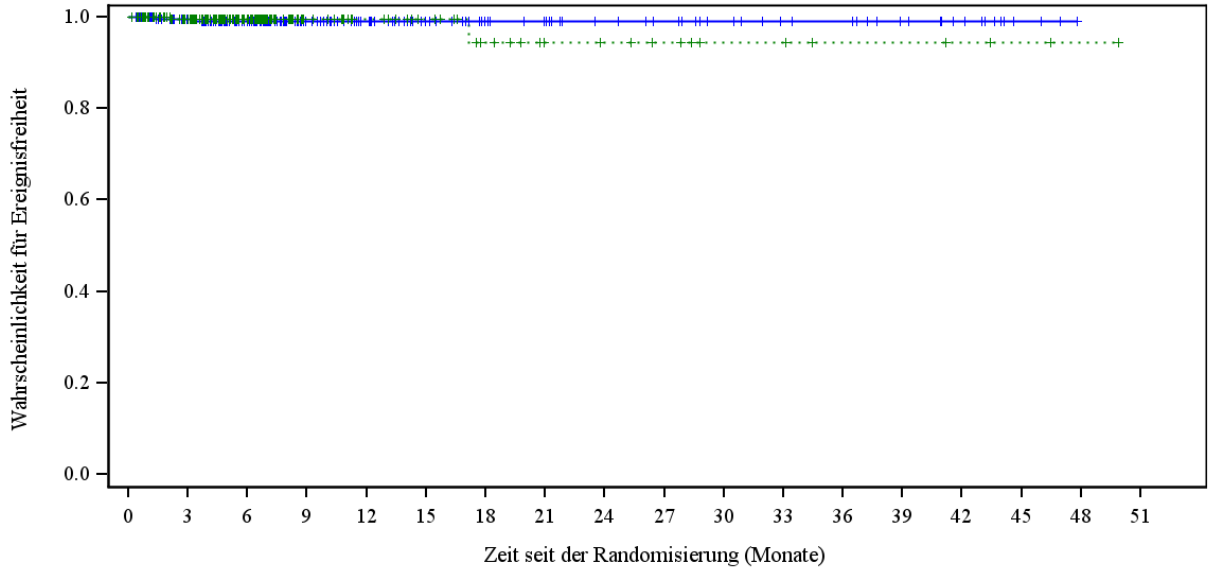
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen des Nervensystems



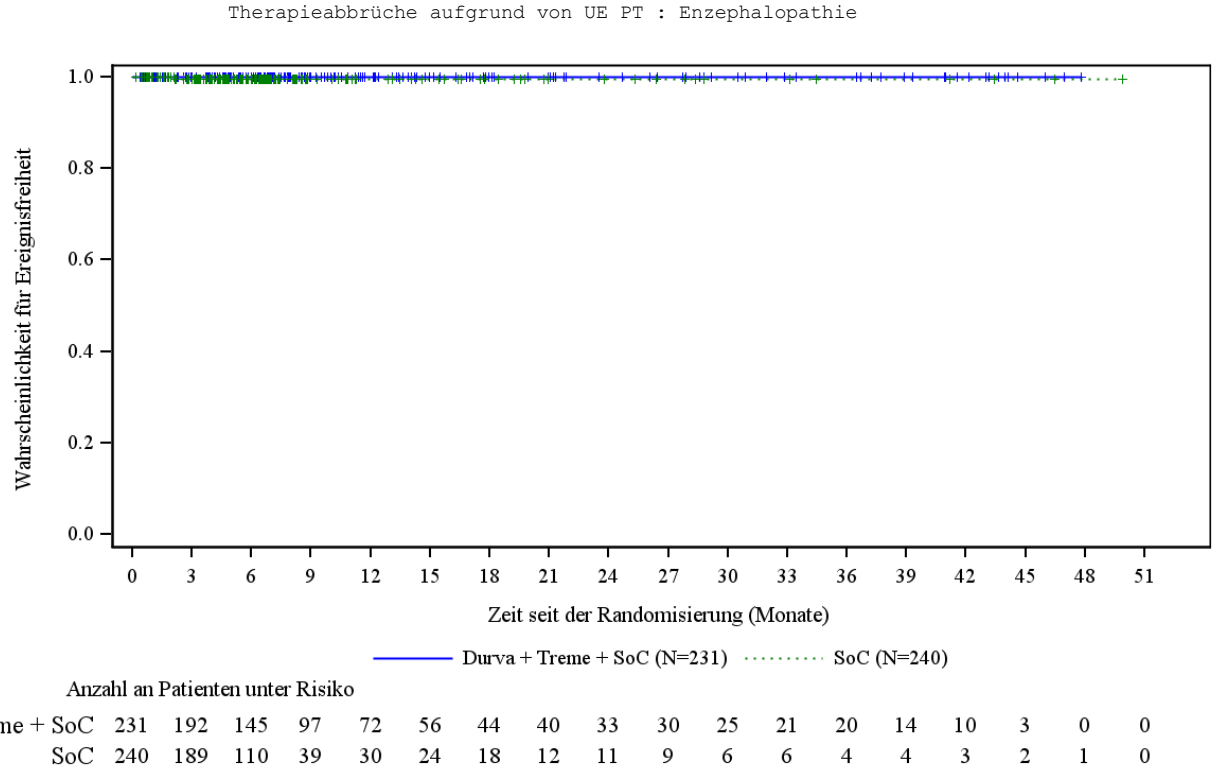
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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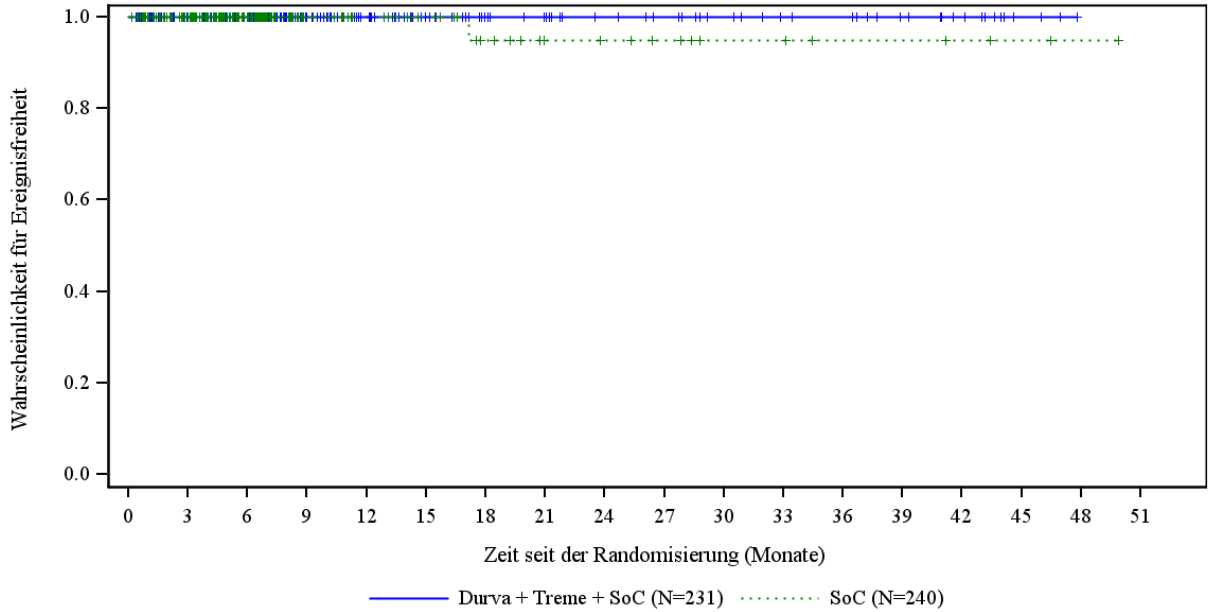
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Erkrankung des Nervensystems



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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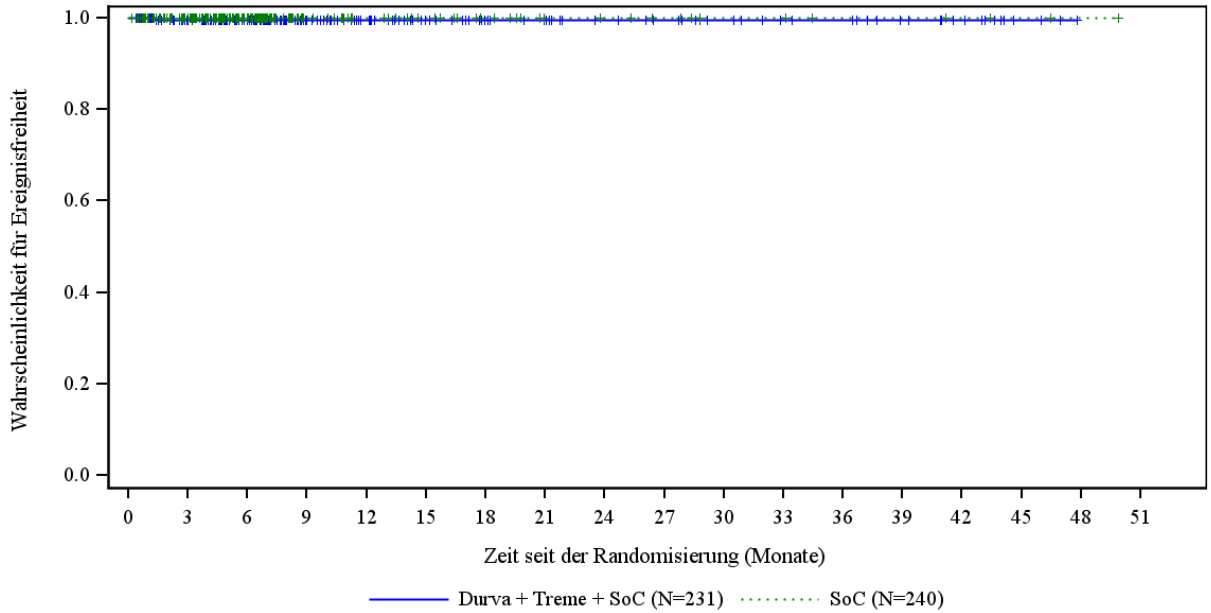
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Haemorrhagischer Schlaganfall



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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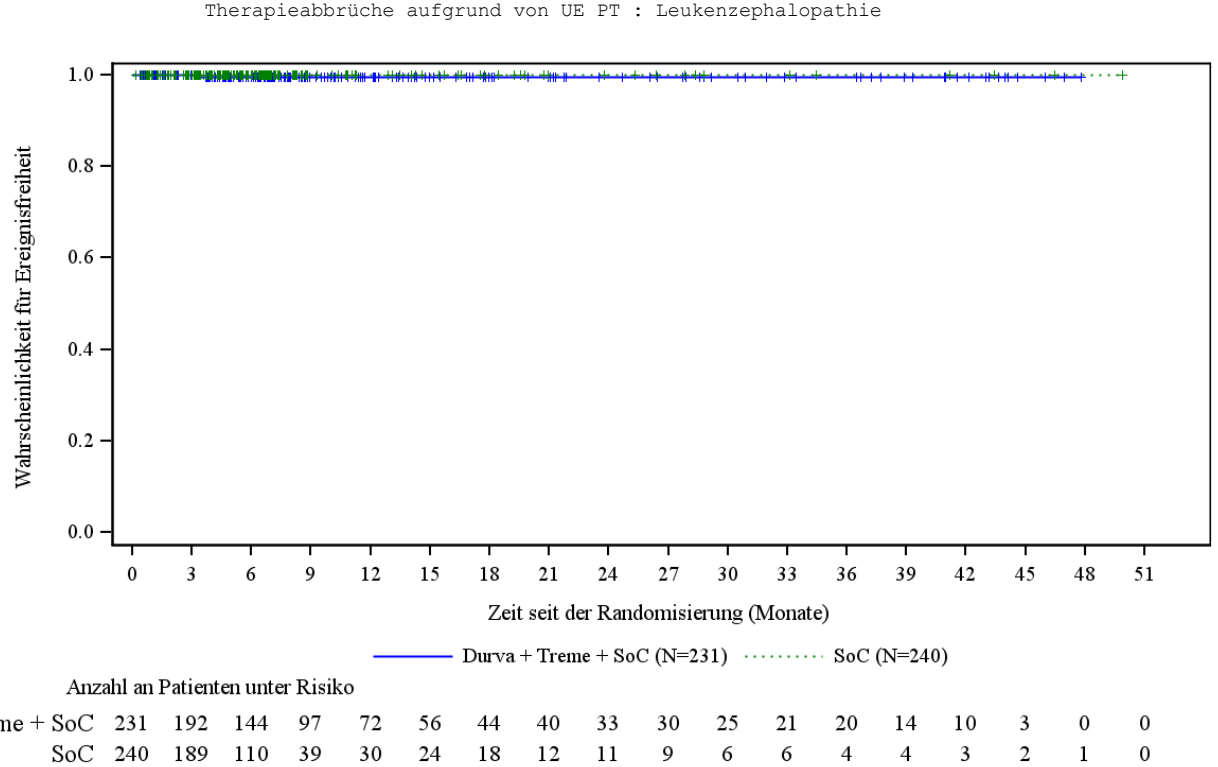
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

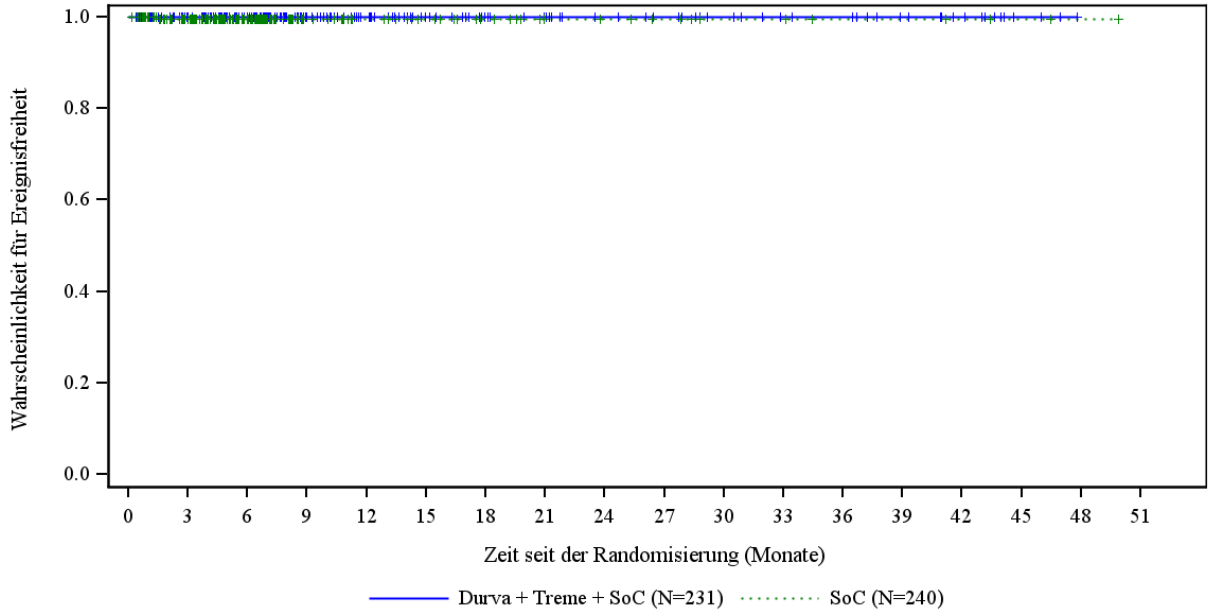


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen des Ohrs und des Labyrinths



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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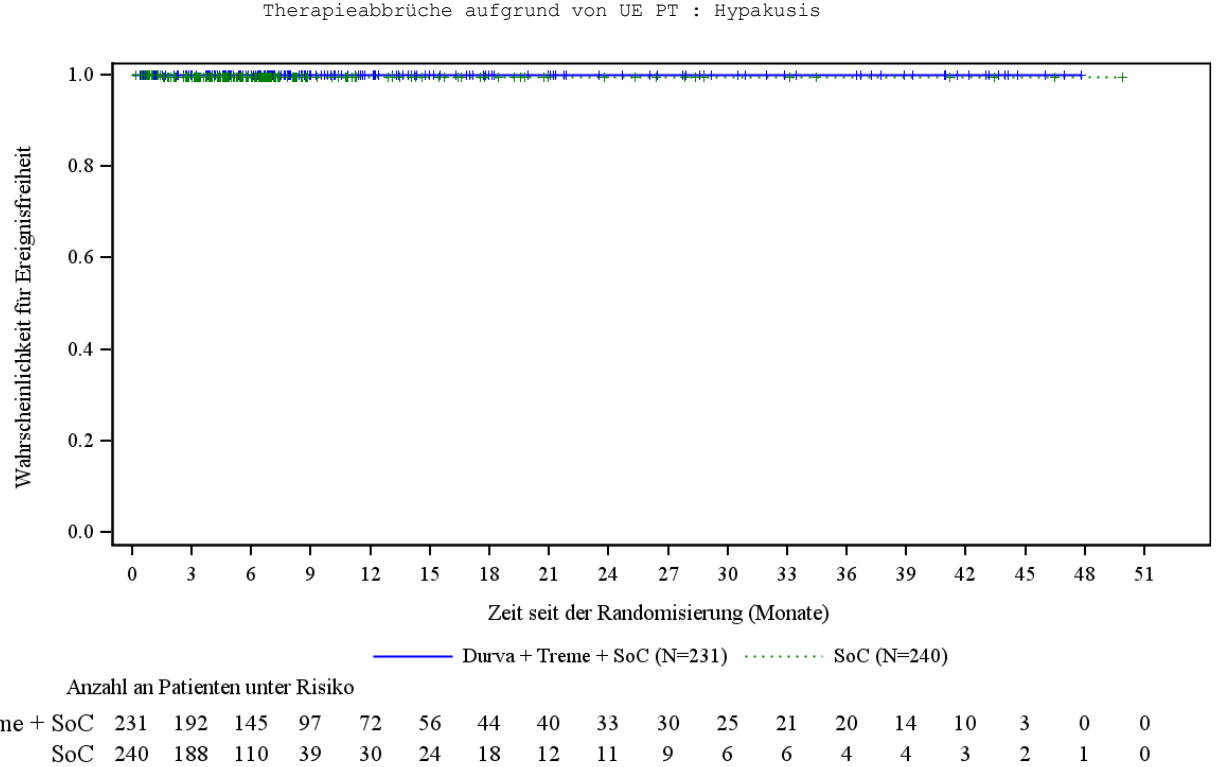
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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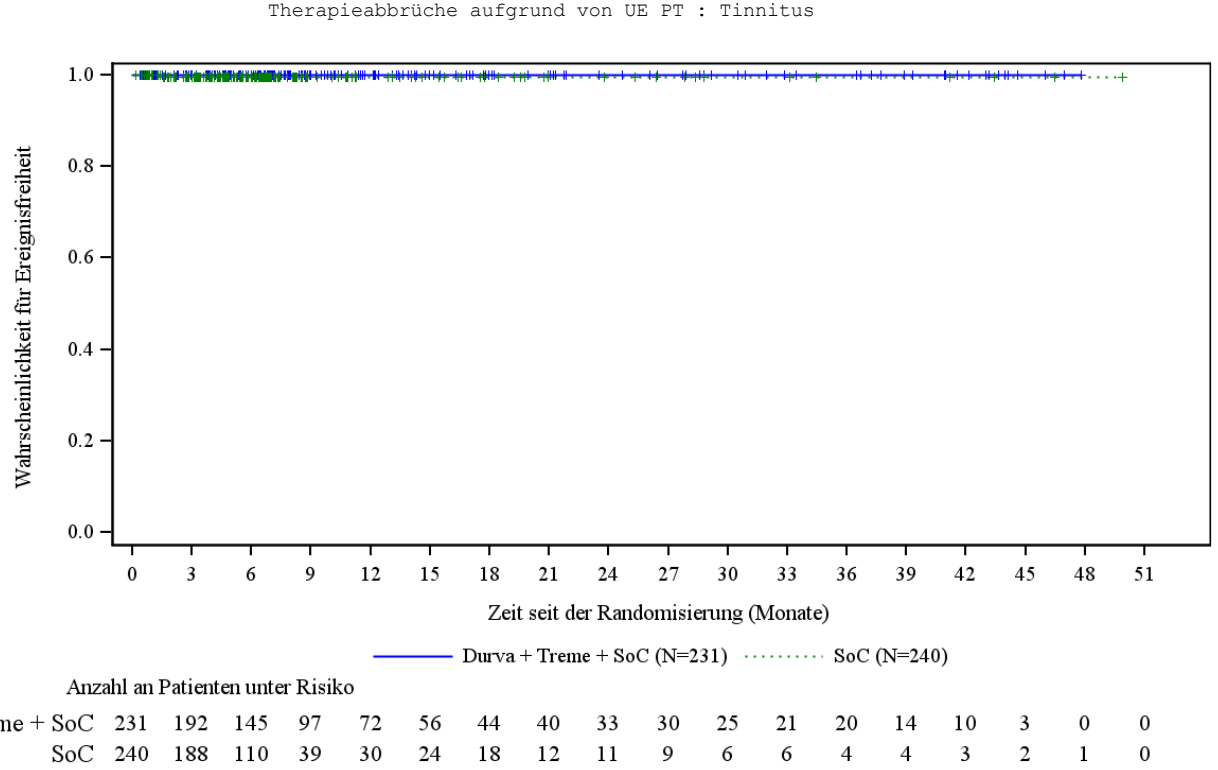
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

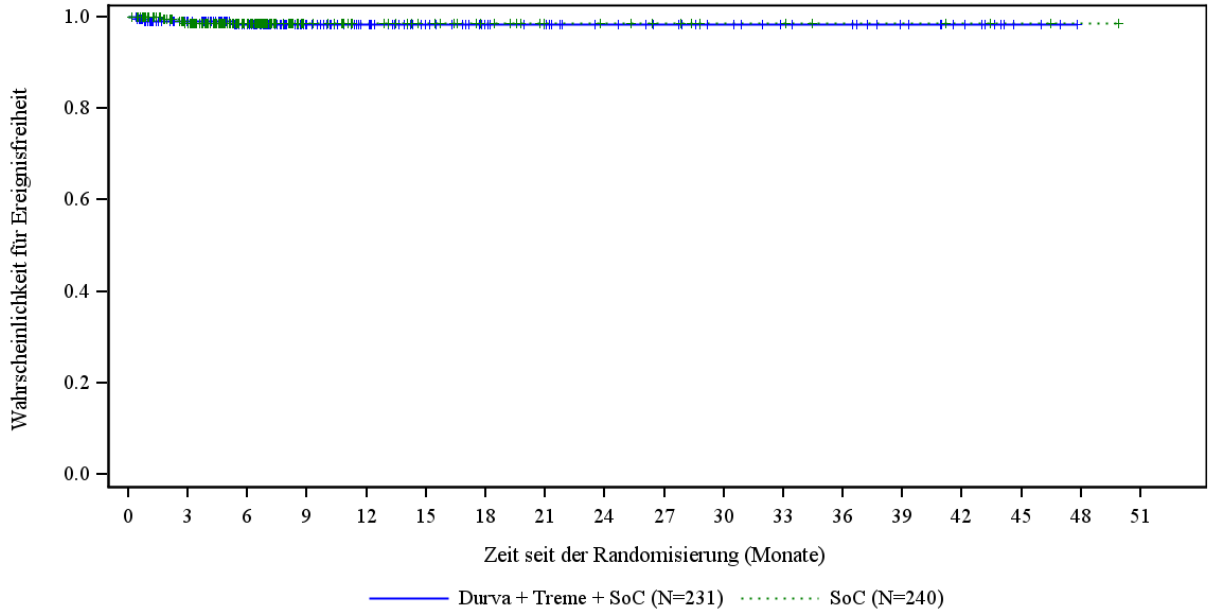


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Herzerkrankungen



Anzahl an Patienten unter Risiko

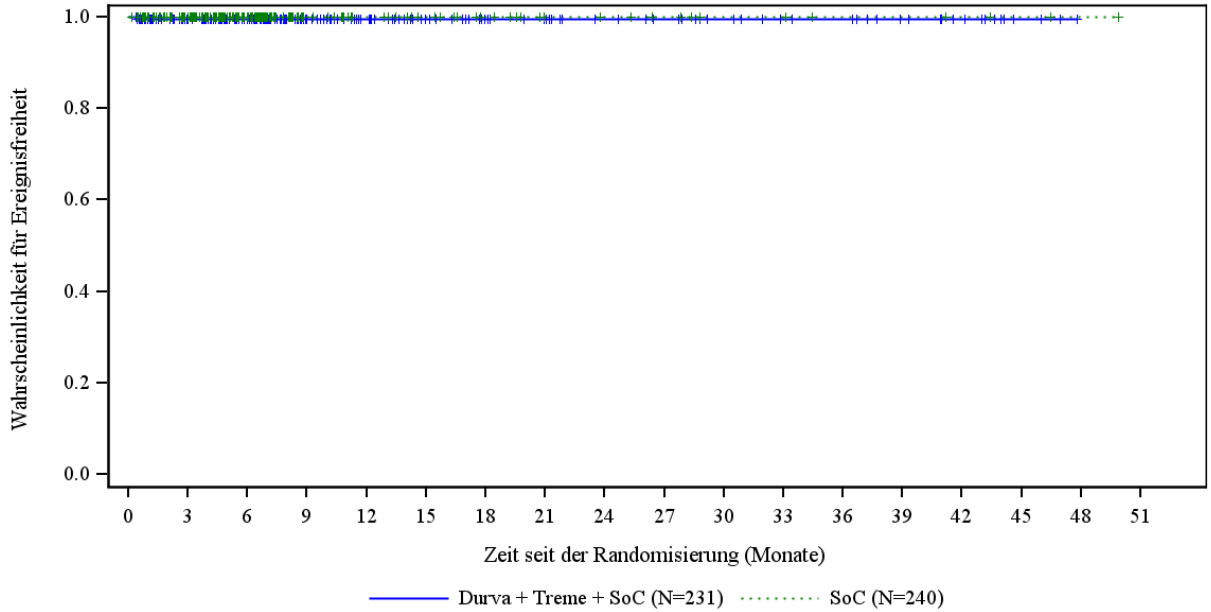
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Akuter Myokardinfarkt



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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Includes treatment-emergent AEs only.

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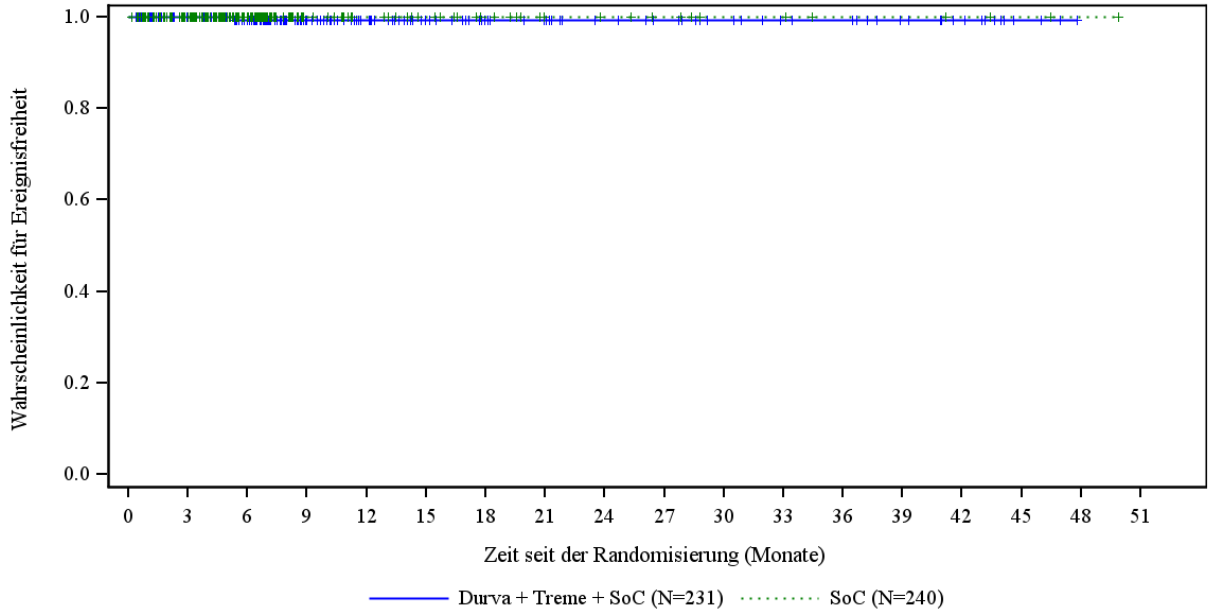
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Akutes Koronarsyndrom



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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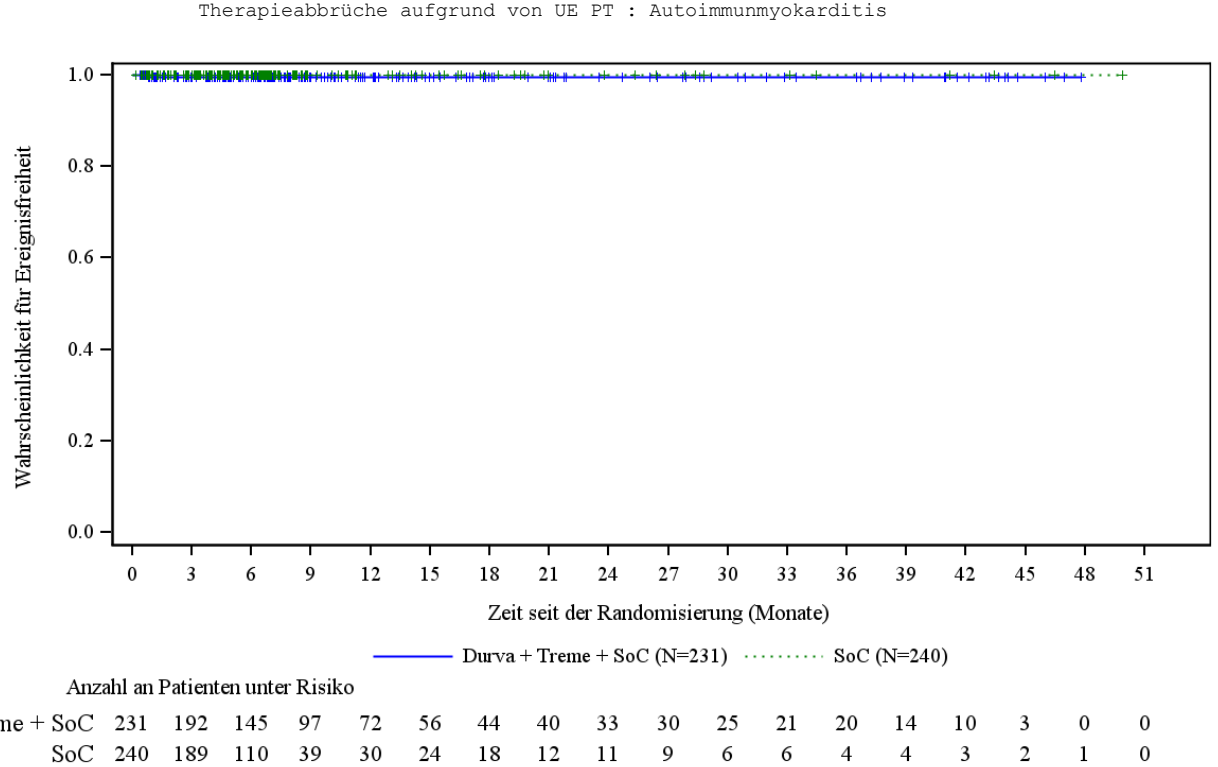
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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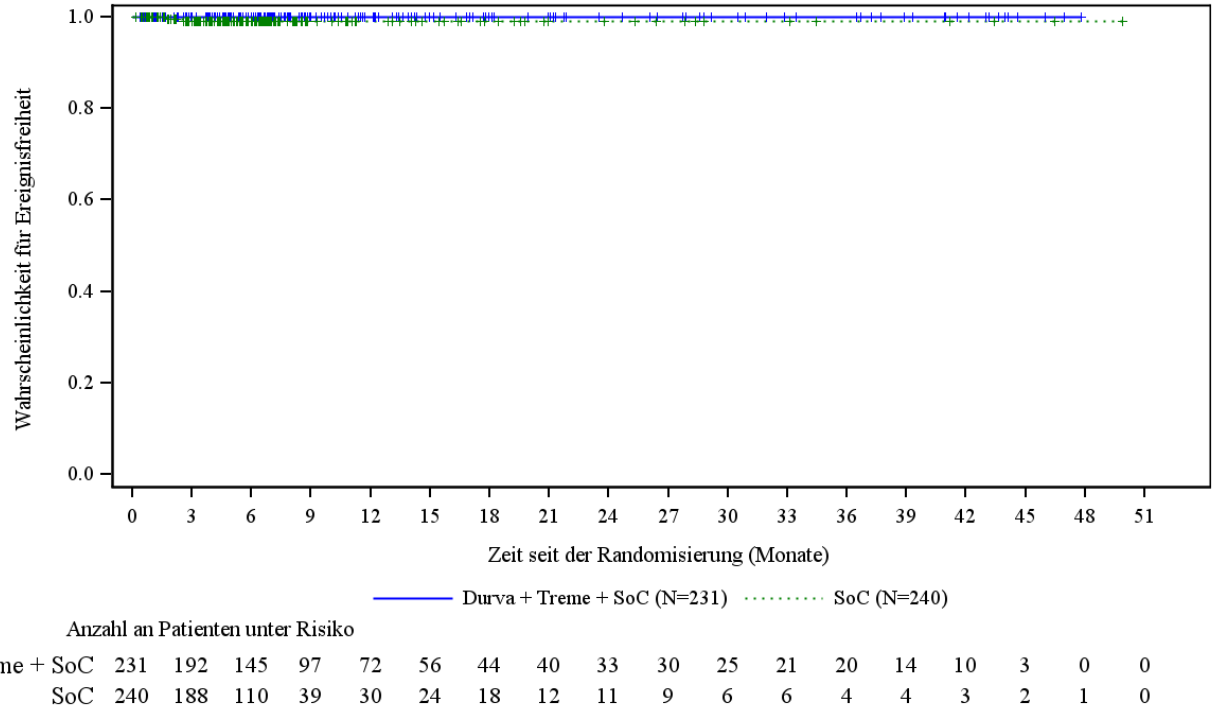
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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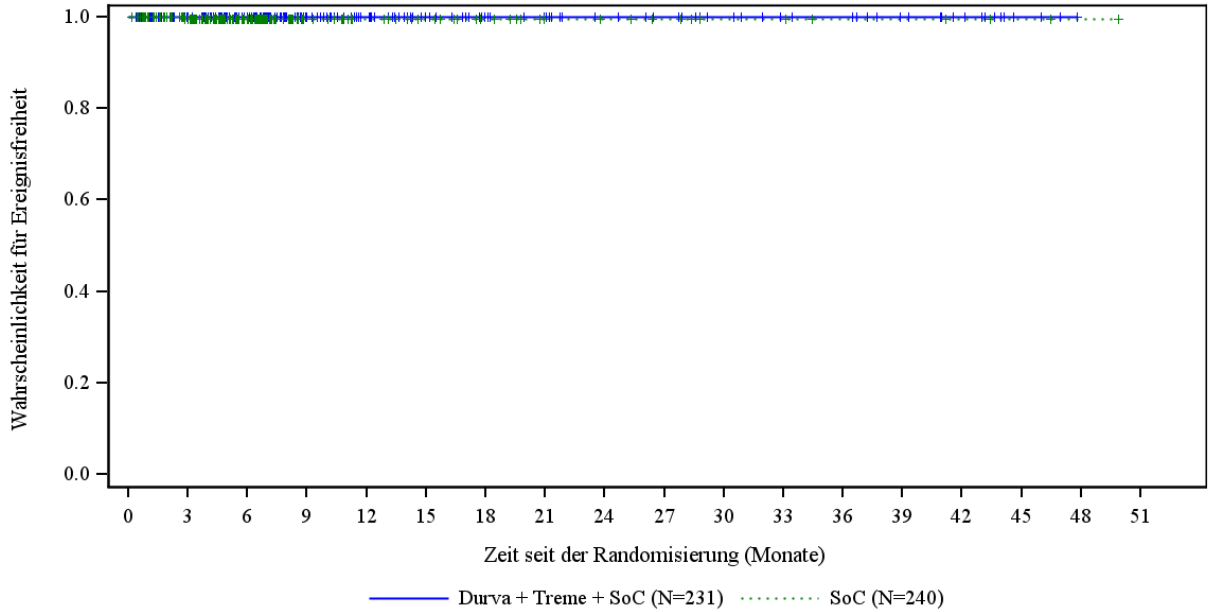
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Kardiopulmonales Versagen



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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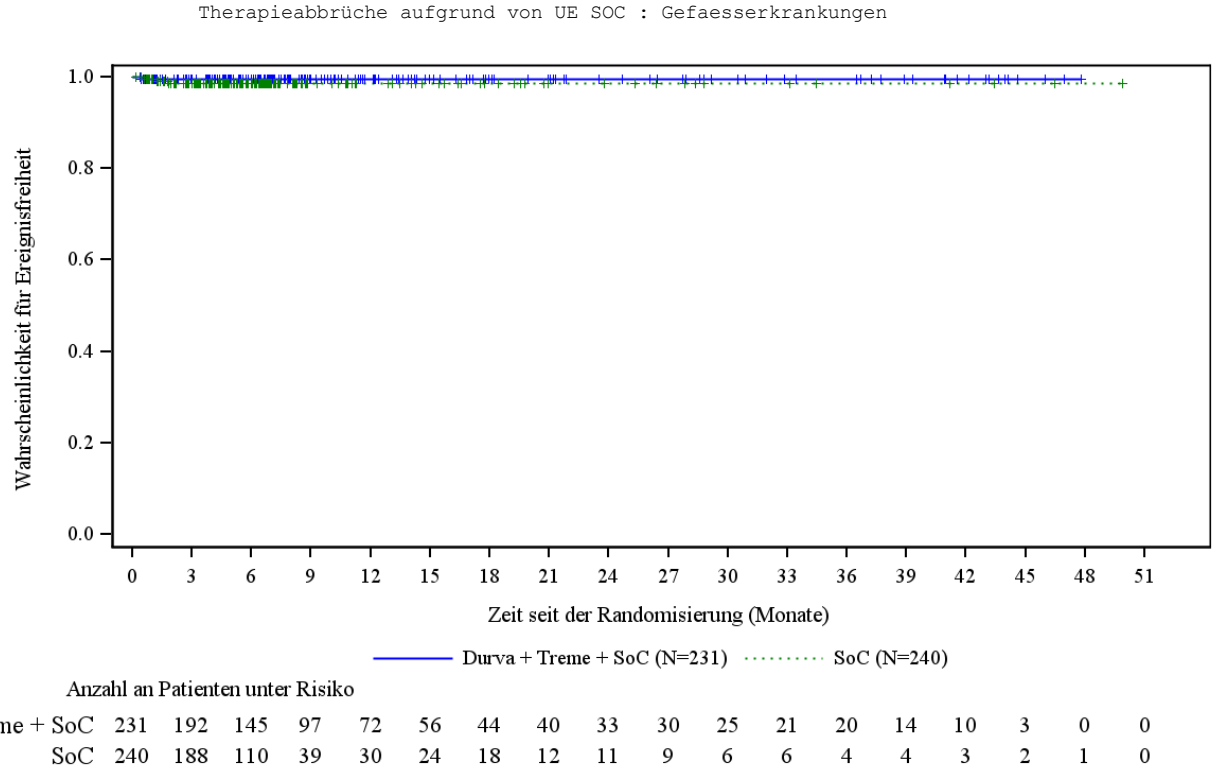
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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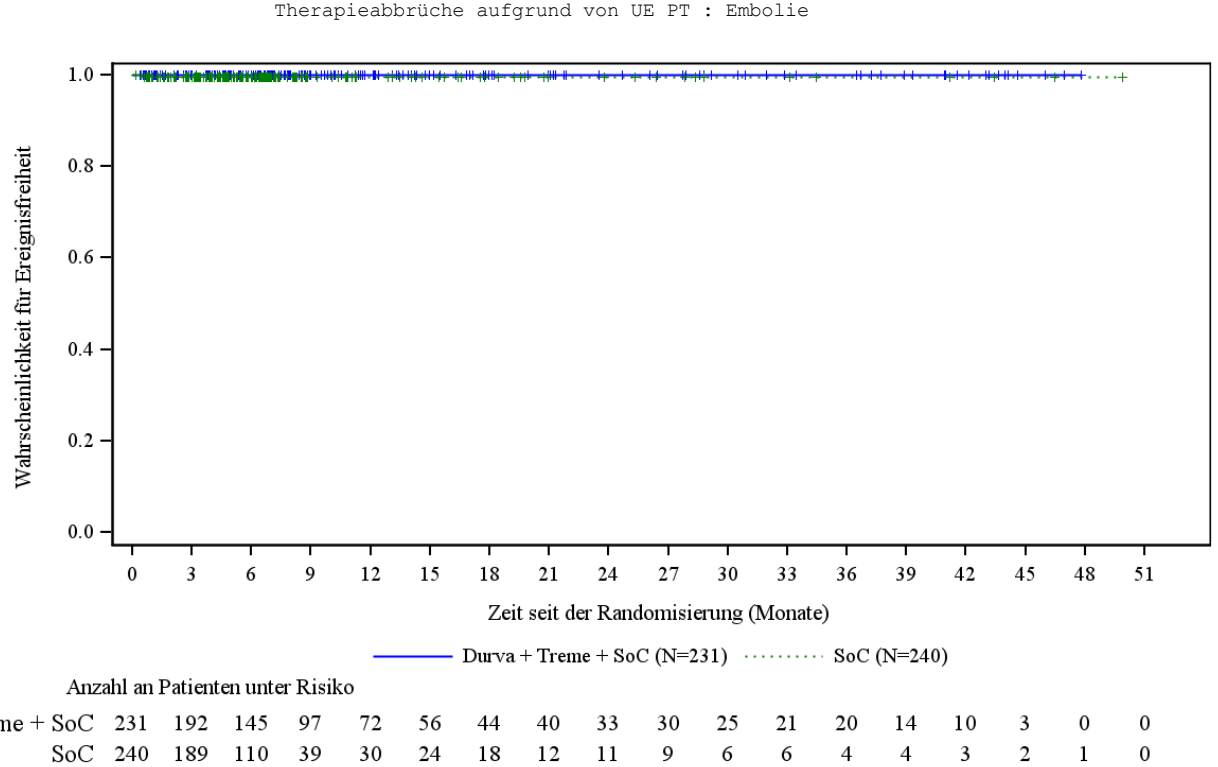
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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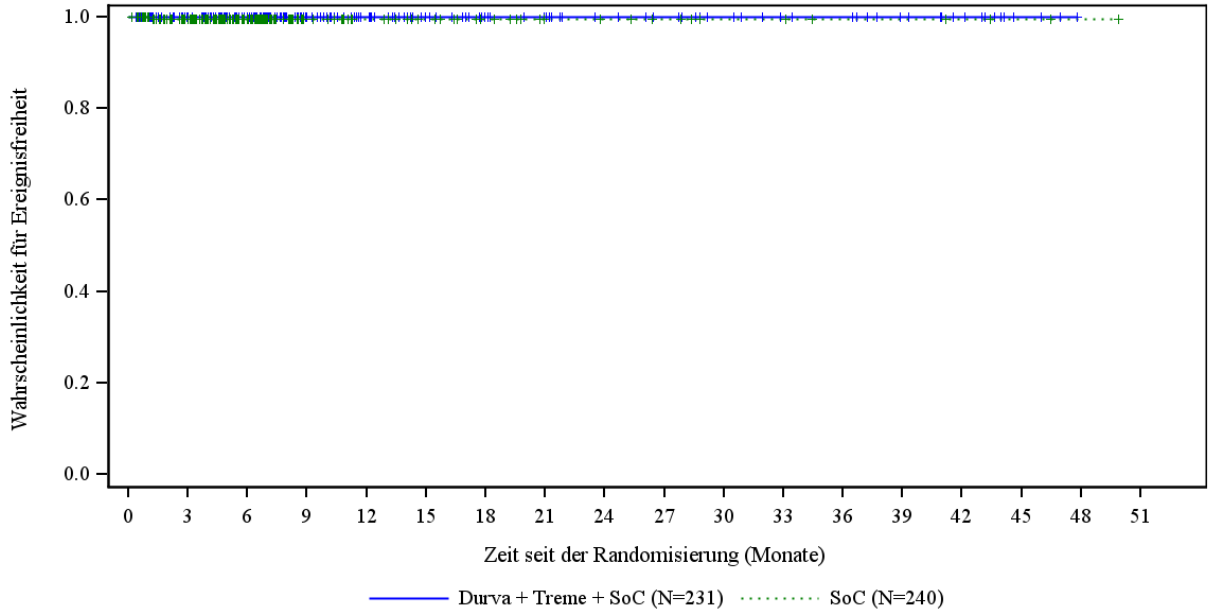
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Haemorrhagischer Schock



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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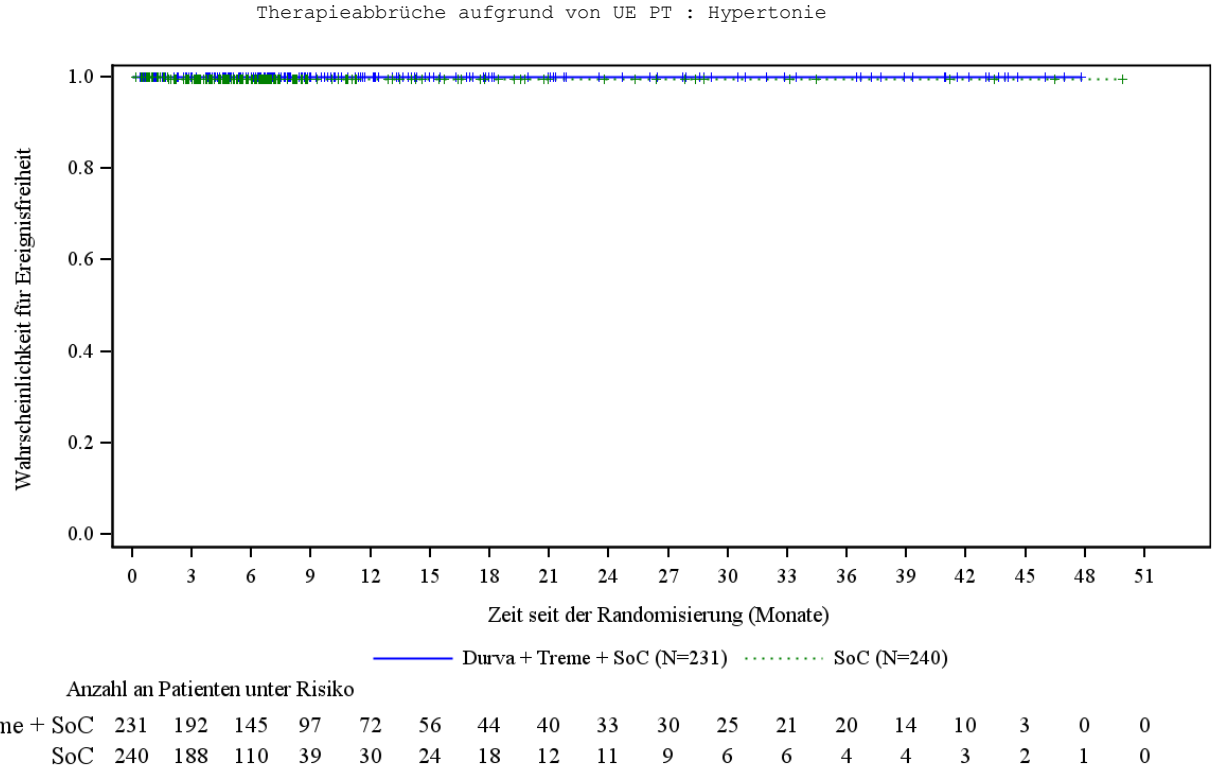
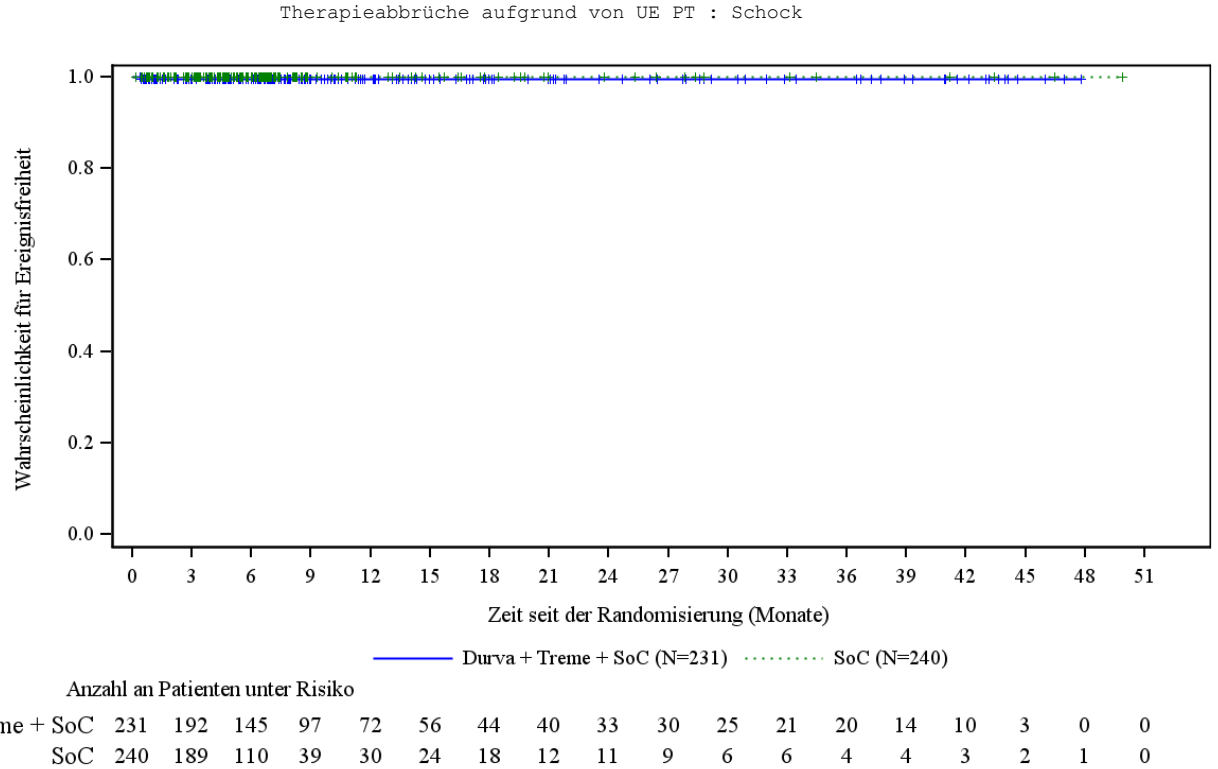
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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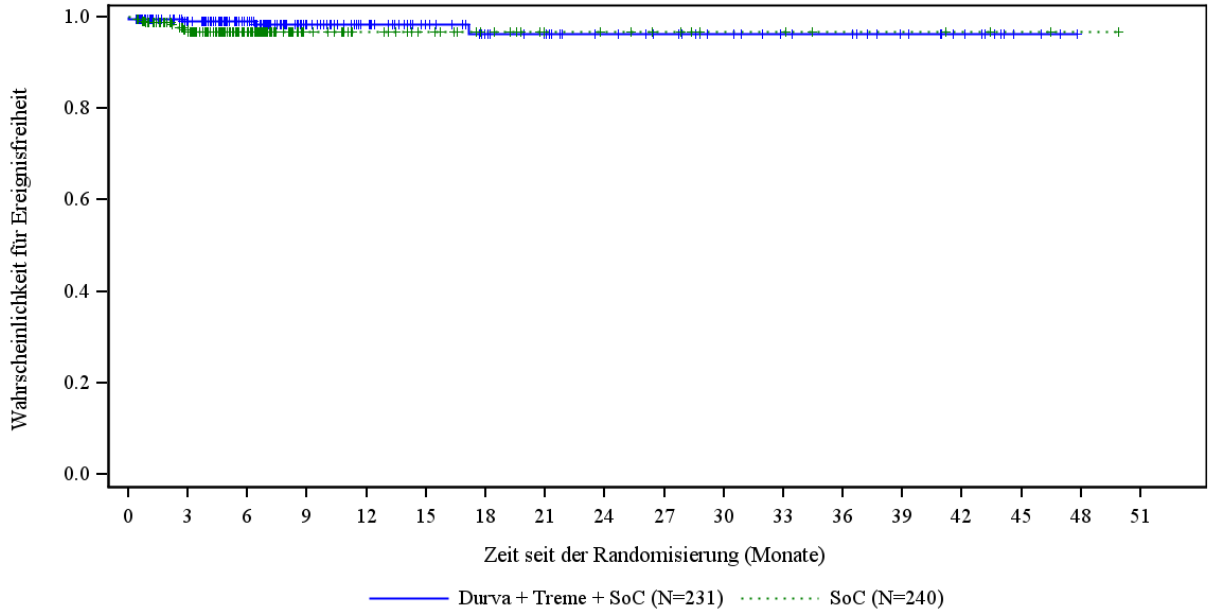
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen der Atemwege, des Brustraums und Mediastinums



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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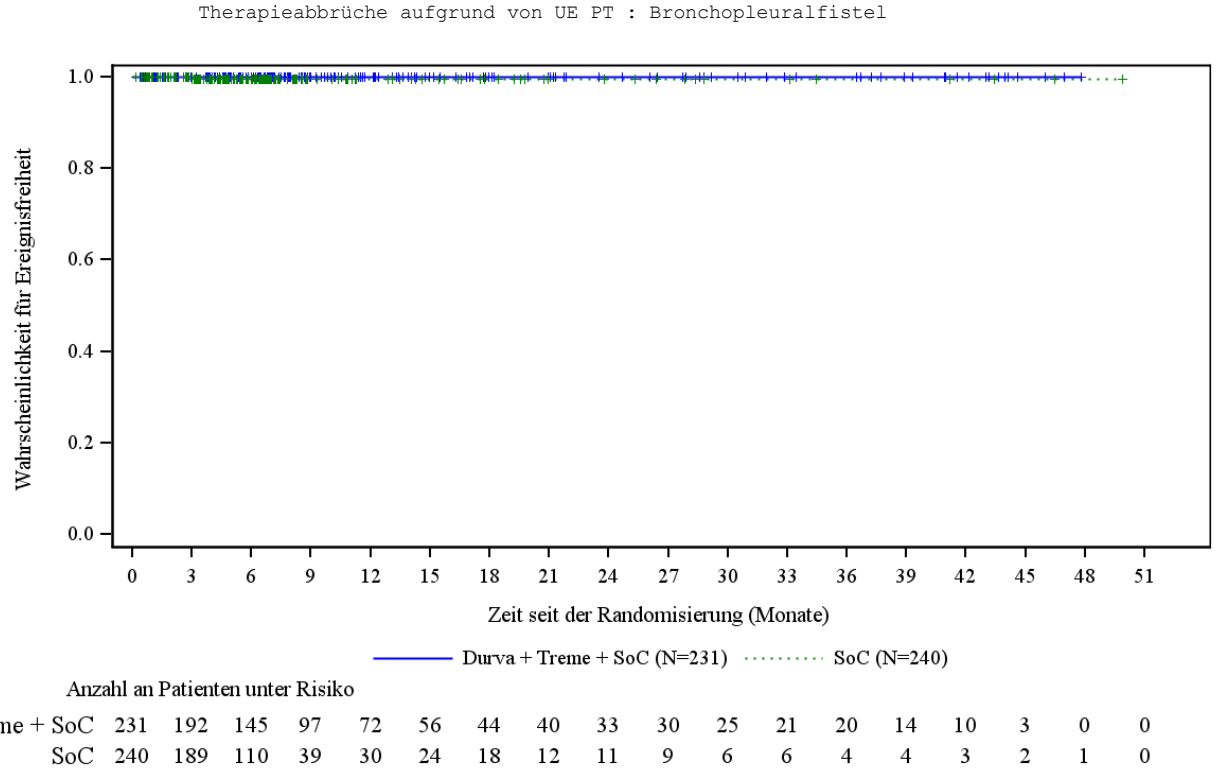
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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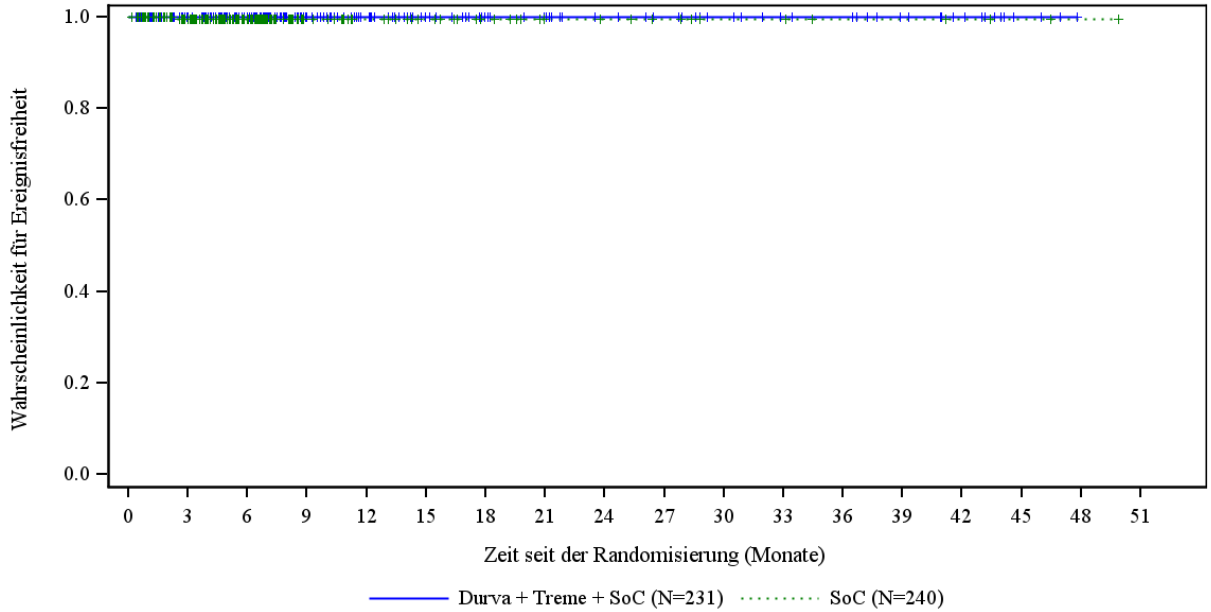
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Interstitielle Lungenerkrankung



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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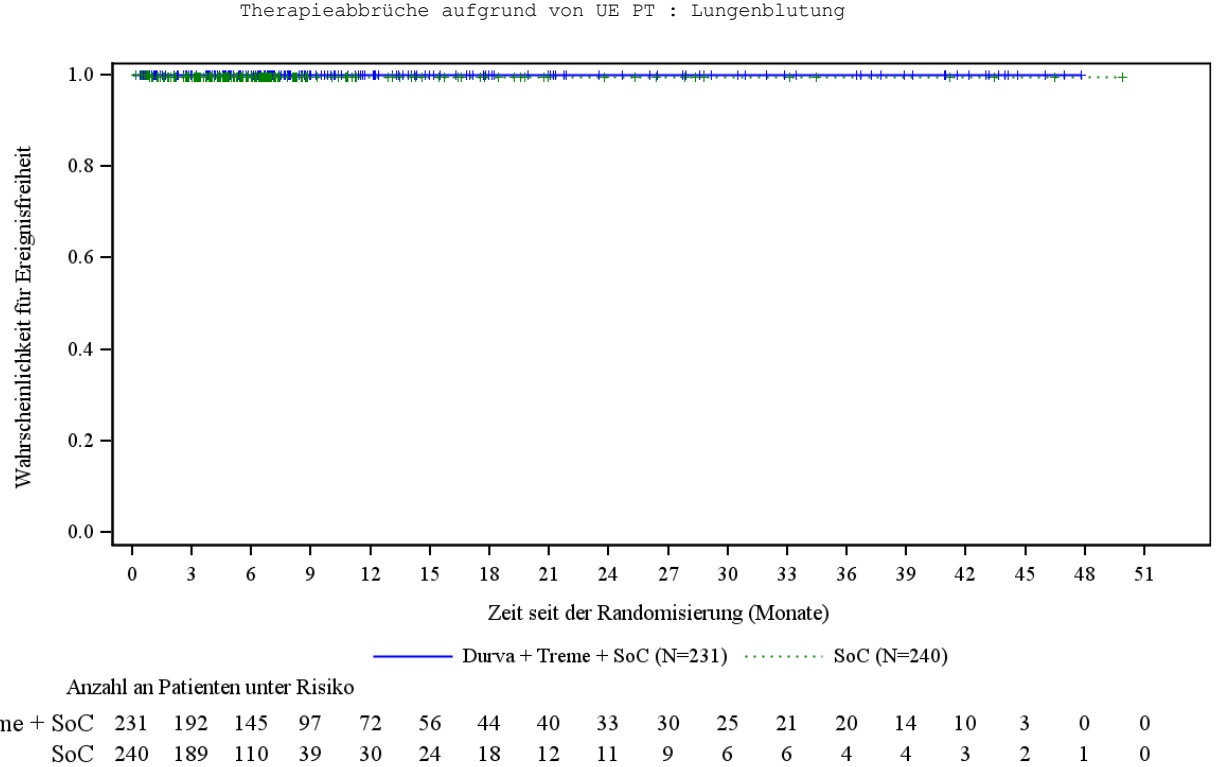
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



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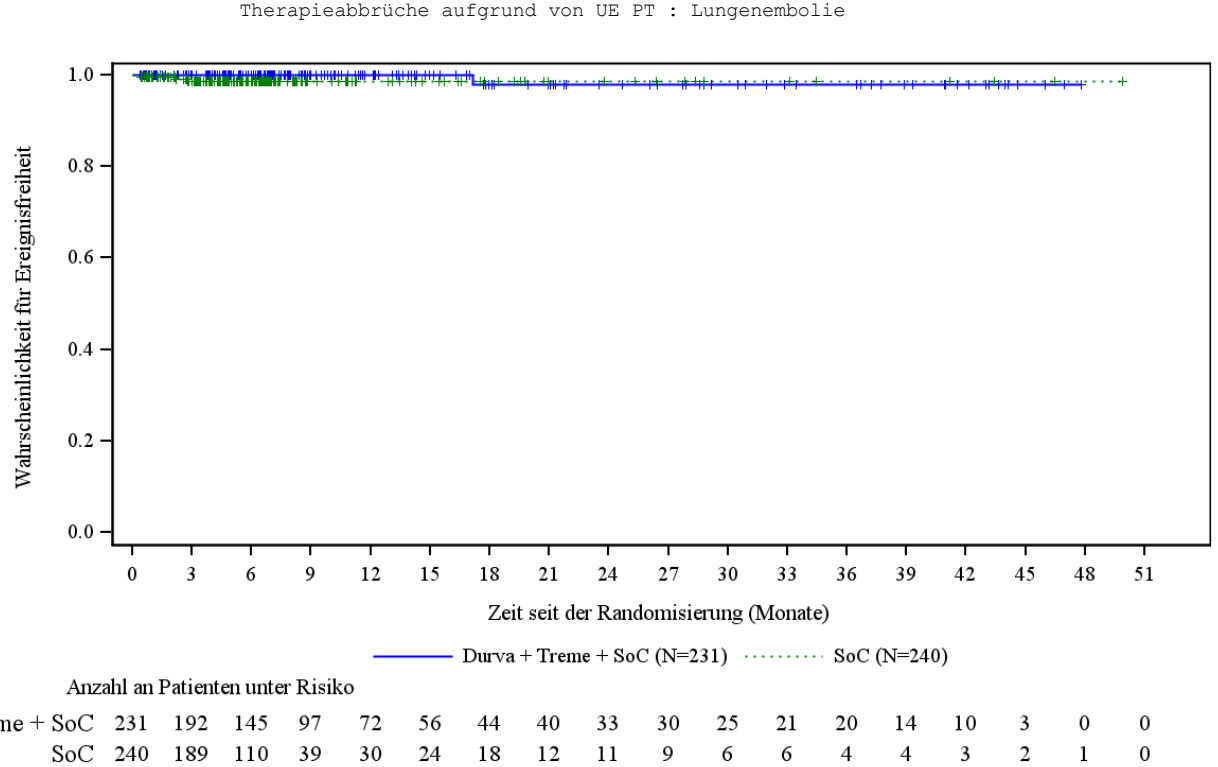
Data Cut-off: 25th October 2021



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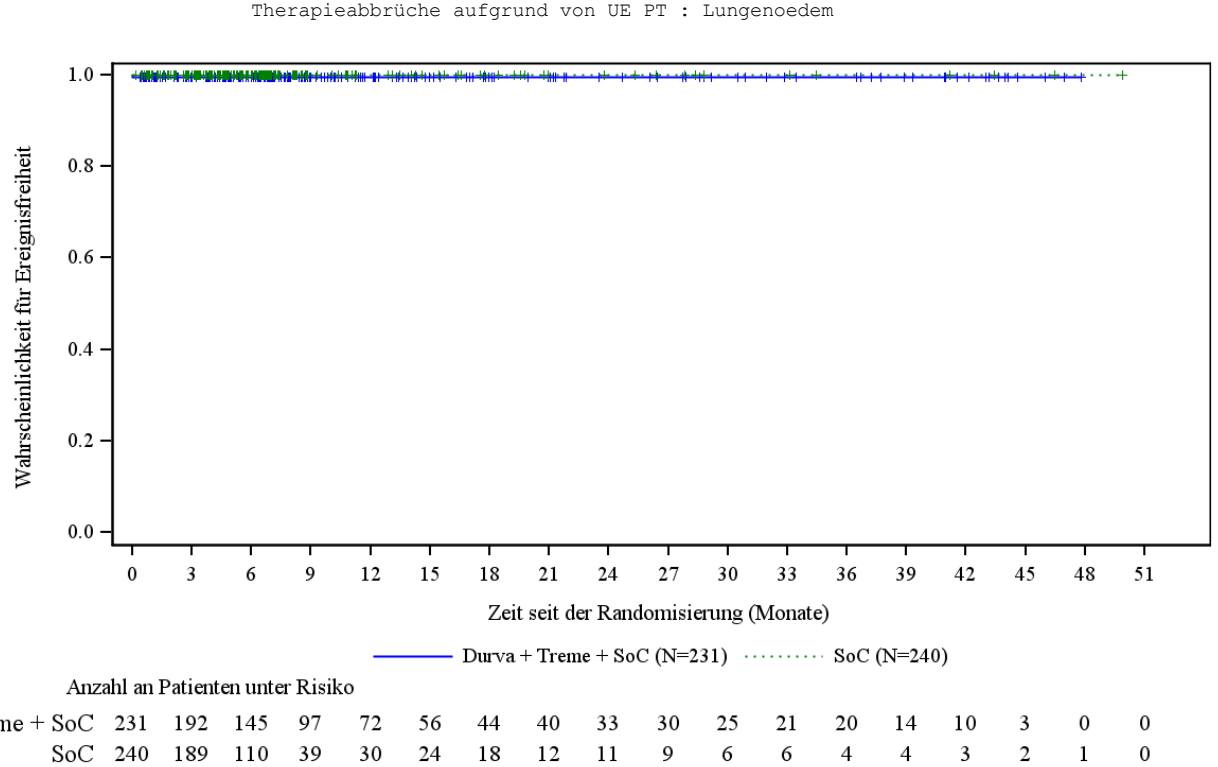
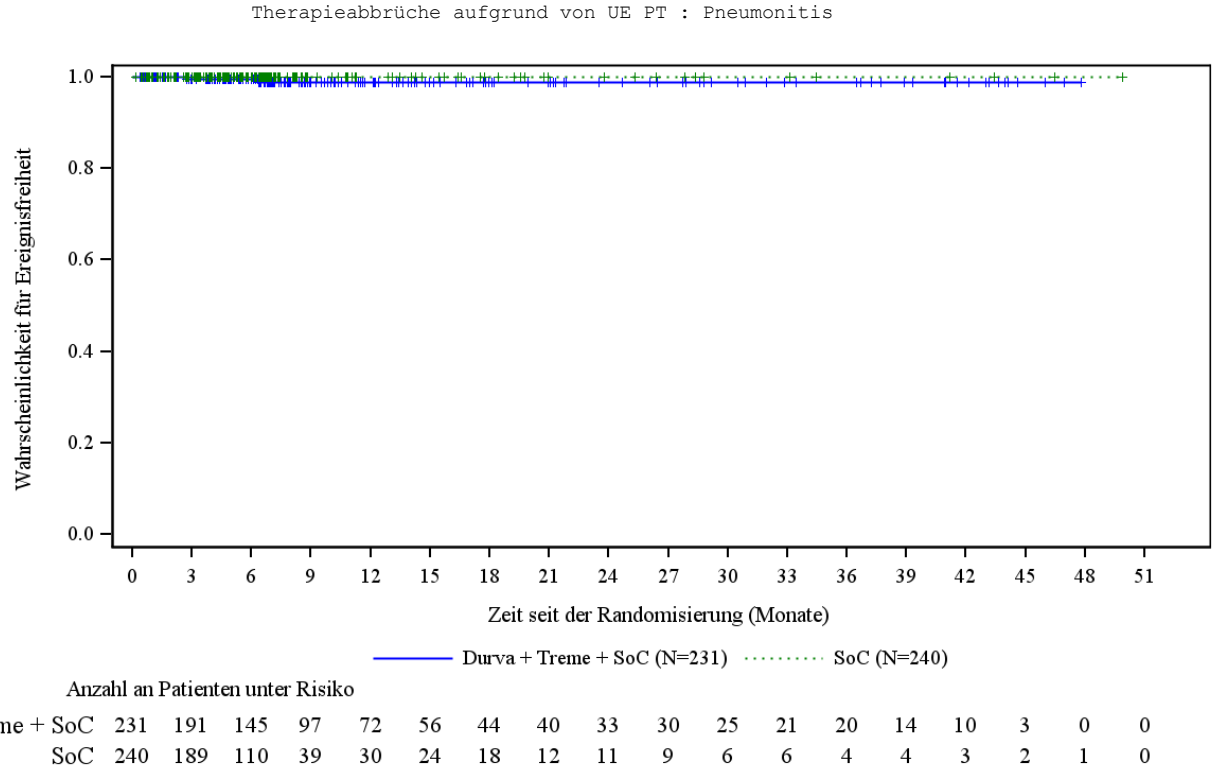
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

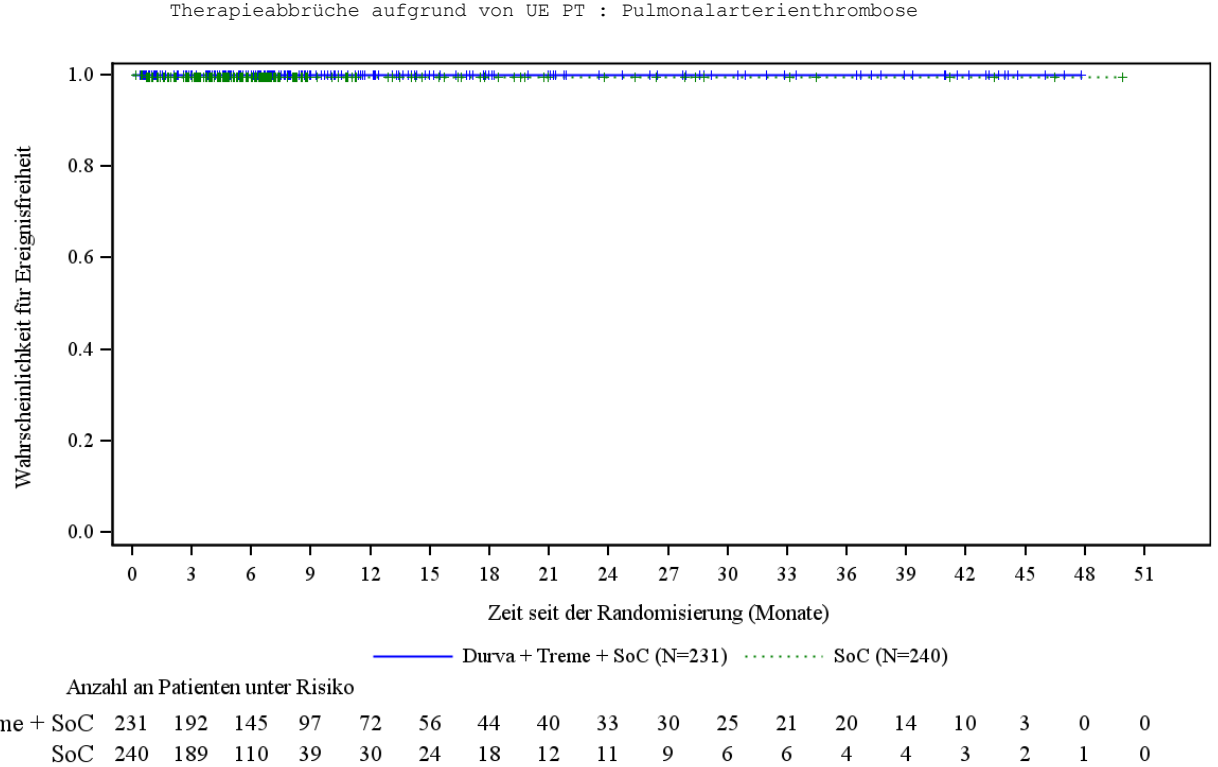

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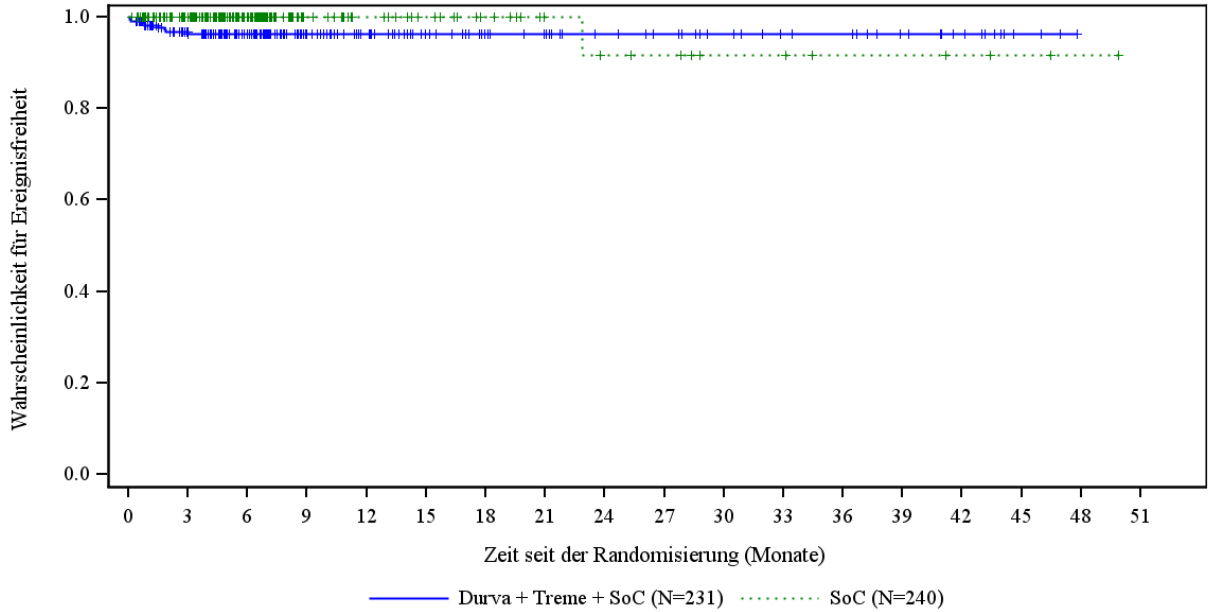
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen des Gastrointestinaltrakts



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	187	141	95	71	55	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	10	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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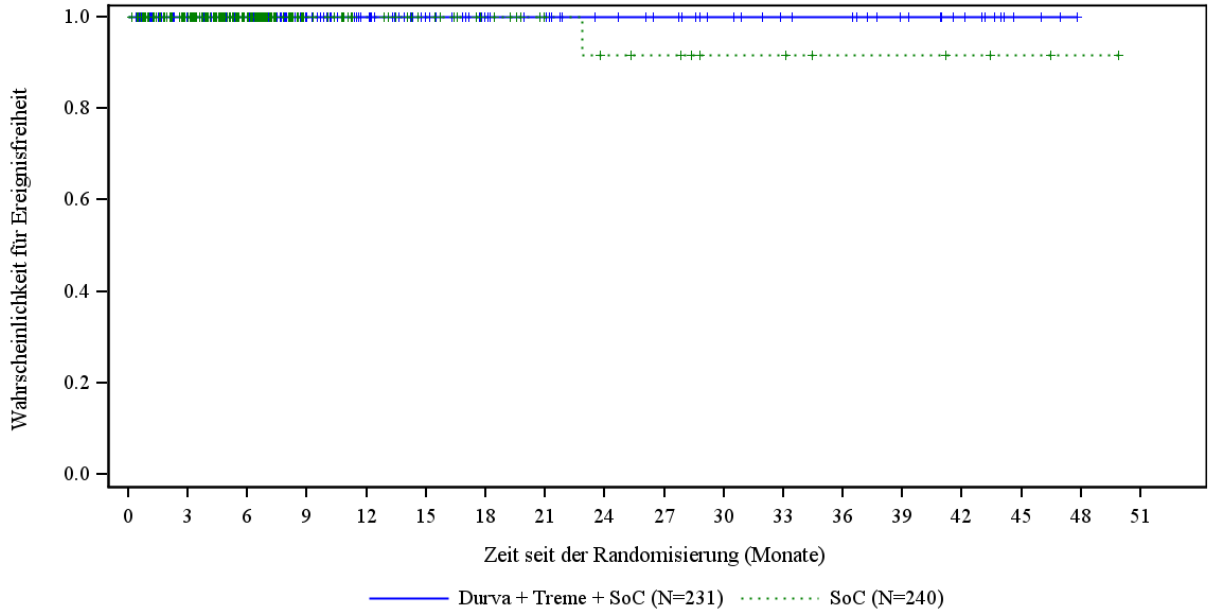
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Abdominalschmerz



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	10	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

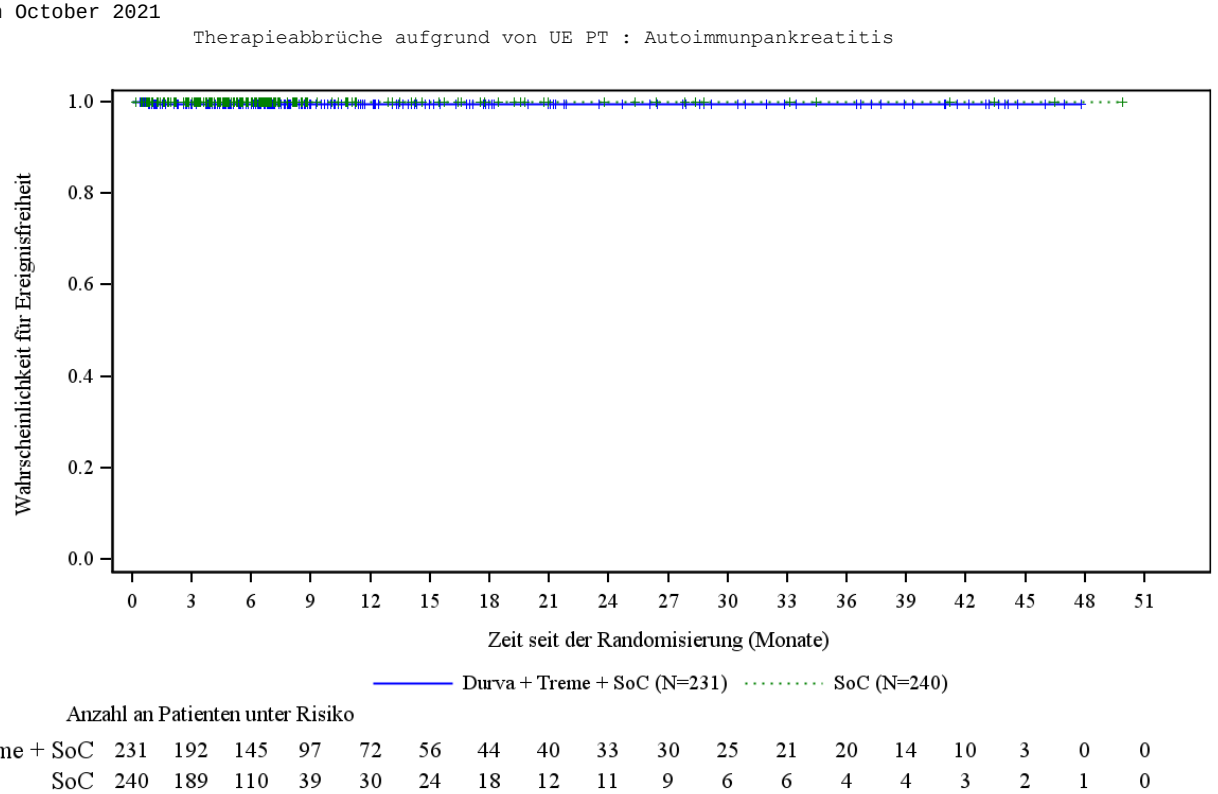

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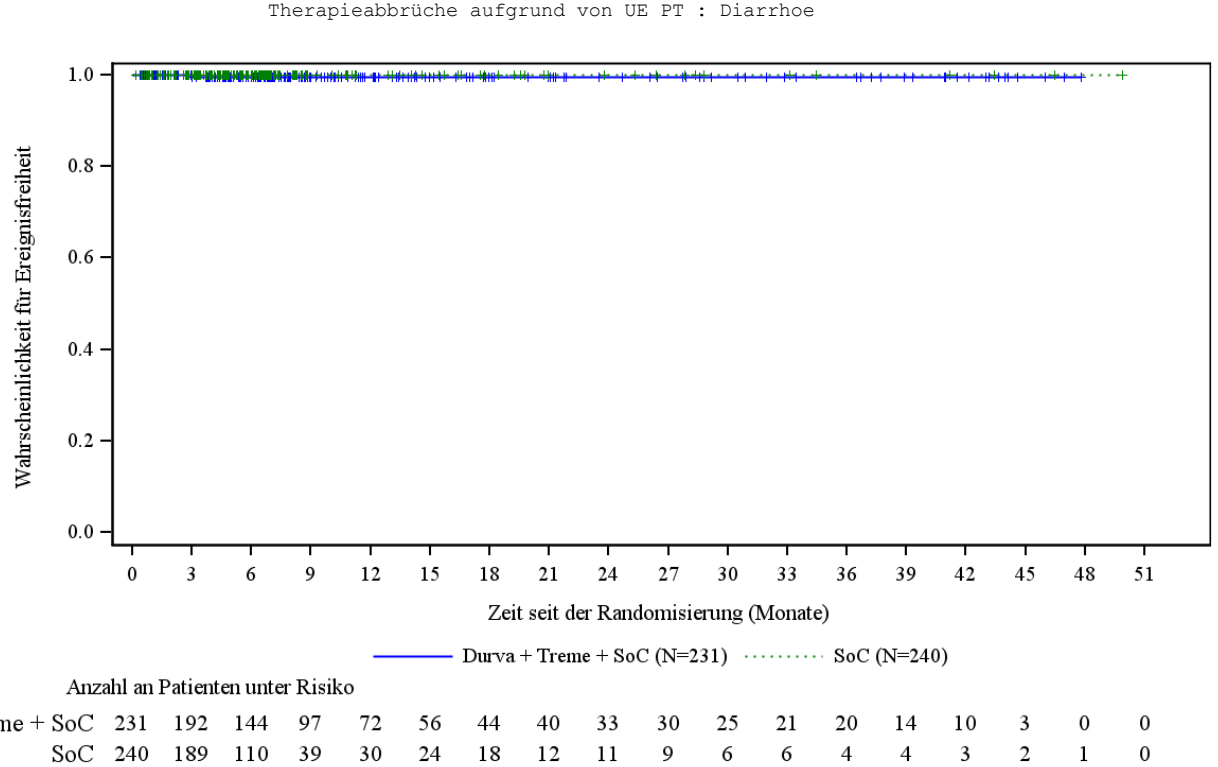
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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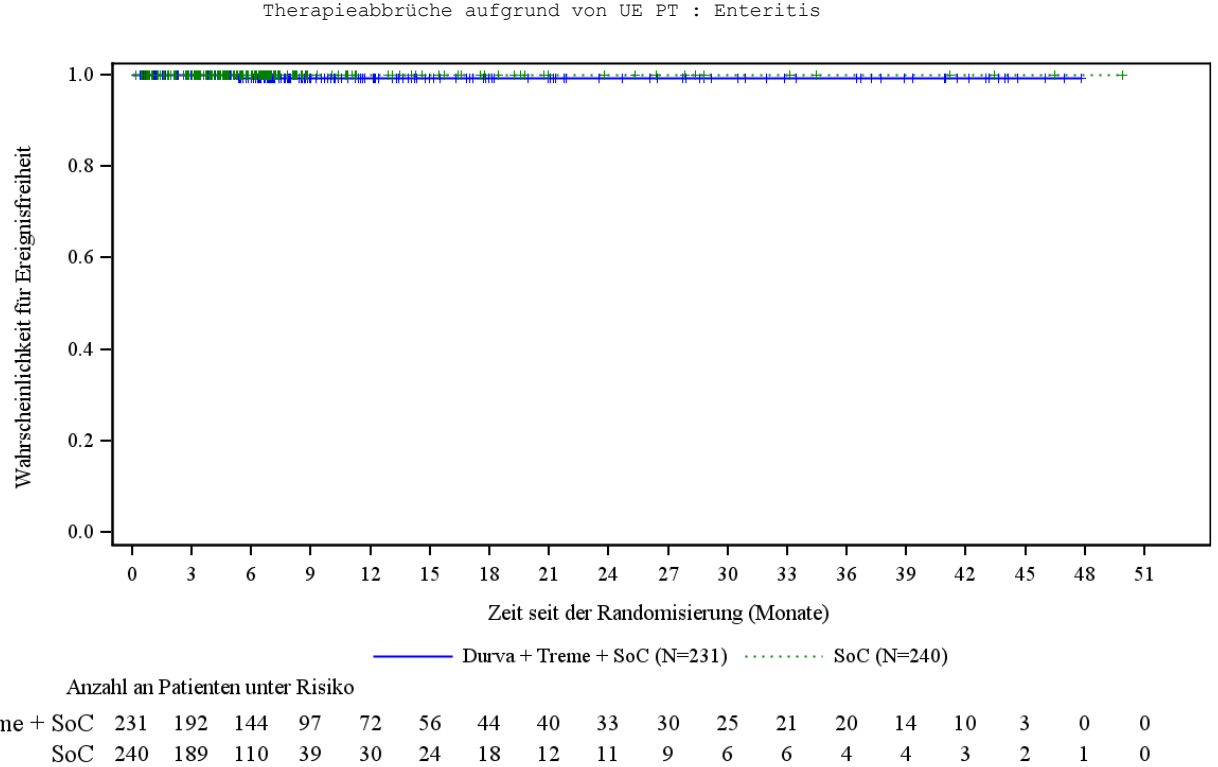
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



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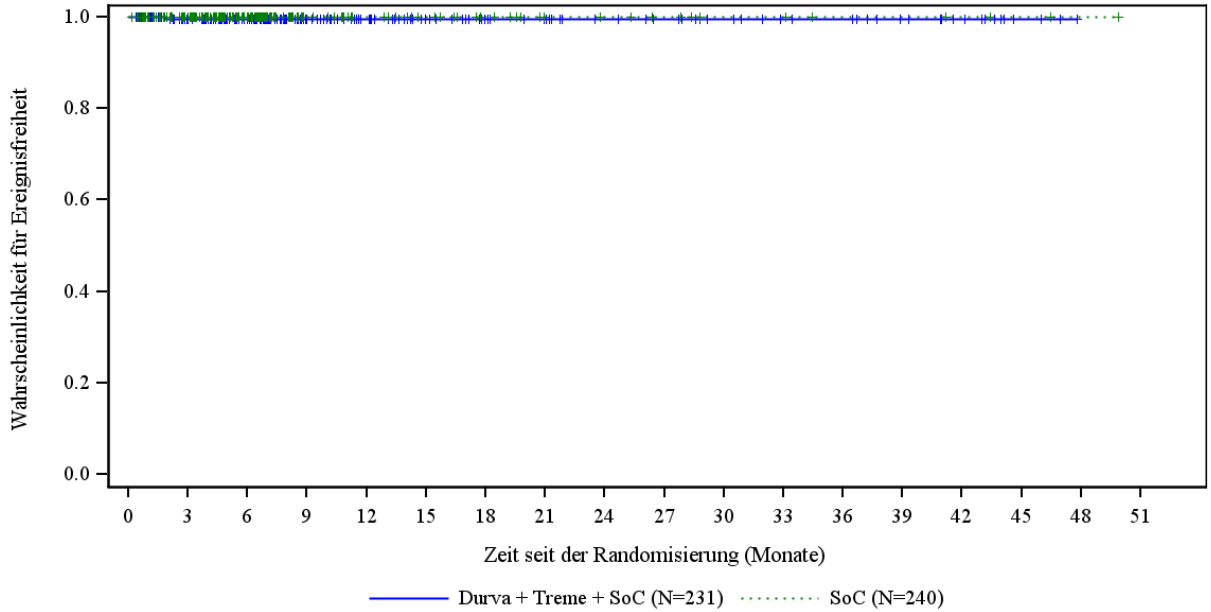
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Enterokolitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	71	55	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
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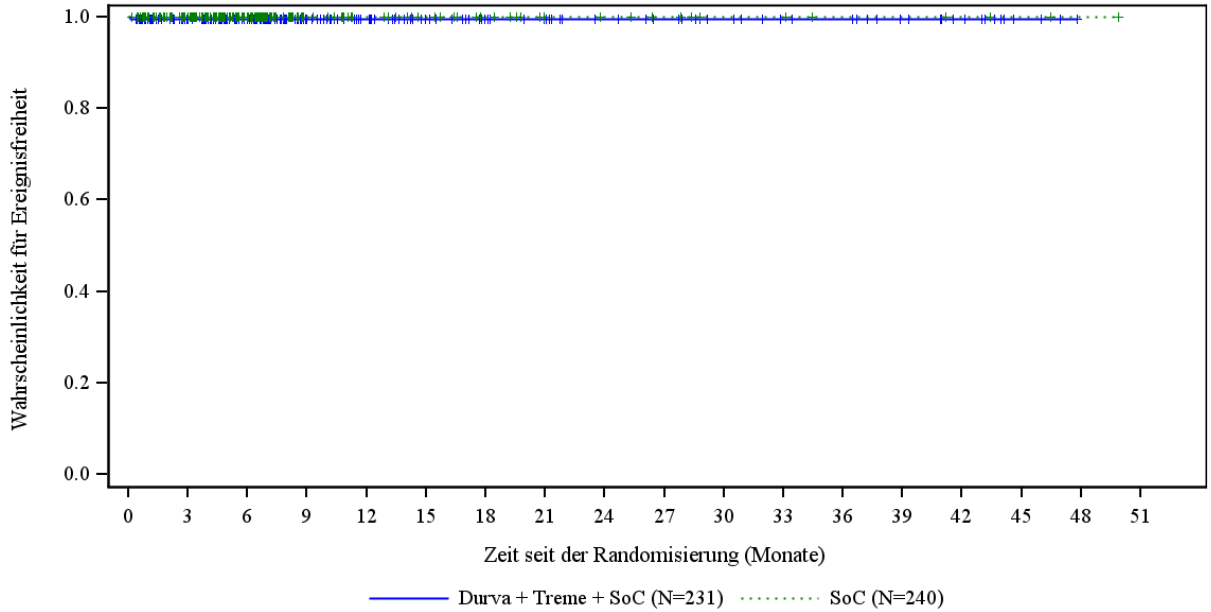
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Erbrechen



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

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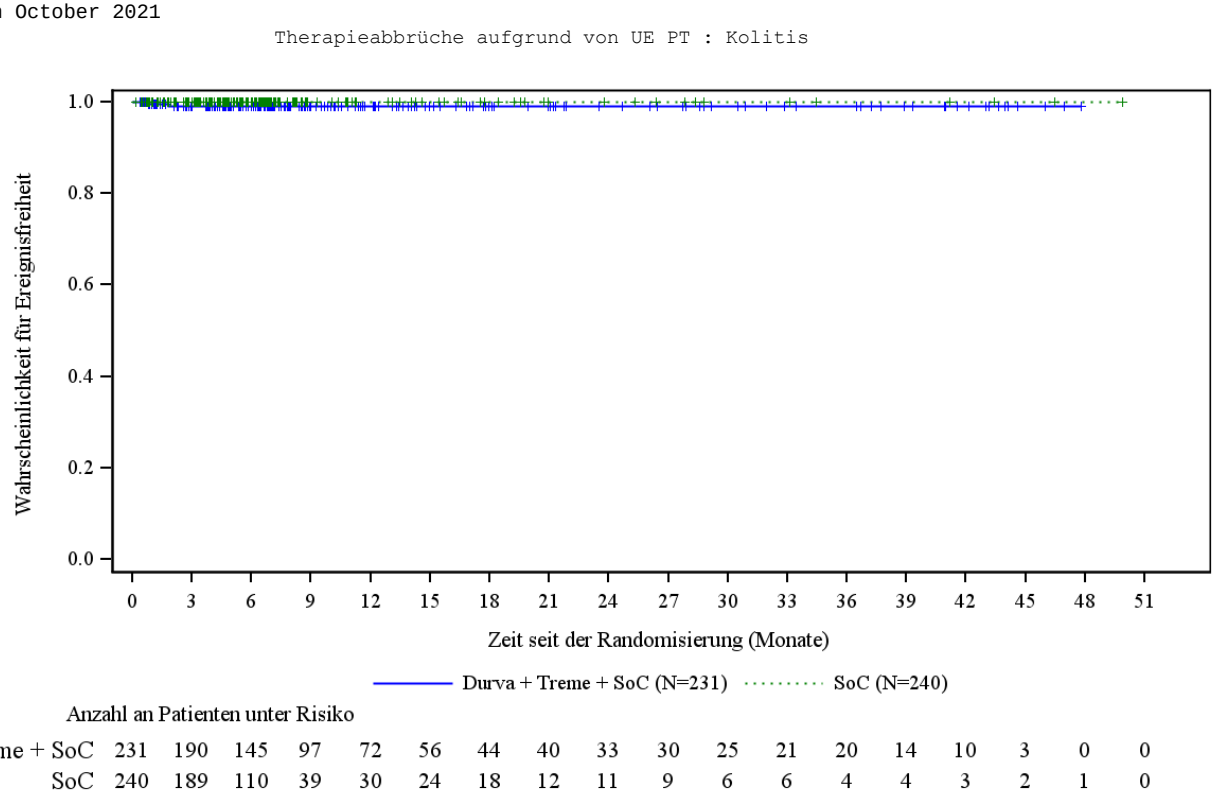
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



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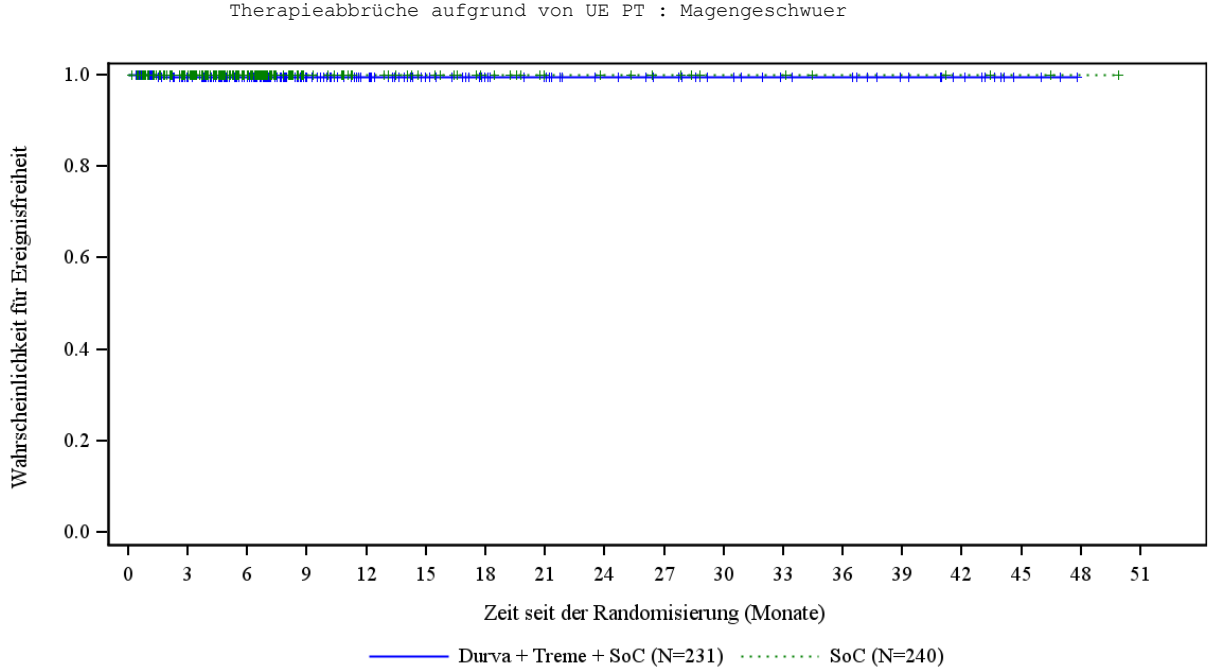
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

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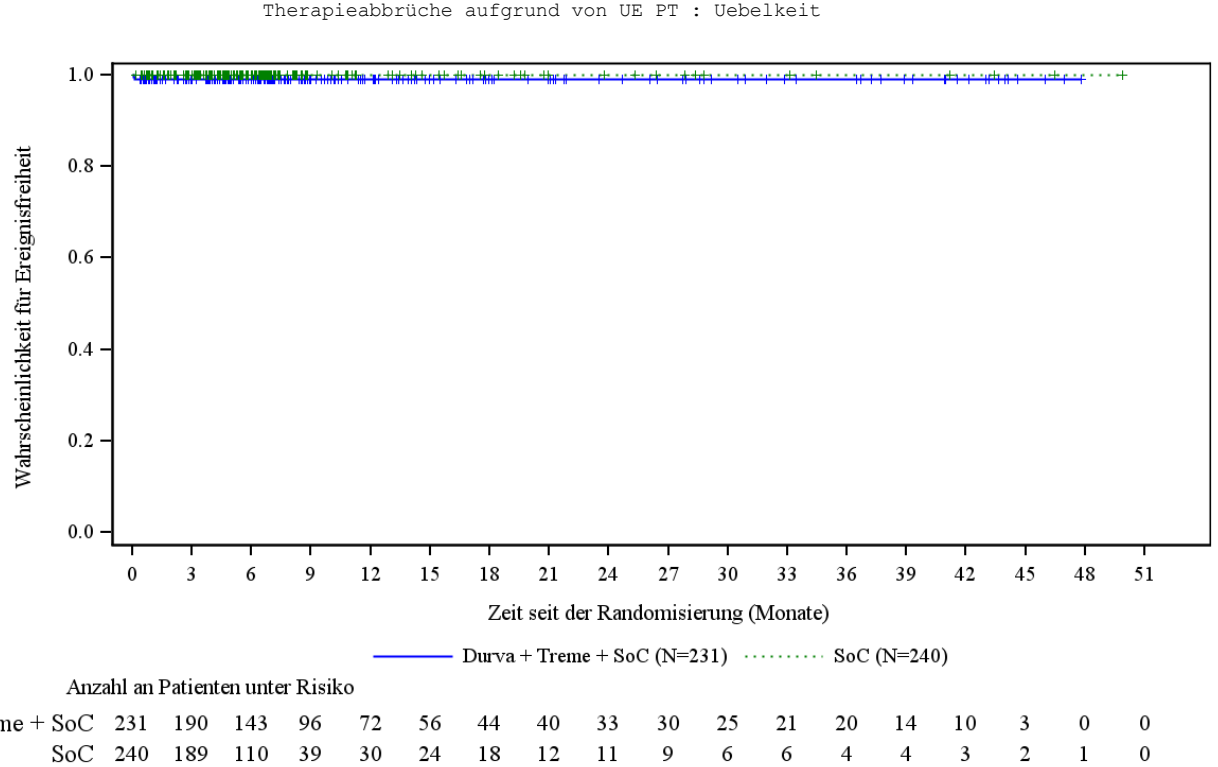
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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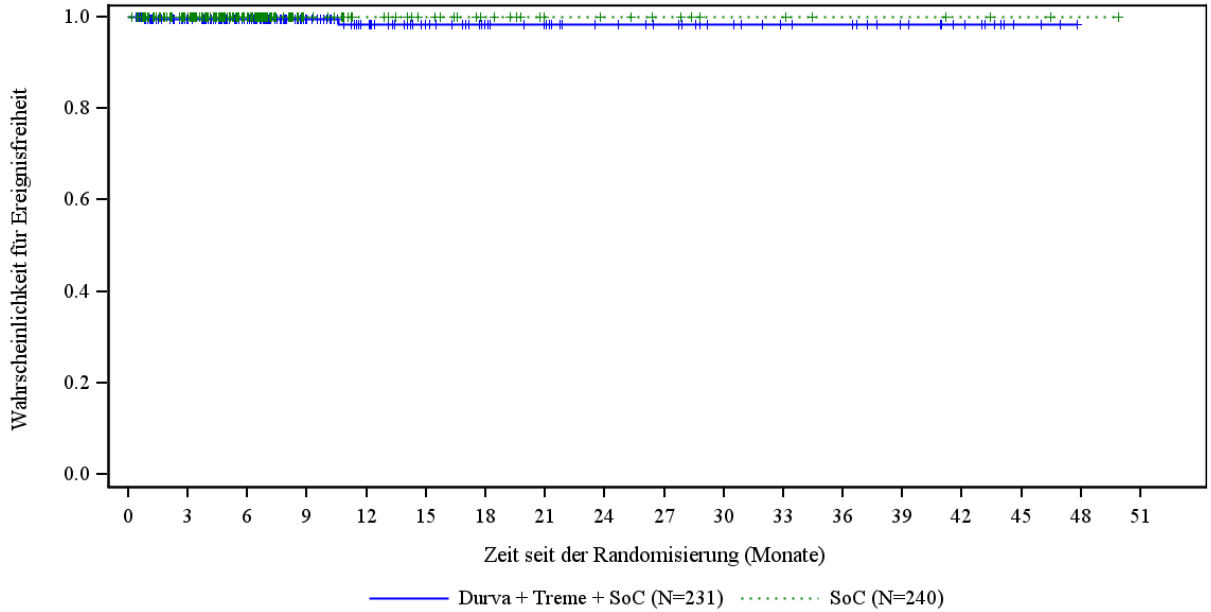
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Leber- und Gallenerkrankungen



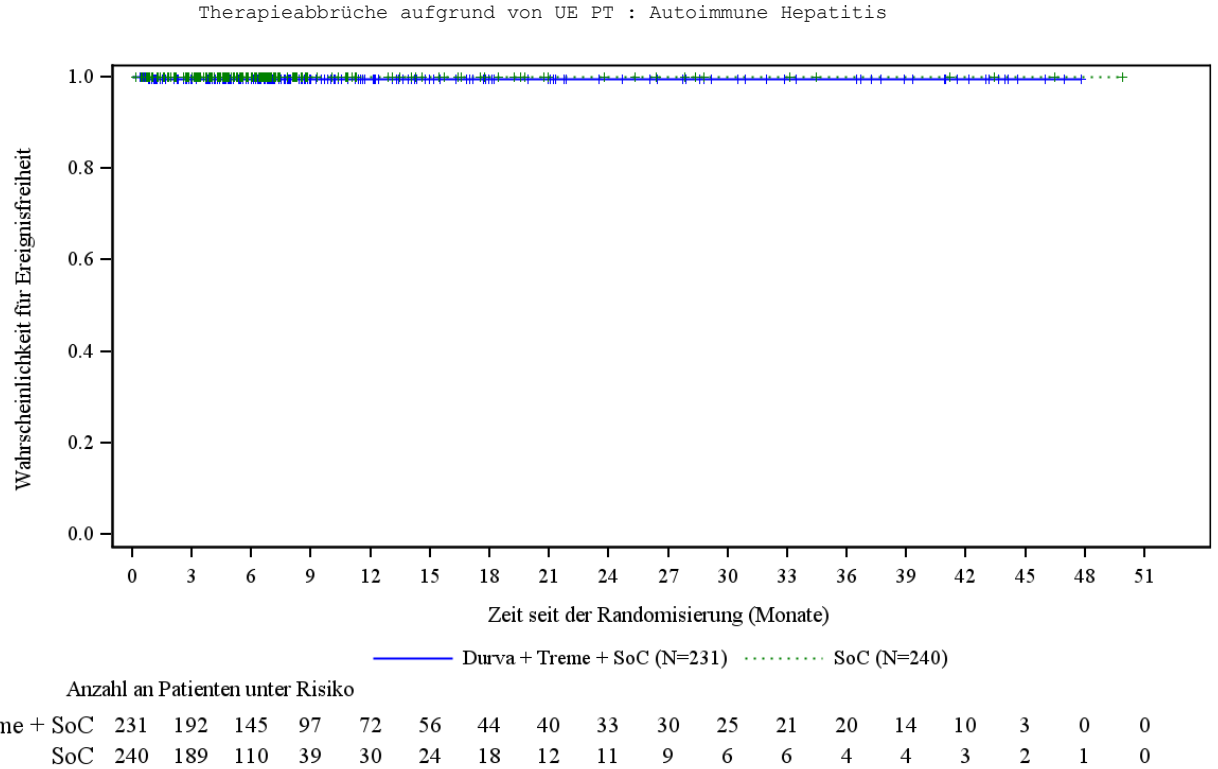
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	71	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

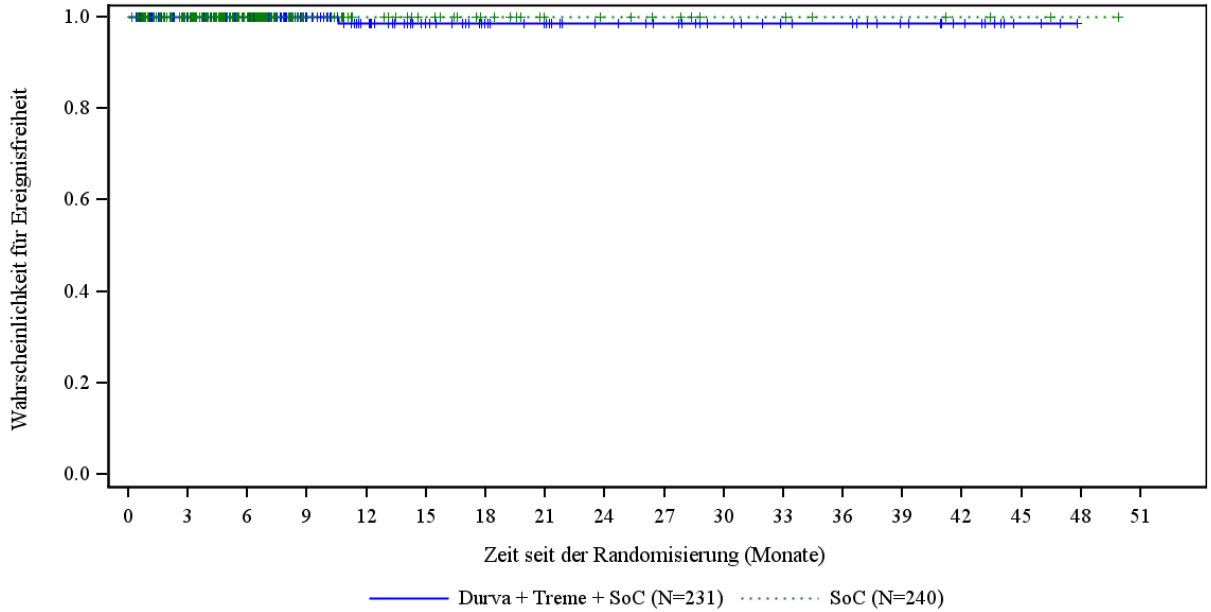


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Immunvermittelte Hepatitis



Anzahl an Patienten unter Risiko

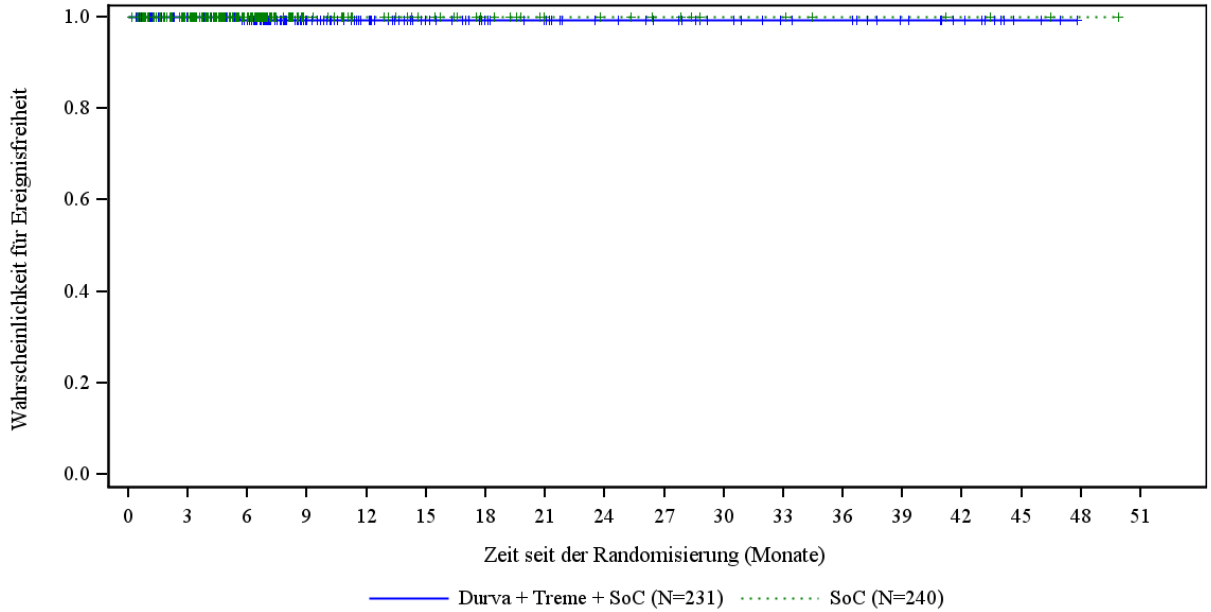
Durva + Treme + SoC	231	192	145	97	71	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen



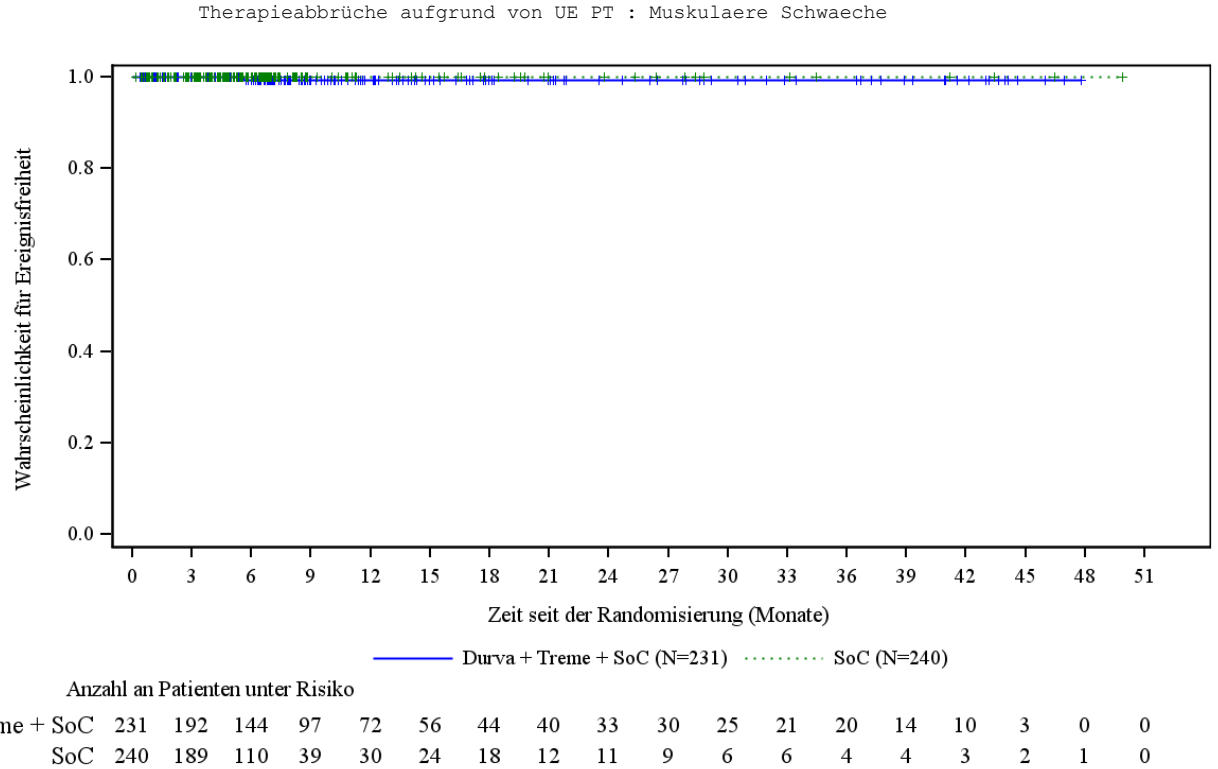
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

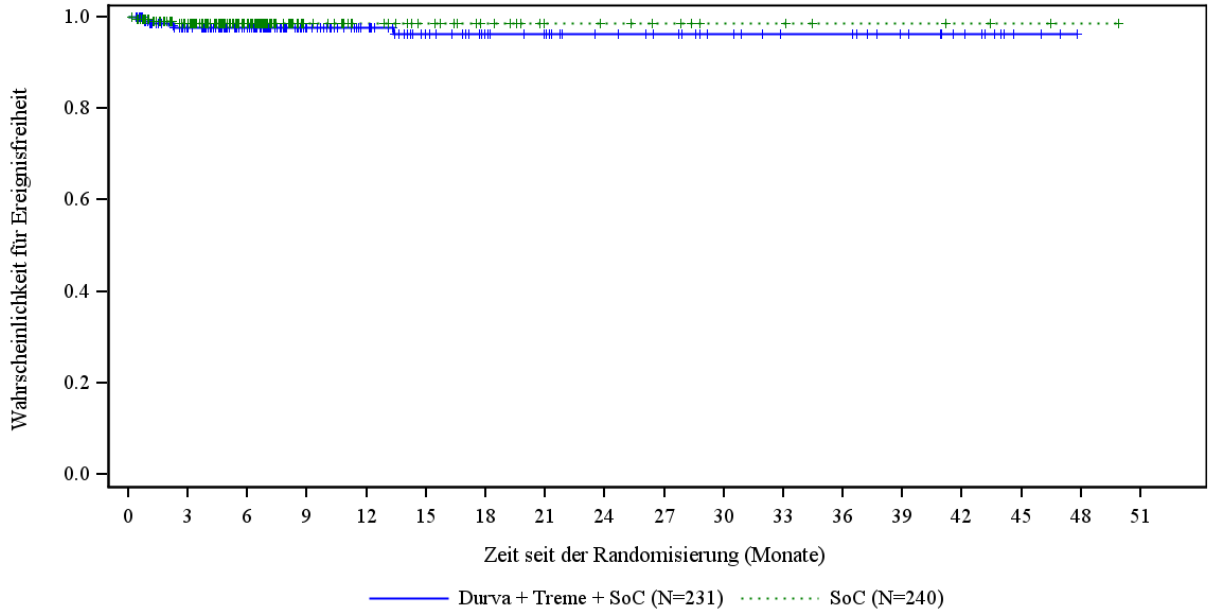


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Erkrankungen der Nieren und Harnwege



Anzahl an Patienten unter Risiko

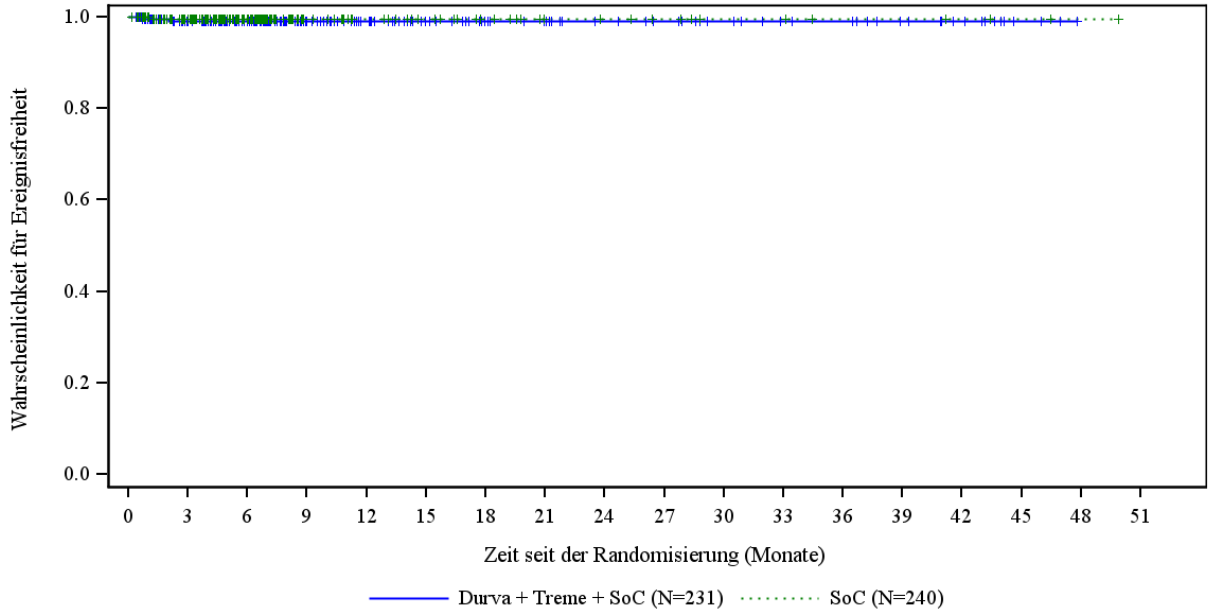
Durva + Treme + SoC	231	191	145	97	72	55	43	39	32	29	24	20	20	14	10	3	0	0
SoC	240	187	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Akute Nierenschaedigung



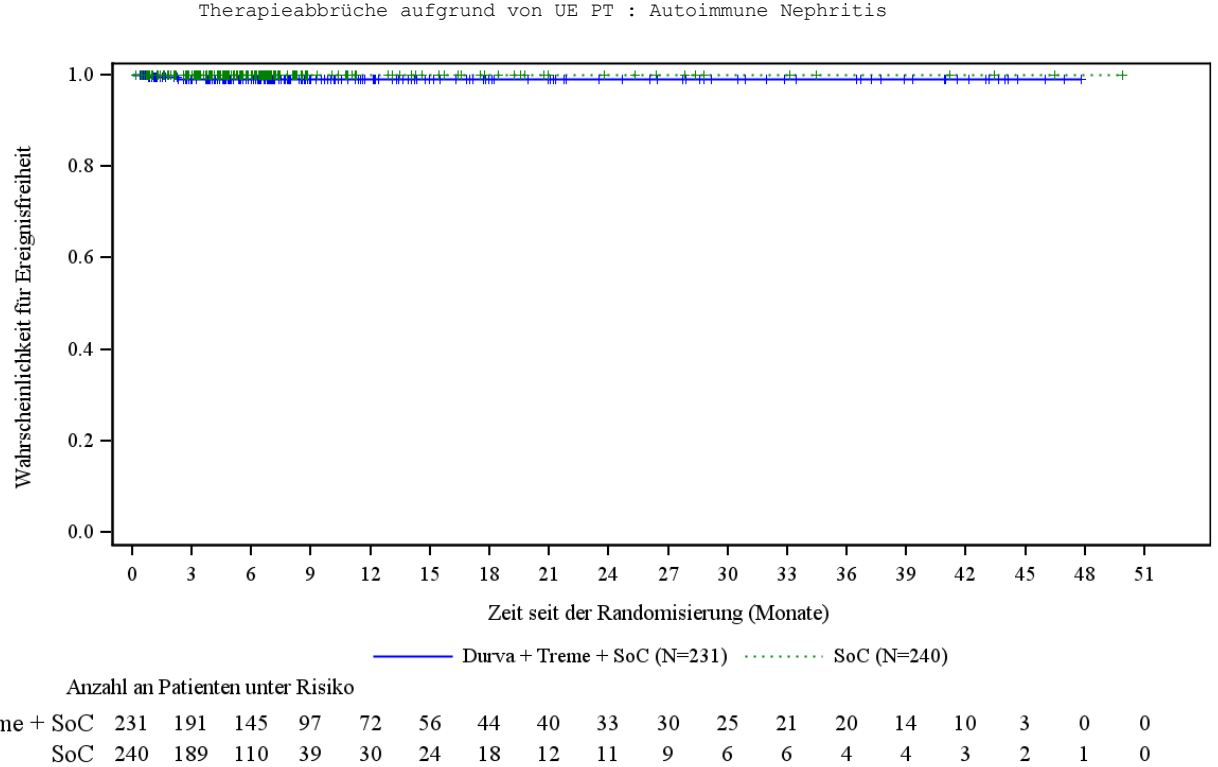
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

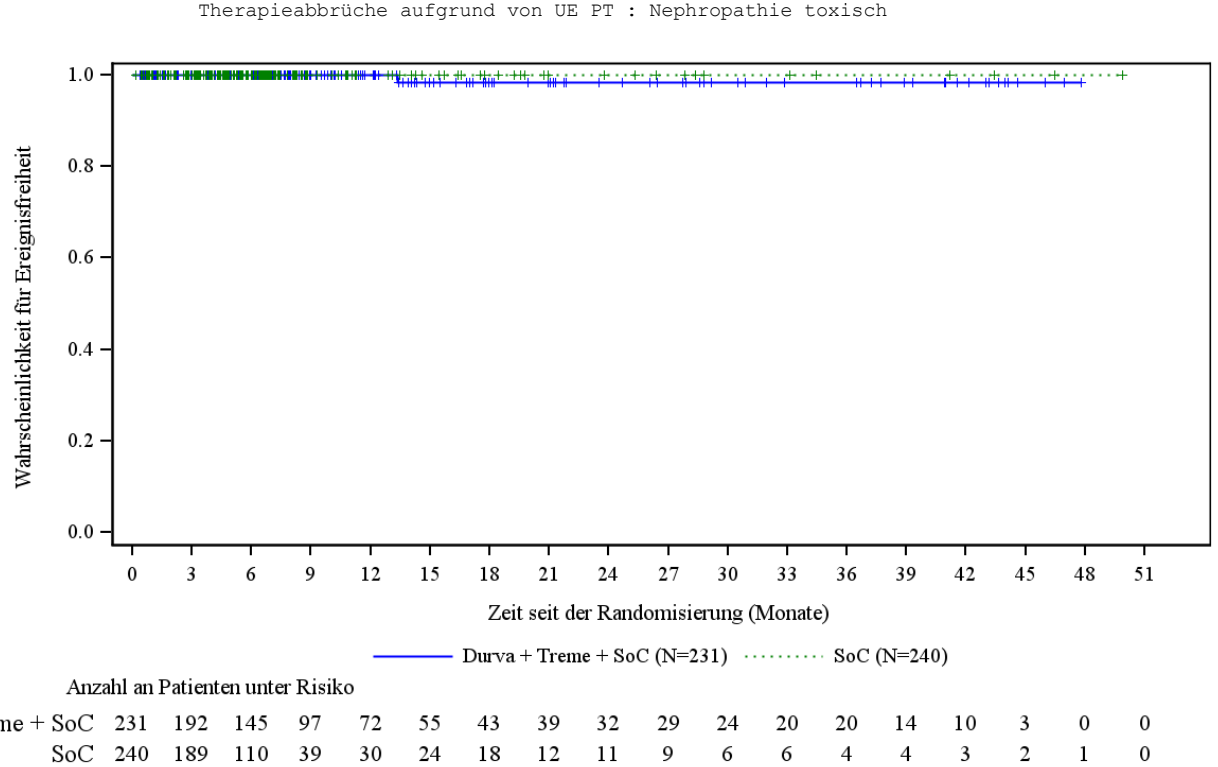
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

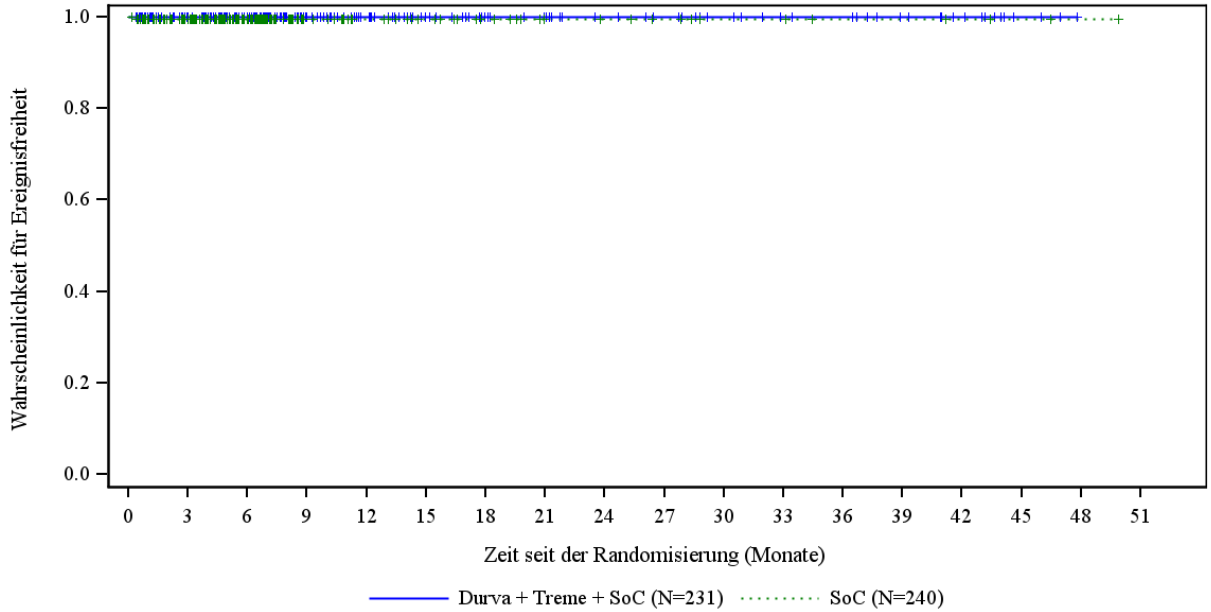


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Nierenfunktionsbeeintraechtigung



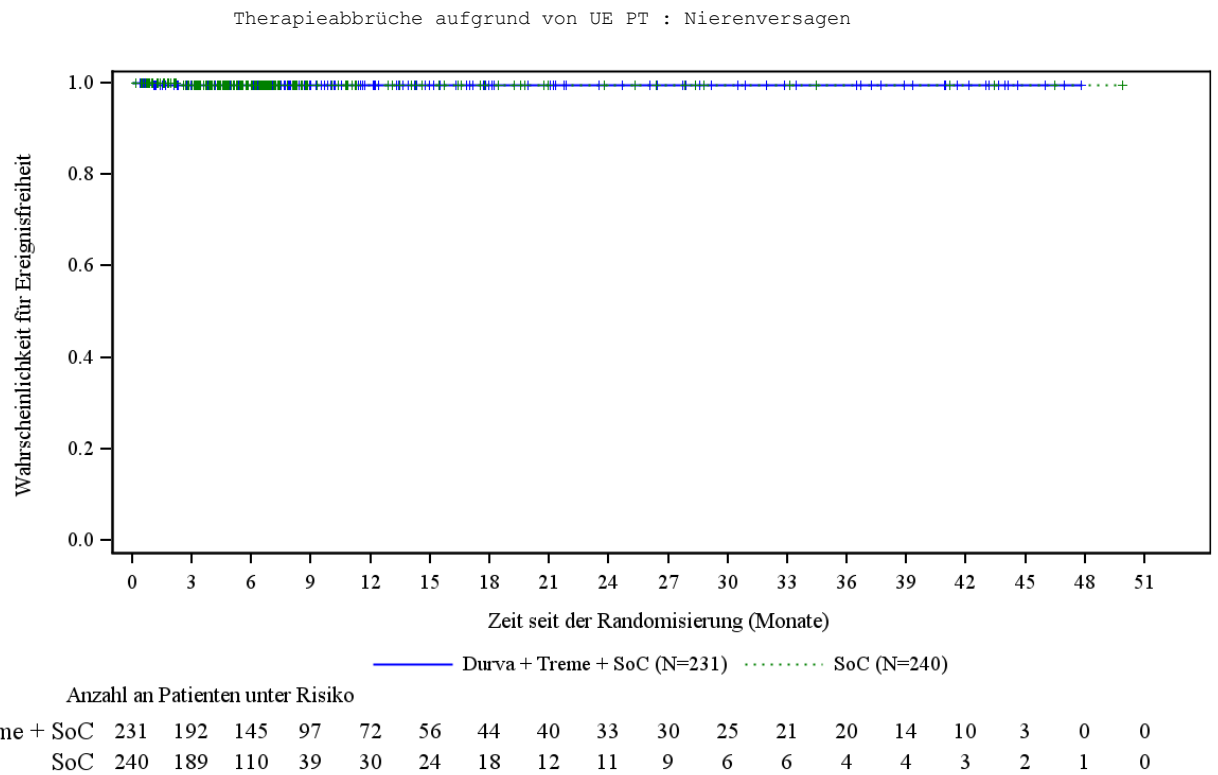
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

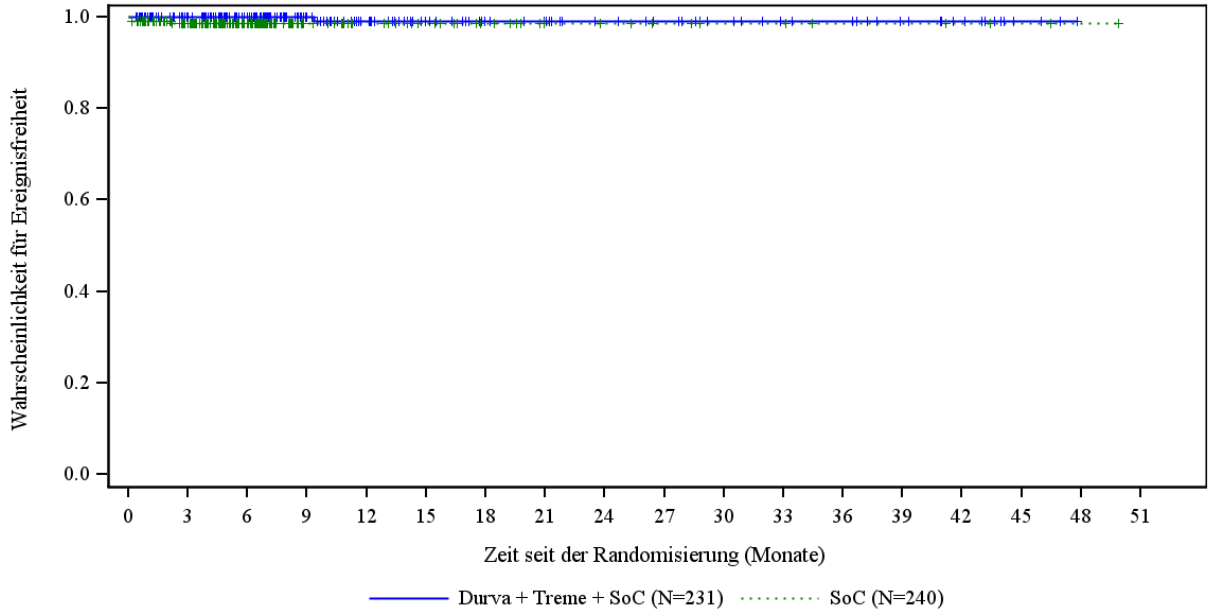


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE SOC : Allgemeine Erkrankungen und Beschwerden am Verabreichungsort



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	71	55	43	40	33	30	25	21	20	14	10	3	0	0
SoC	240	187	109	38	29	23	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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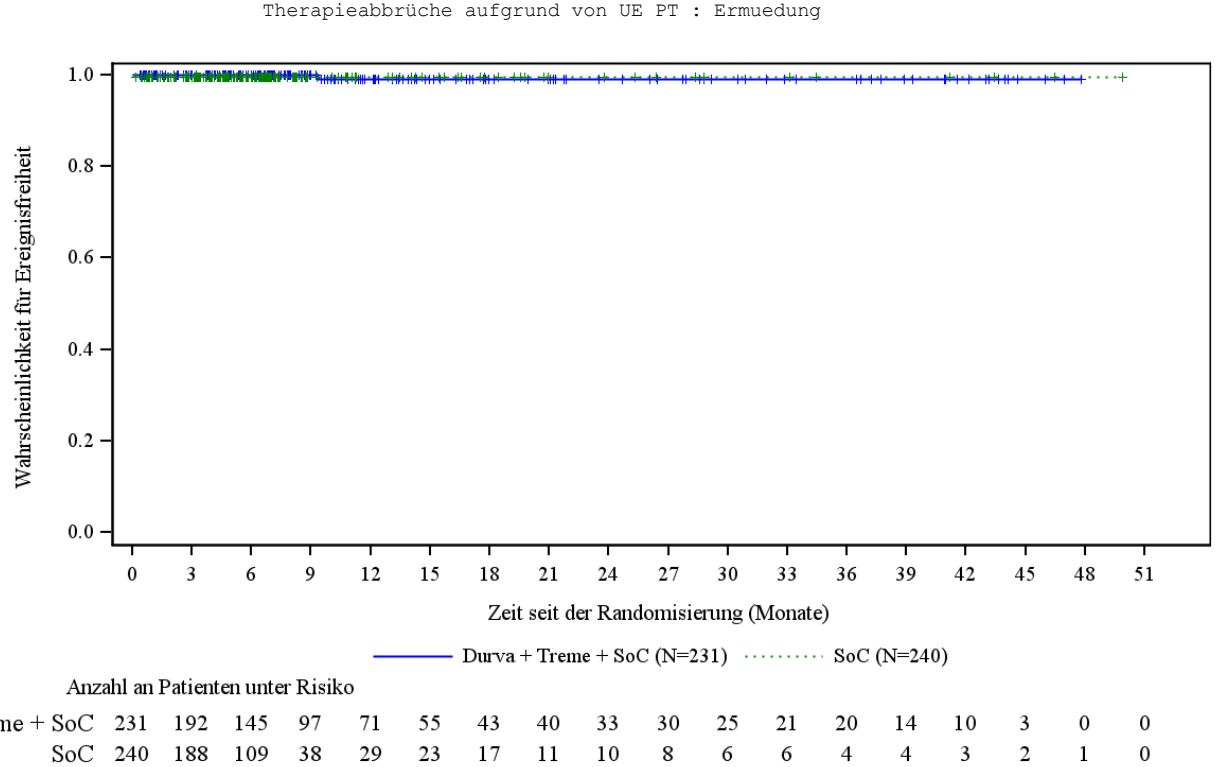
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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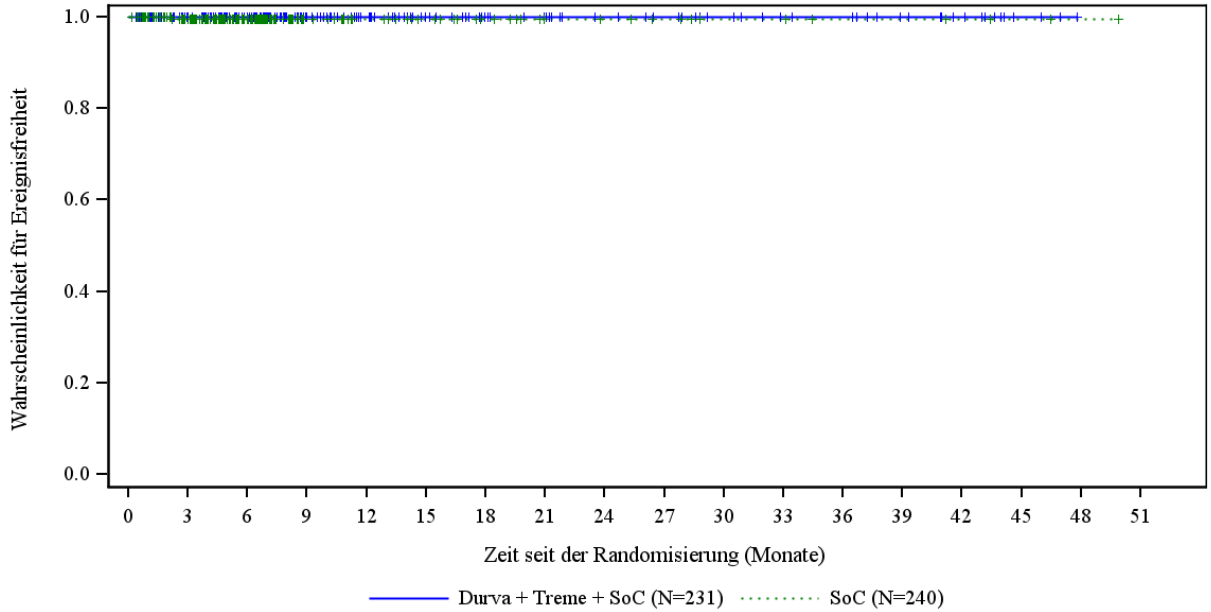
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021
Therapieabbrüche aufgrund von UE PT : Generelle Verschlechterung des physischen Gesundheitszustandes



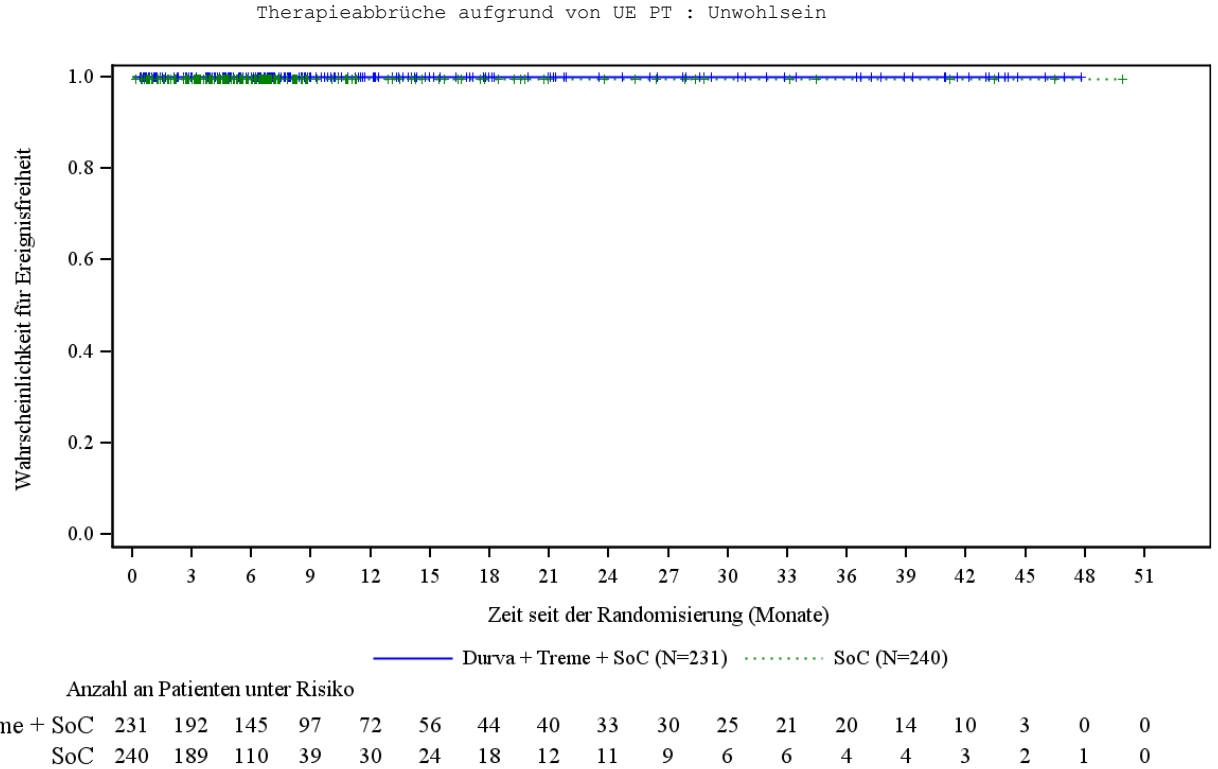
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

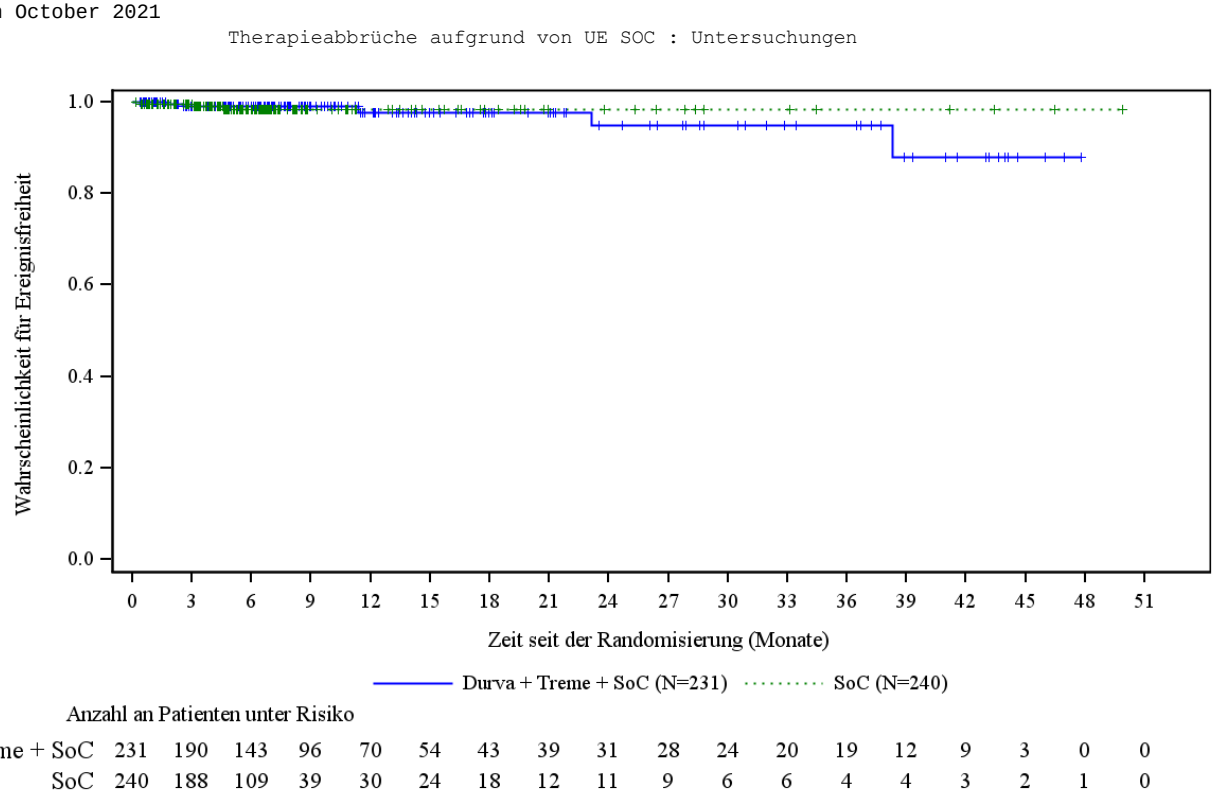
Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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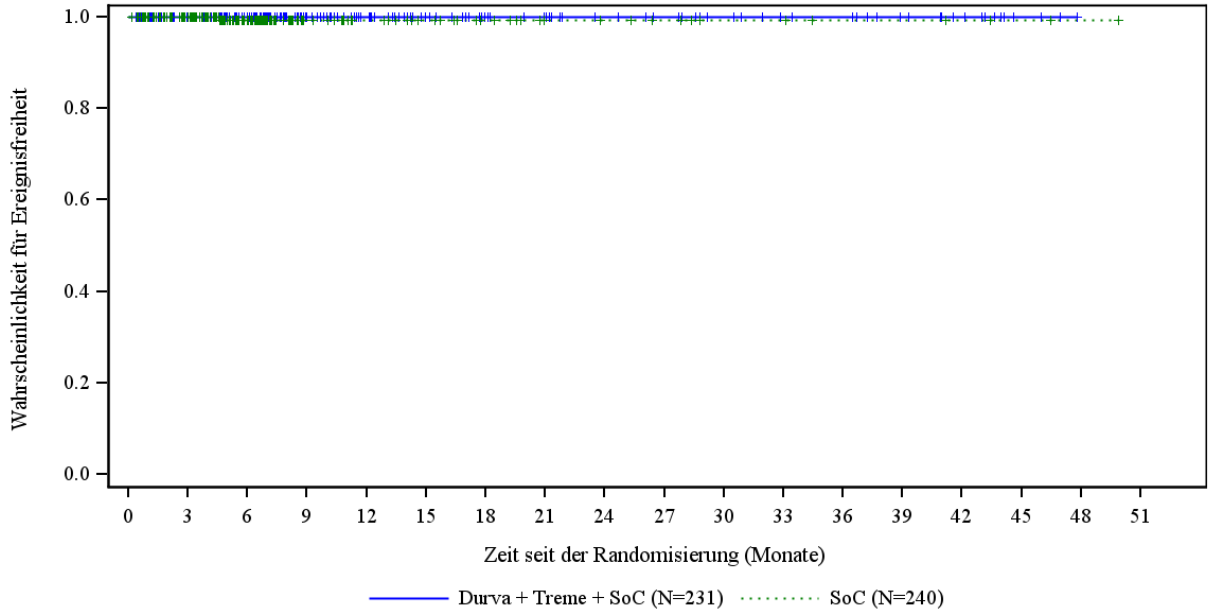
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Alaninaminotransferase erhoeht



Anzahl an Patienten unter Risiko

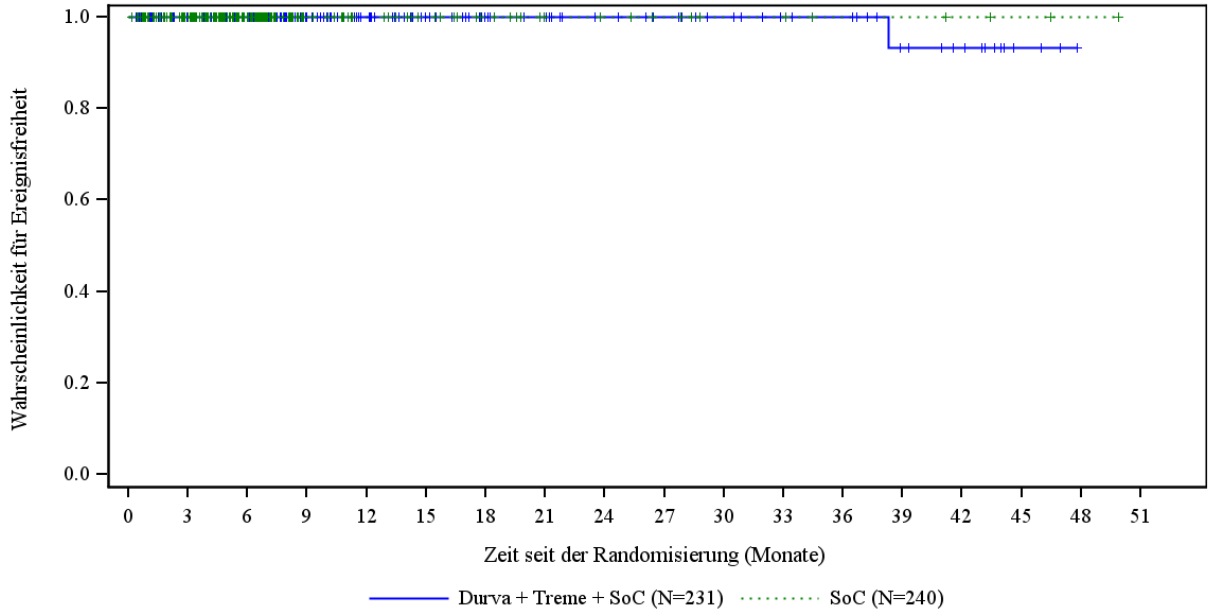
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Gewicht erniedrigt



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	13	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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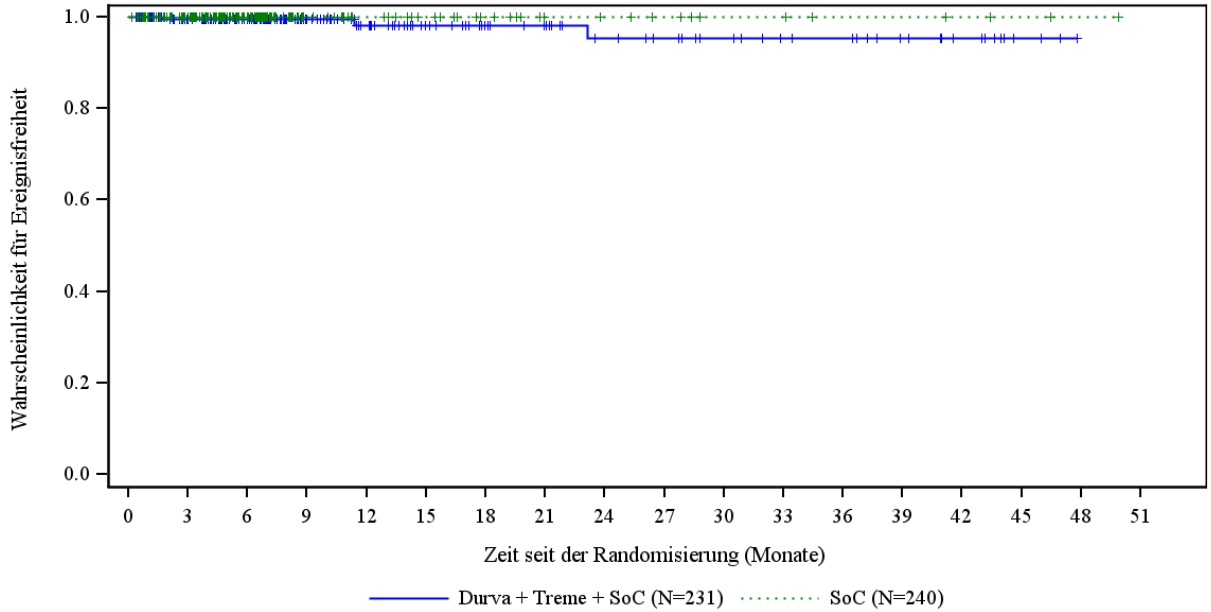
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Kreatinin im Blut erhoeht



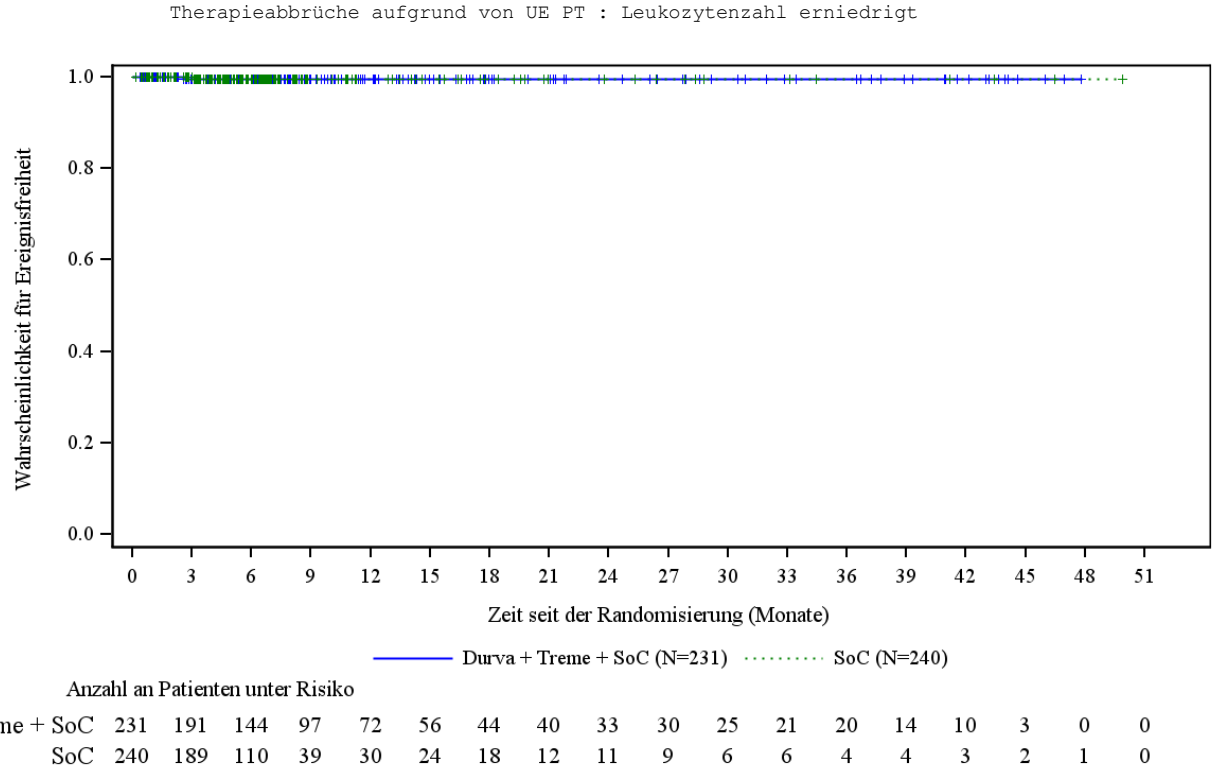
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	70	54	43	39	31	28	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

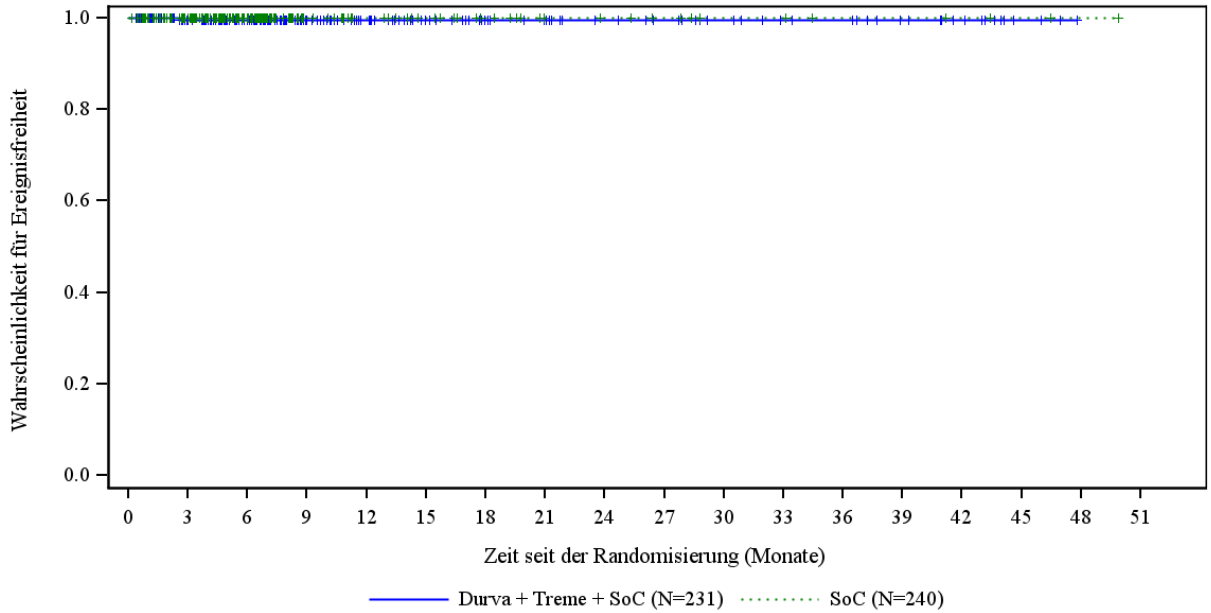
Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Neutrophilenzahl erniedrigt



Anzahl an Patienten unter Risiko

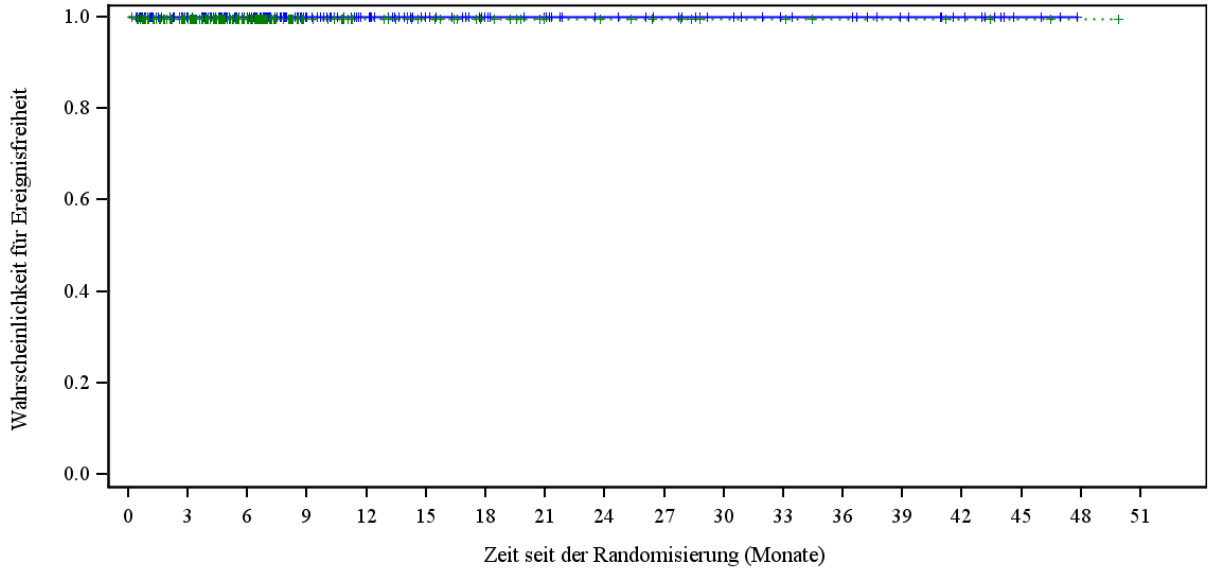
Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Therapieabbrüche aufgrund von UE PT : Thrombozytenzahl vermindert



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae326g.sas Executed : 2022-11-22T130149

Anhang 4-G 1.2.1.3: Schwere unerwünschte Ereignisse (CTCAE-Grad ≥ 3) nach SOC und PT

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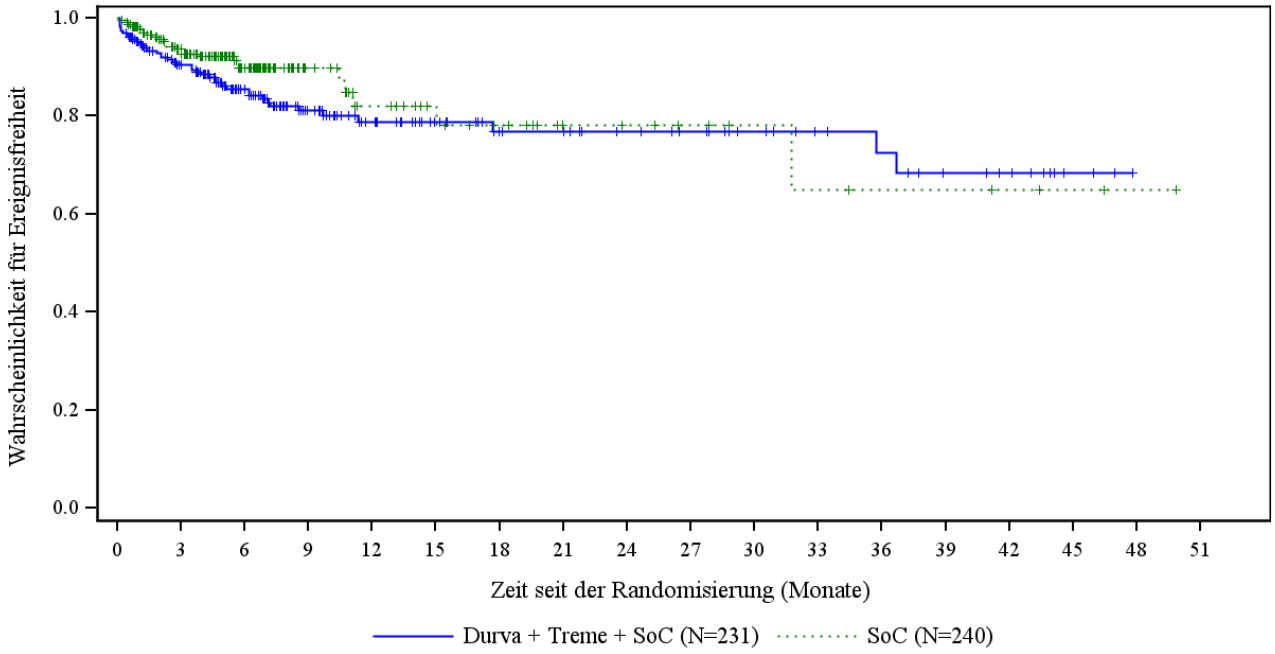
Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Infektionen und parasitaere Erkrankungen



Anzahl an Patienten unter Risiko

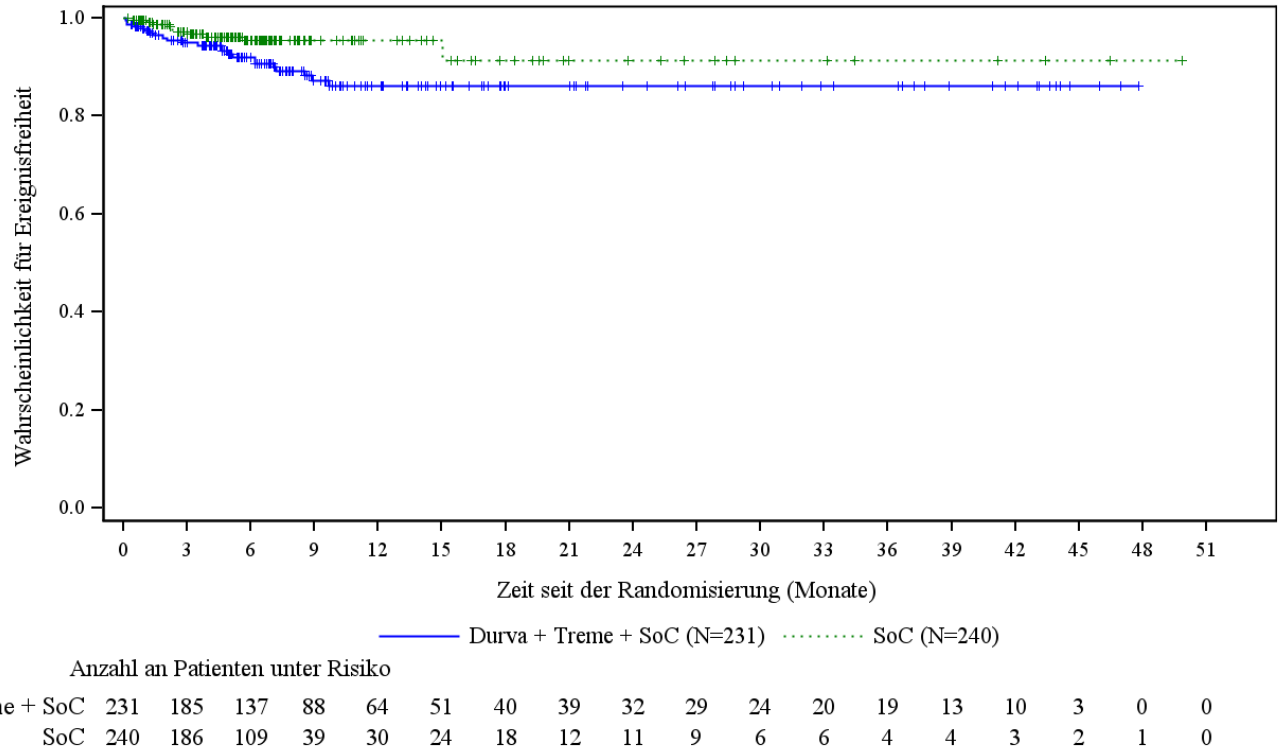
Durva + Treme + SoC	231	178	131	84	60	47	38	37	31	28	23	19	17	12	9	3	0	0
SoC	240	182	106	39	27	21	17	11	10	8	6	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 PT : Pneumonie



Anzahl an Patienten unter Risiko

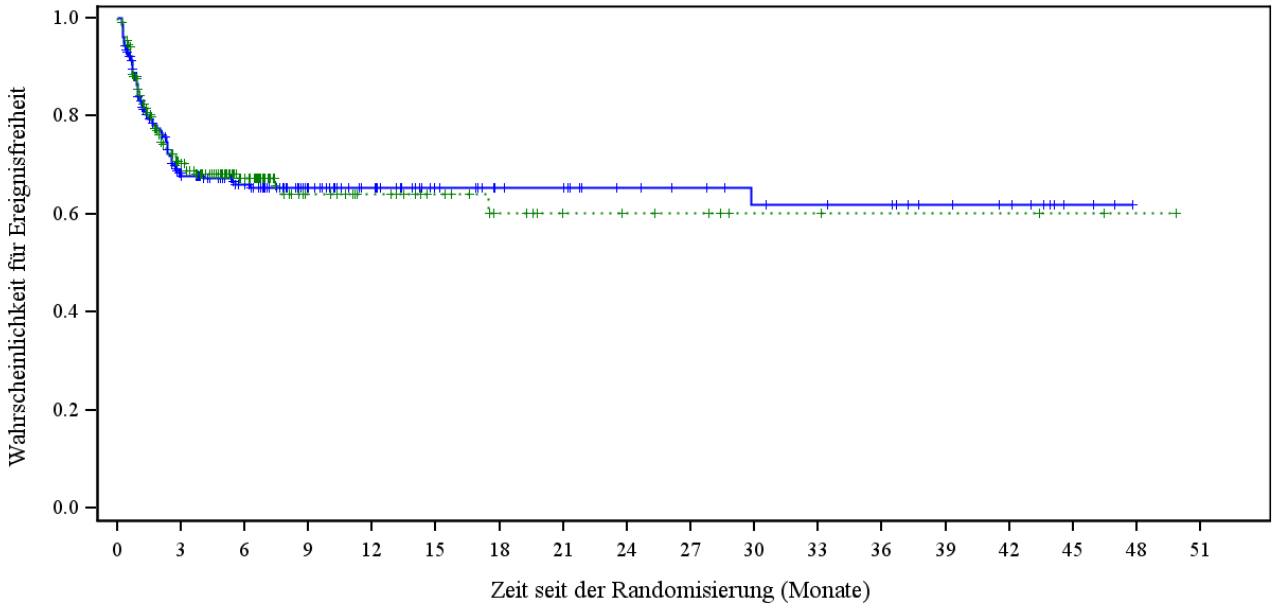
Durva + Treme + SoC	231	185	137	88	64	51	40	39	32	29	24	20	19	13	10	3	0	0
SoC	240	186	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Erkrankungen des Blutes und des Lymphsystems



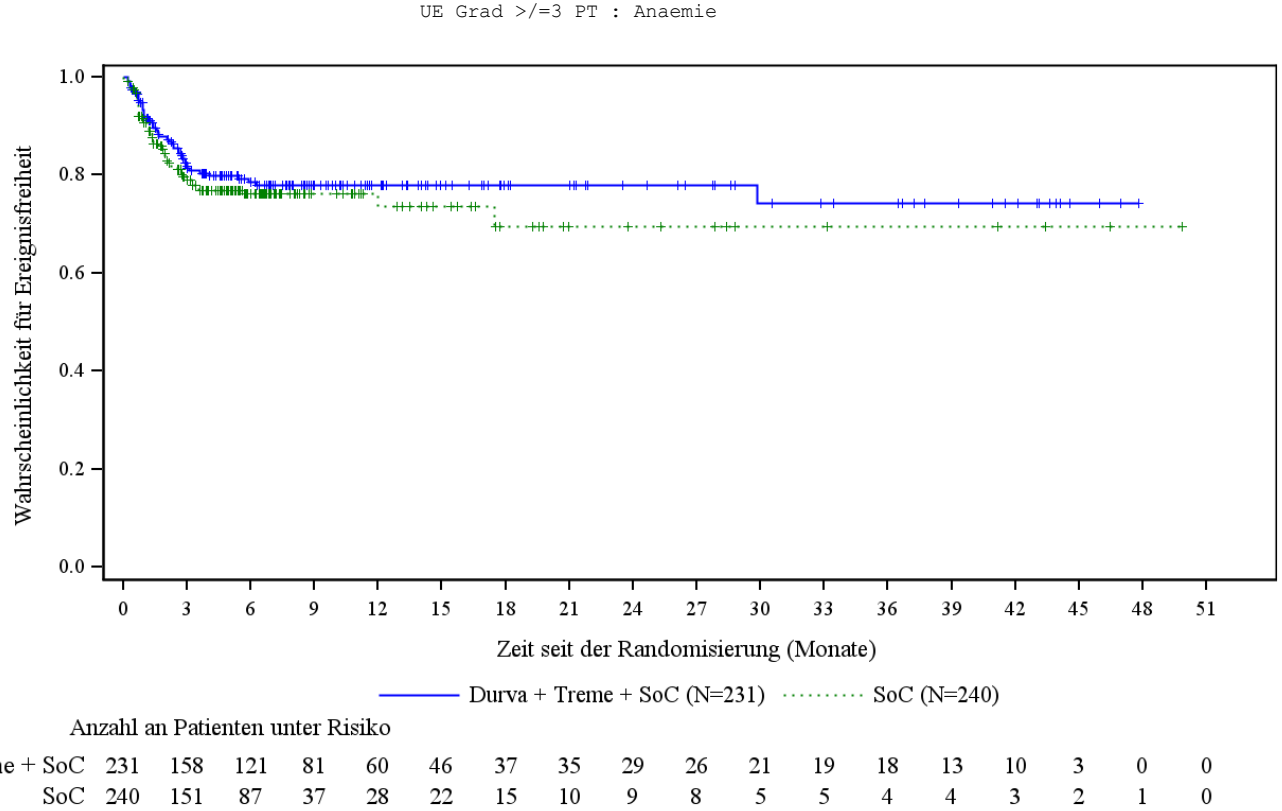
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	130	102	66	49	36	30	29	23	21	18	17	16	11	9	3	0	0
SoC	240	134	75	31	25	19	13	9	8	7	4	4	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

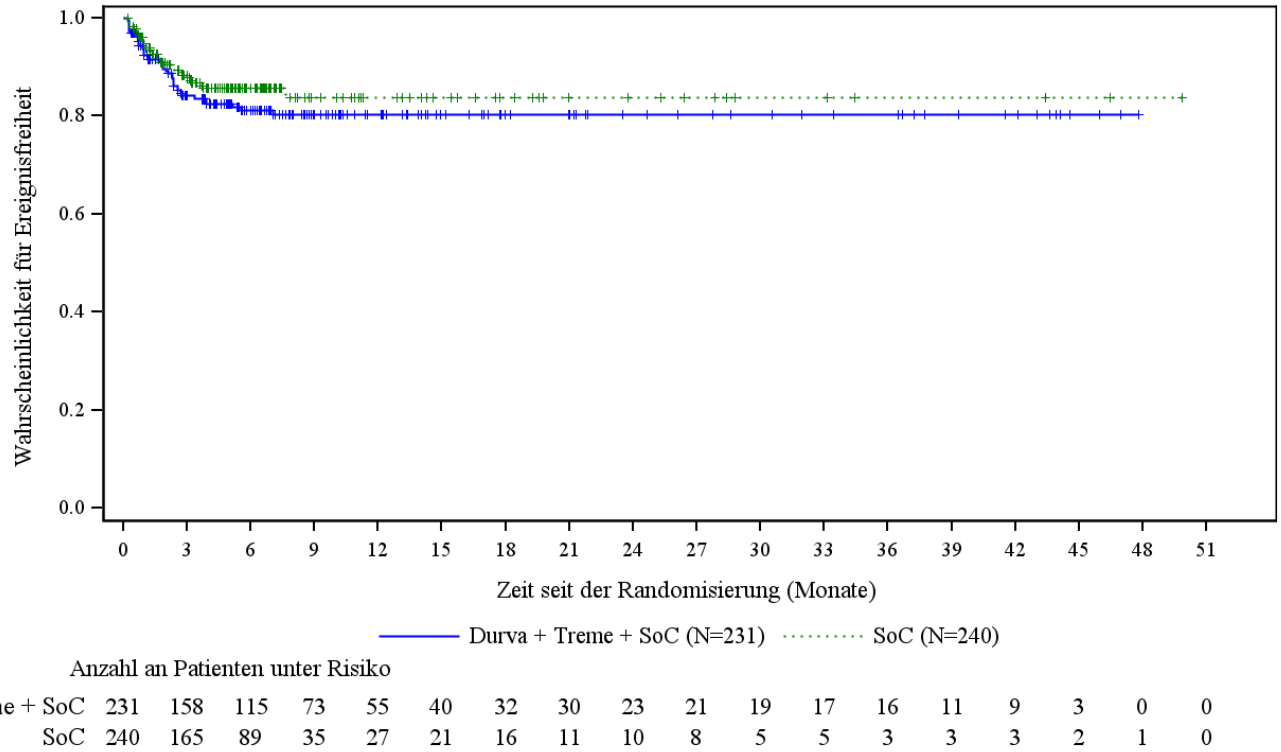


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 PT : Neutropenie



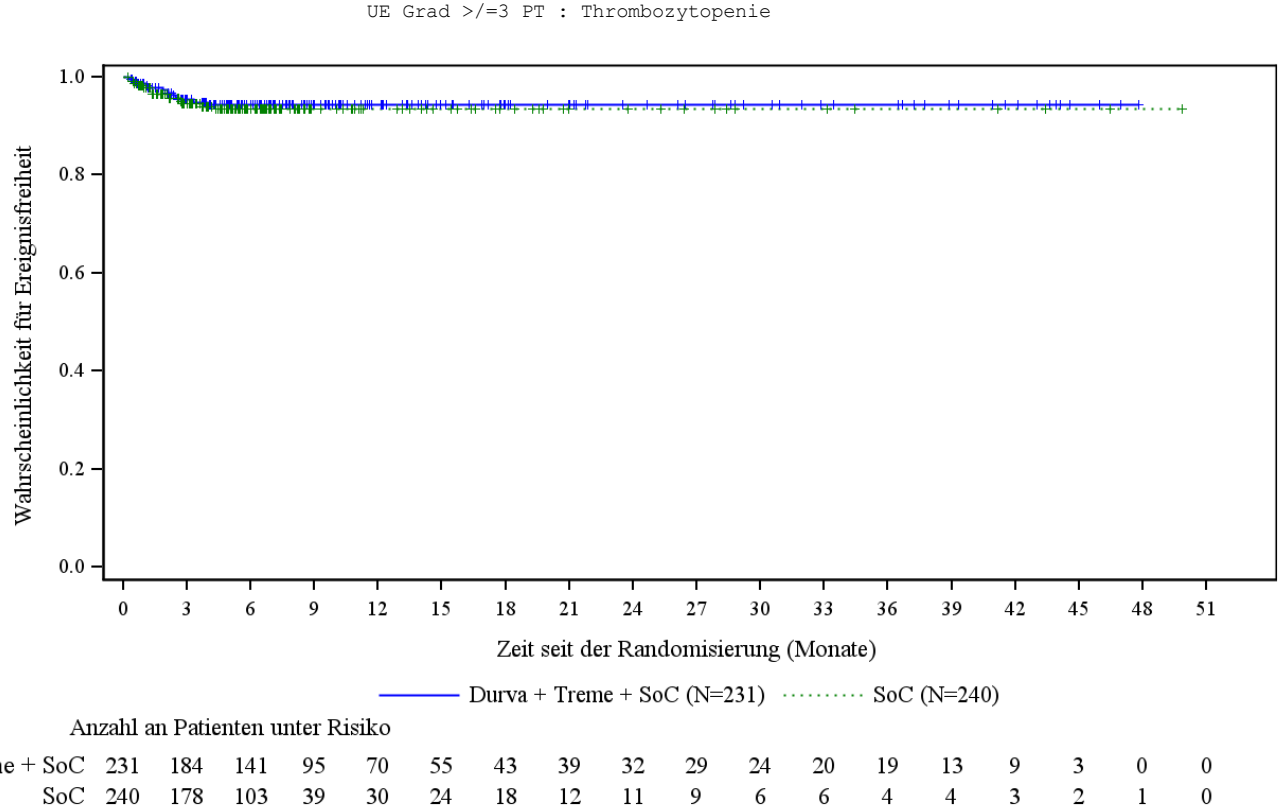
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	158	115	73	55	40	32	30	23	21	19	17	16	11	9	3	0	0
SoC	240	165	89	35	27	21	16	11	10	8	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	184	141	95	70	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	178	103	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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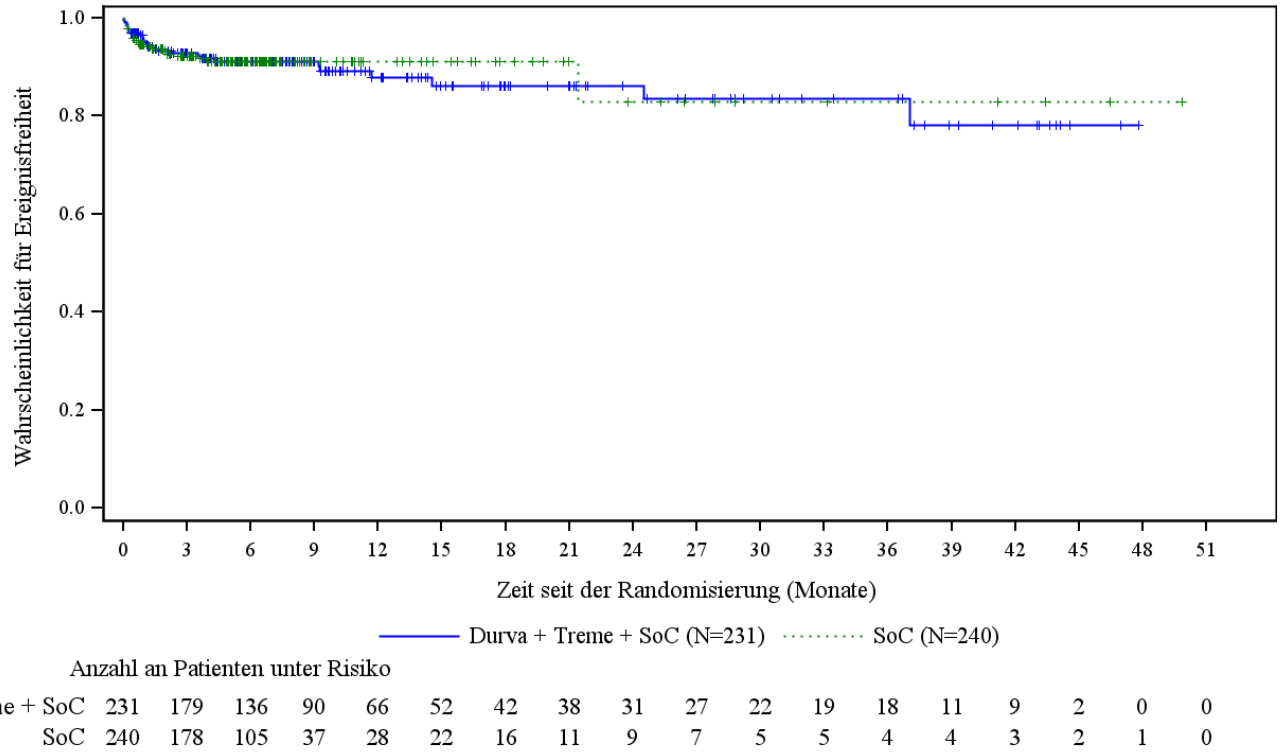
Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Stoffwechsel- und Ernaehrungsstoerungen



Anzahl an Patienten unter Risiko

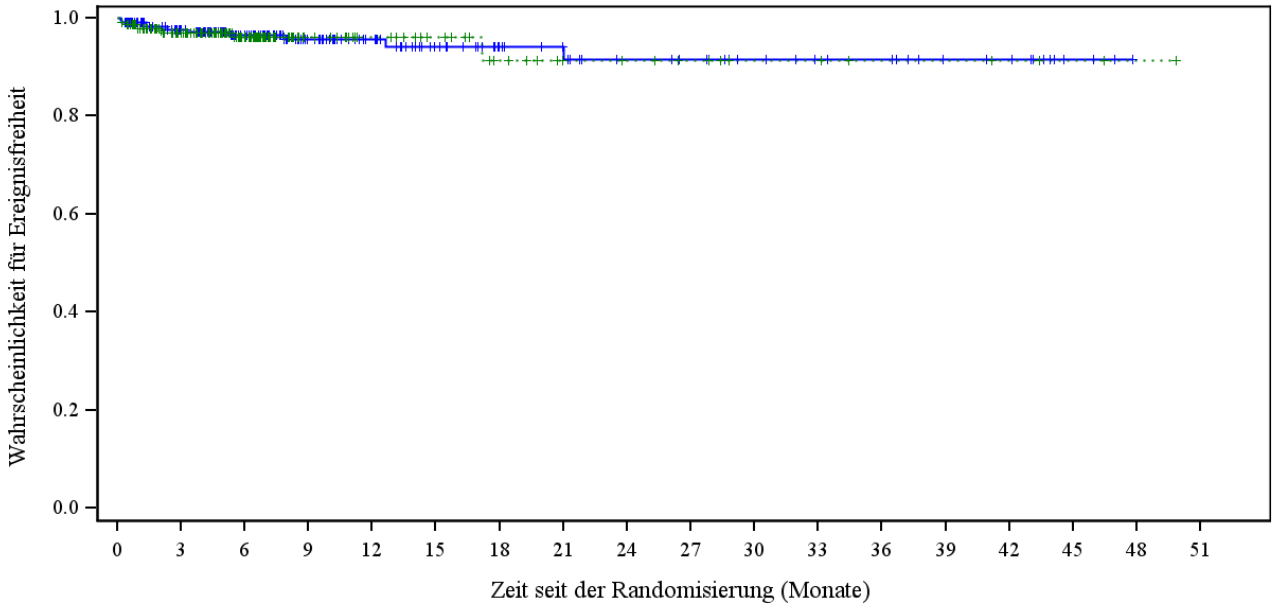
Durva + Treme + SoC	231	179	136	90	66	52	42	38	31	27	22	19	18	11	9	2	0	0
SoC	240	178	105	37	28	22	16	11	9	7	5	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Erkrankungen des Nervensystems



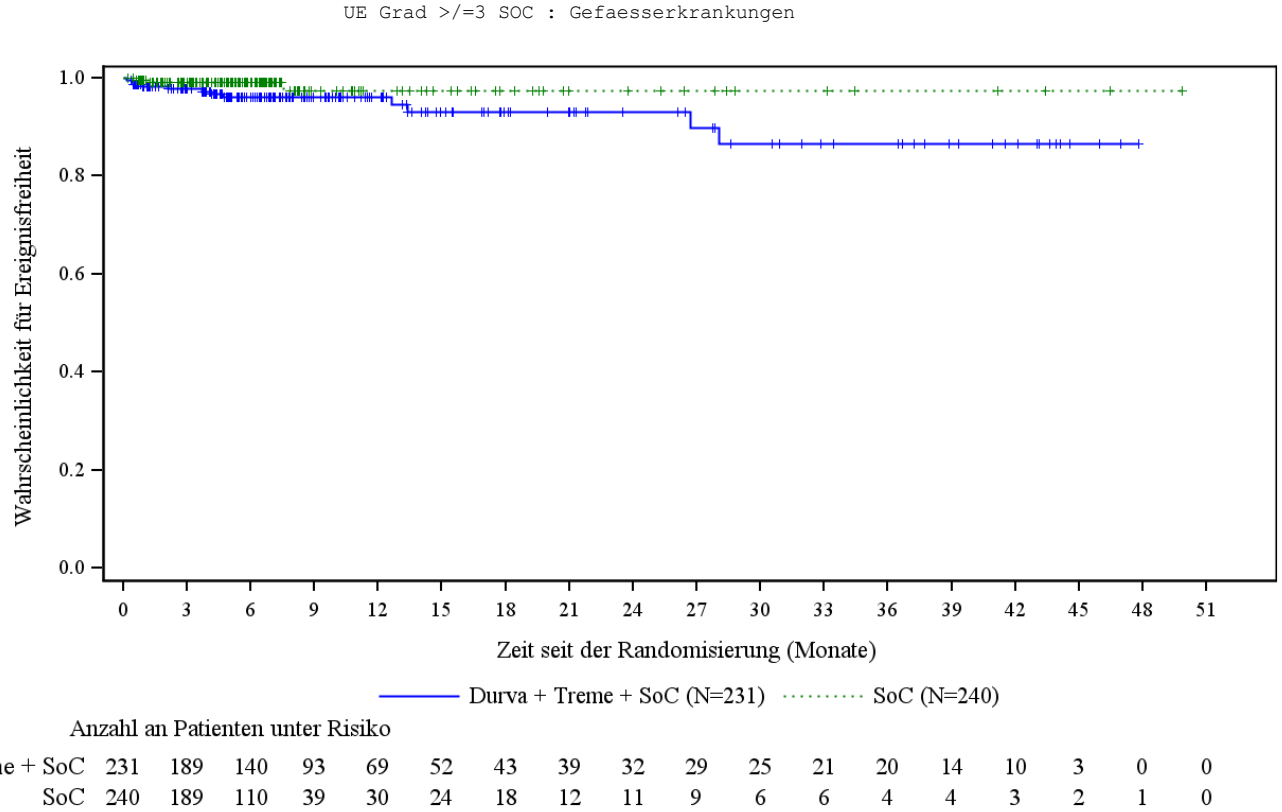
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	188	140	93	69	52	40	36	29	27	22	19	18	12	10	3	0	0
SoC	240	185	108	39	30	24	17	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	140	93	69	52	43	39	32	29	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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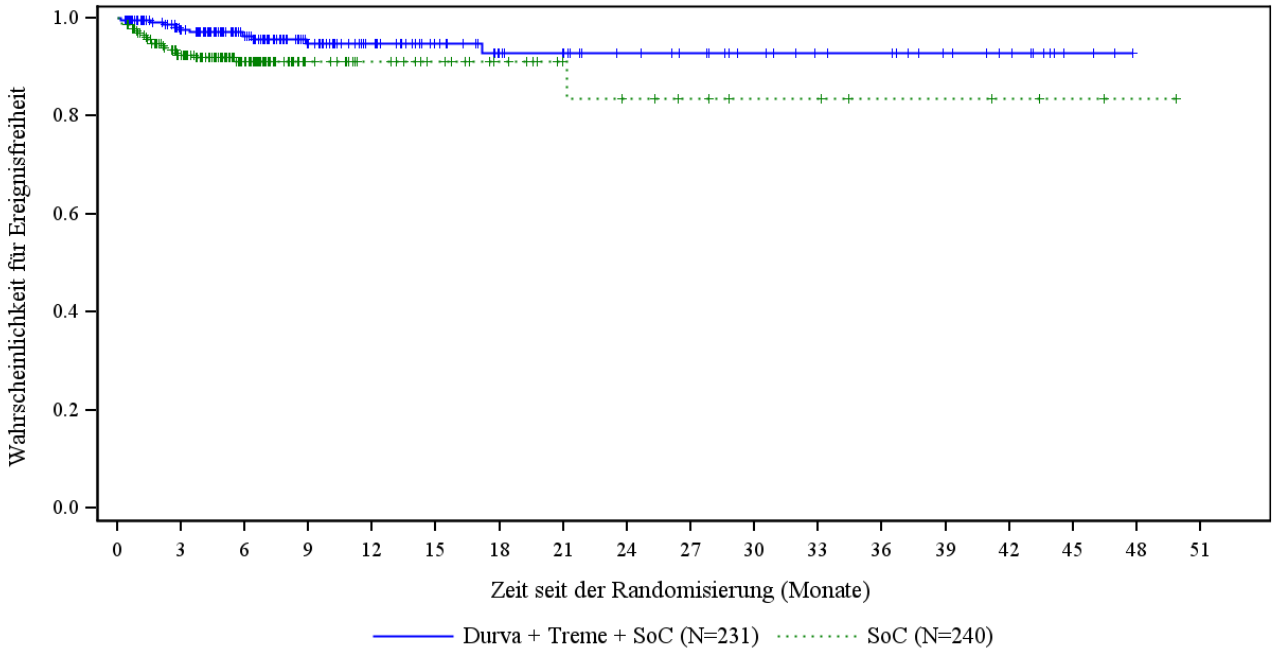
Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 10 of 16

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Erkrankungen der Atemwege, des Brustraums und Mediastinums



Anzahl an Patienten unter Risiko

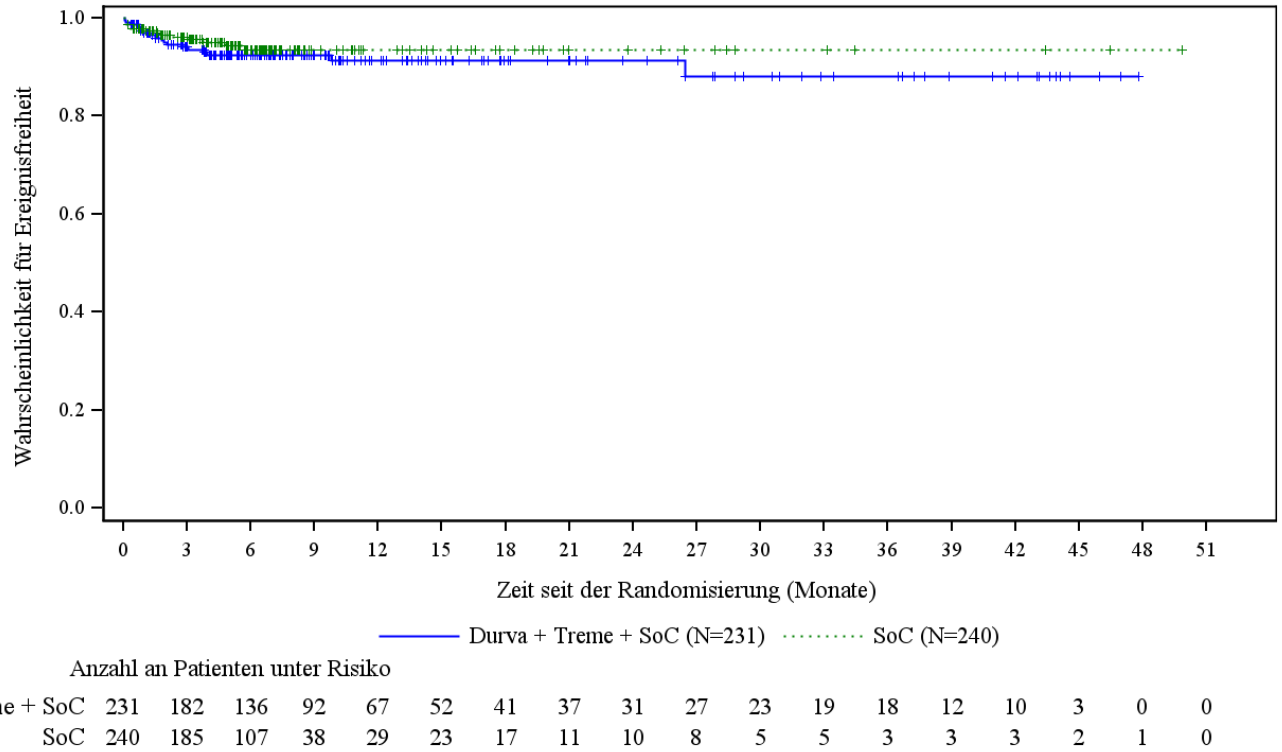
Durva + Treme + SoC	231	187	143	95	70	54	43	40	33	30	25	21	20	14	10	3	0	0
SoC	240	182	107	39	30	24	18	12	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Erkrankungen des Gastrointestinaltrakts



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	182	136	92	67	52	41	37	31	27	23	19	18	12	10	3	0	0
SoC	240	185	107	38	29	23	17	11	10	8	5	5	3	3	3	2	1	0

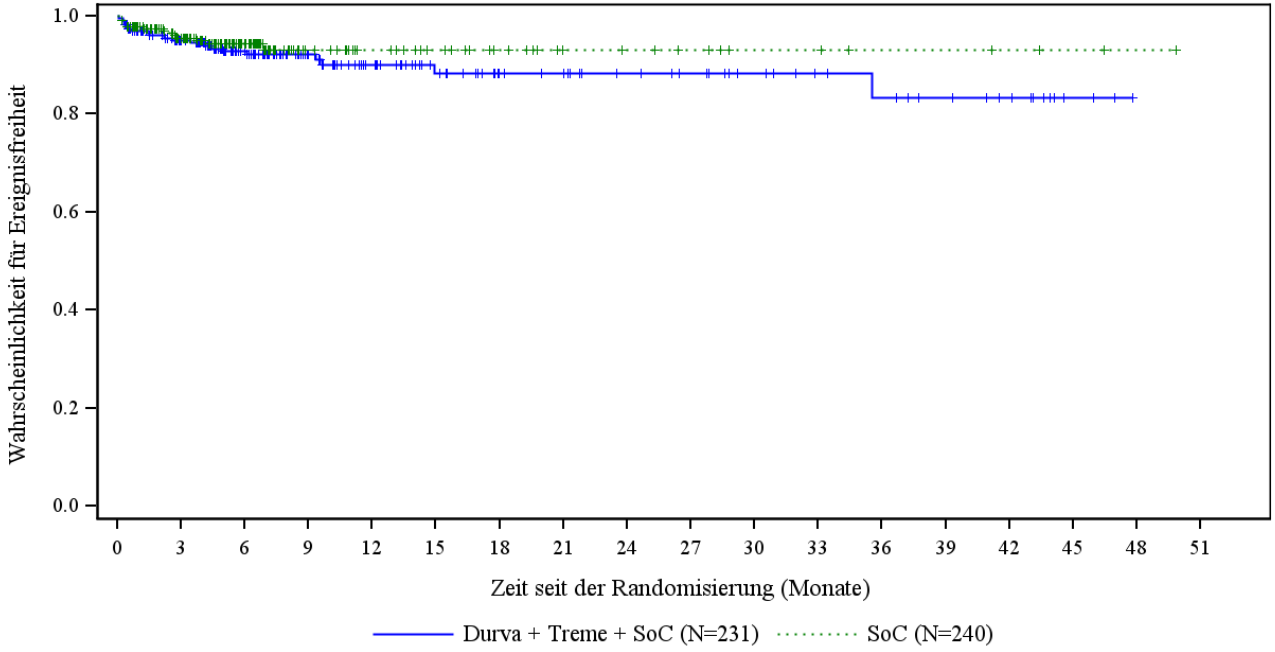
Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 12 of 16

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Allgemeine Erkrankungen und Beschwerden am Verabreichungsort



Anzahl an Patienten unter Risiko

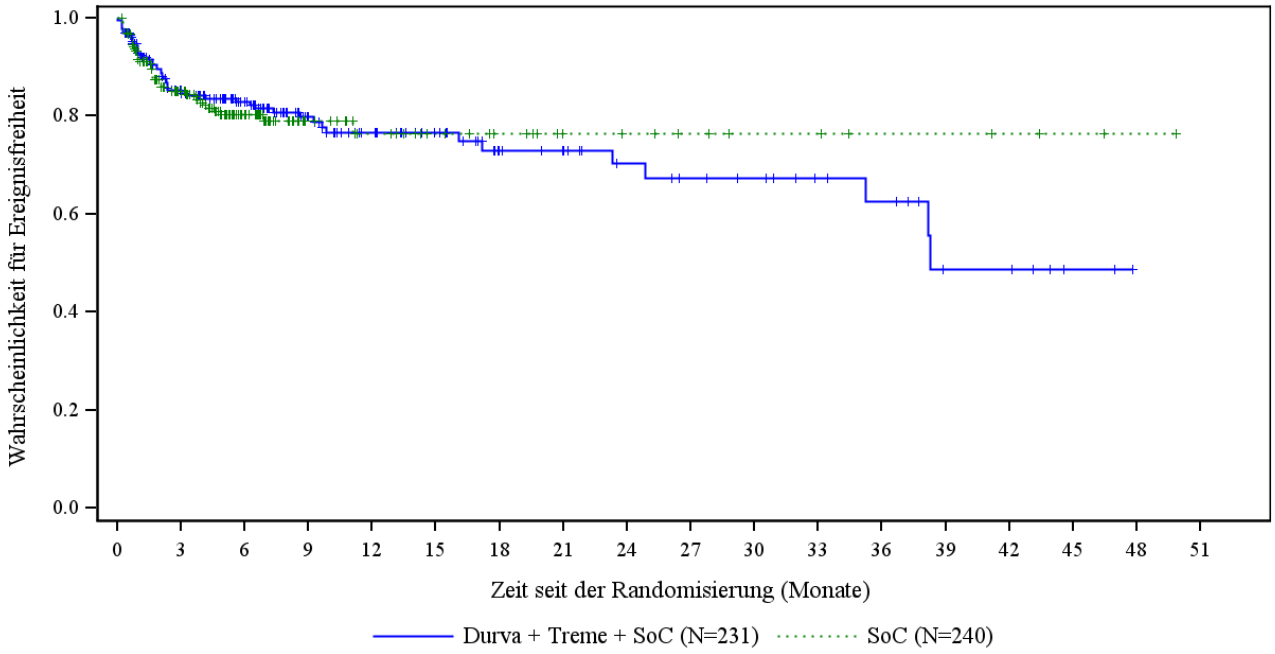
Durva + Treme + SoC	231	185	139	92	67	51	40	38	31	28	23	19	17	13	10	3	0	0
SoC	240	182	106	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 SOC : Untersuchungen



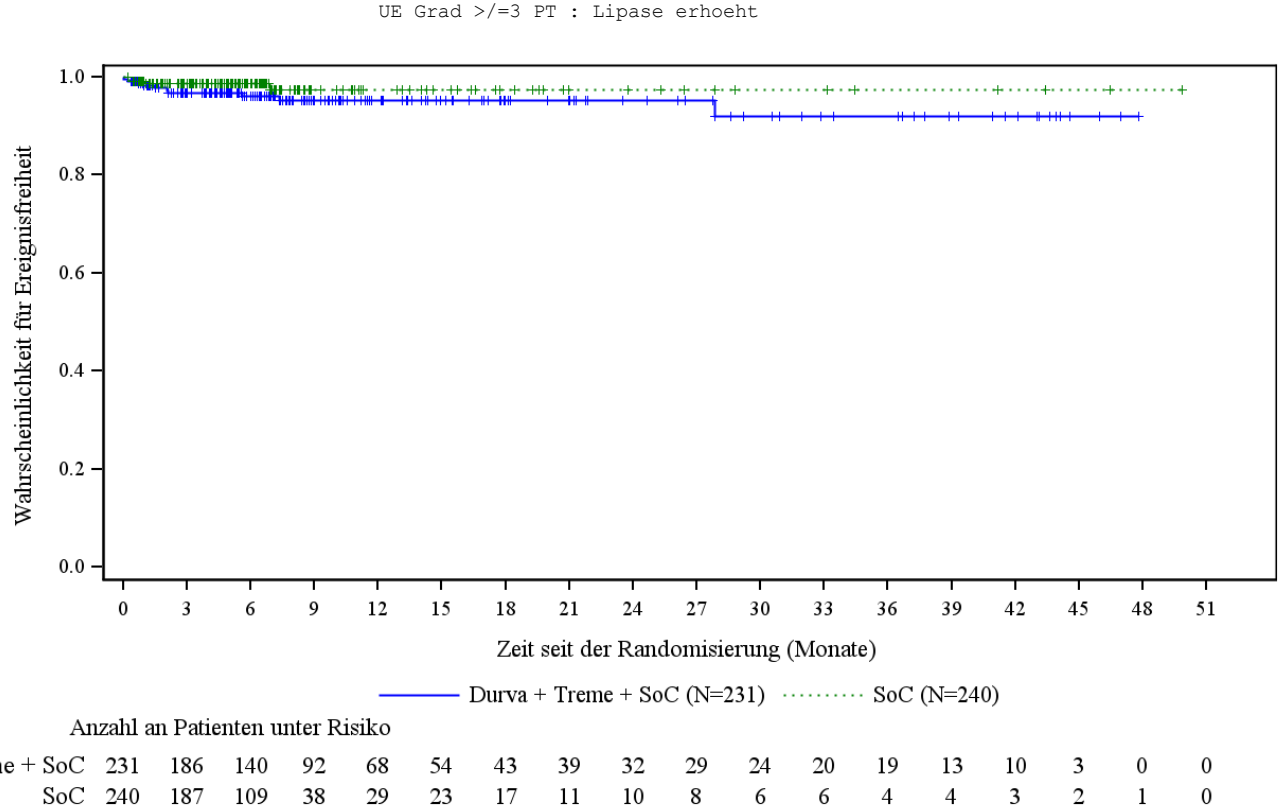
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	163	122	79	58	47	34	31	24	21	19	15	13	6	6	2	0	0
SoC	240	160	90	35	26	20	16	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	140	92	68	54	43	39	32	29	24	20	19	13	10	3	0	0
SoC	240	187	109	38	29	23	17	11	10	8	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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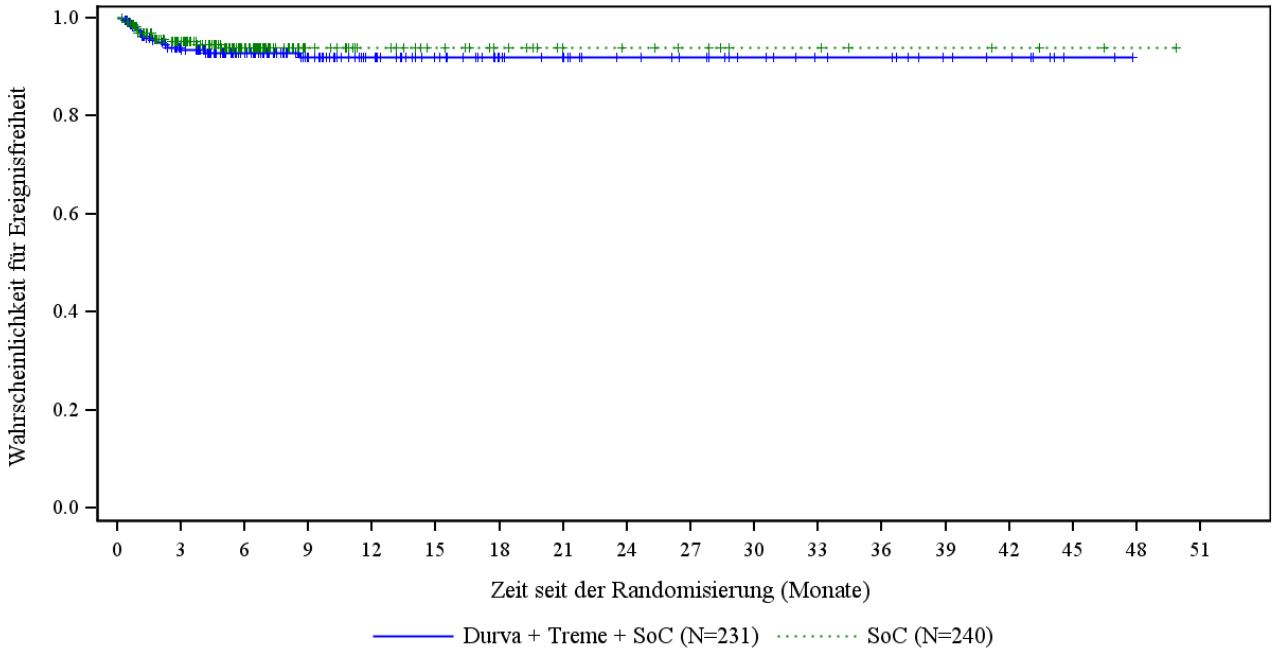
Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 15 of 16

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UE Grad >/=3 PT : Neutrophilenzahl erniedrigt



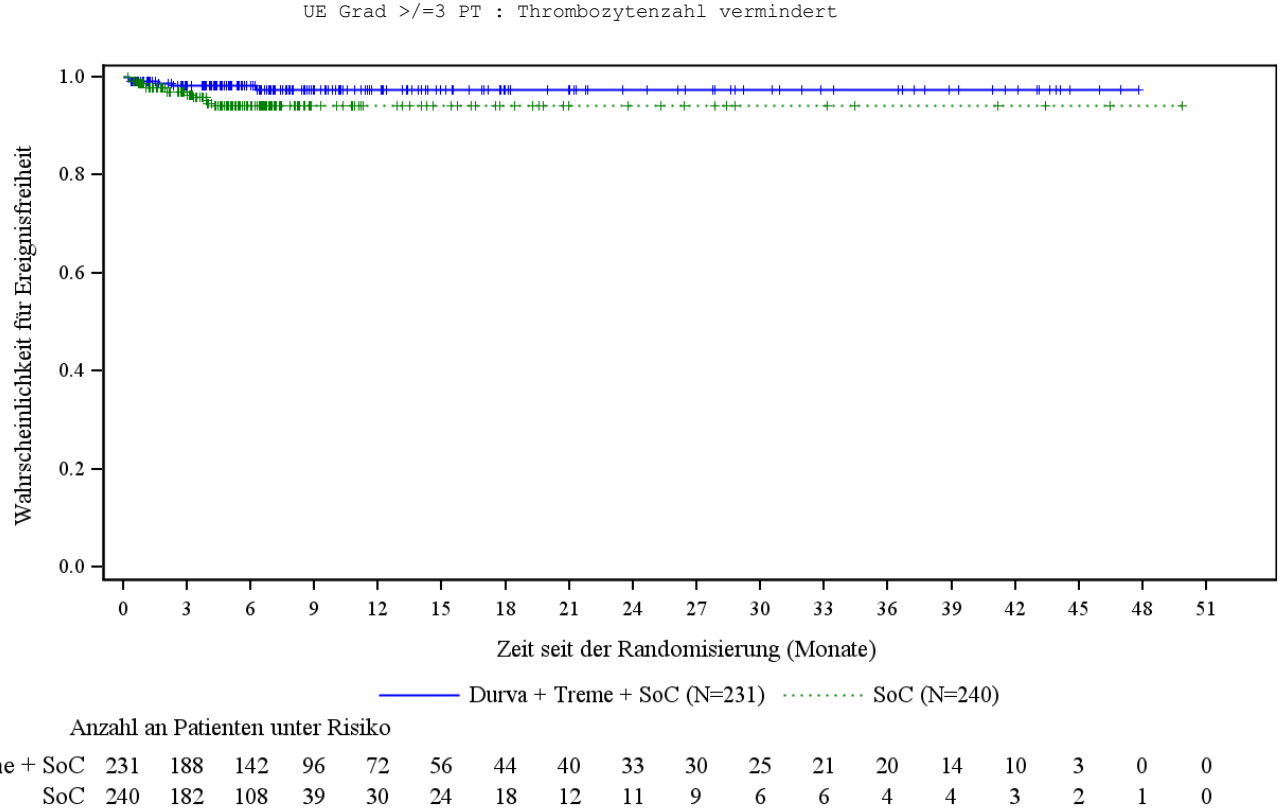
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	179	134	90	66	53	41	37	30	27	22	18	17	11	8	2	0	0
SoC	240	178	103	38	29	23	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Figure 4.3.2.4 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 by SOC/PT (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

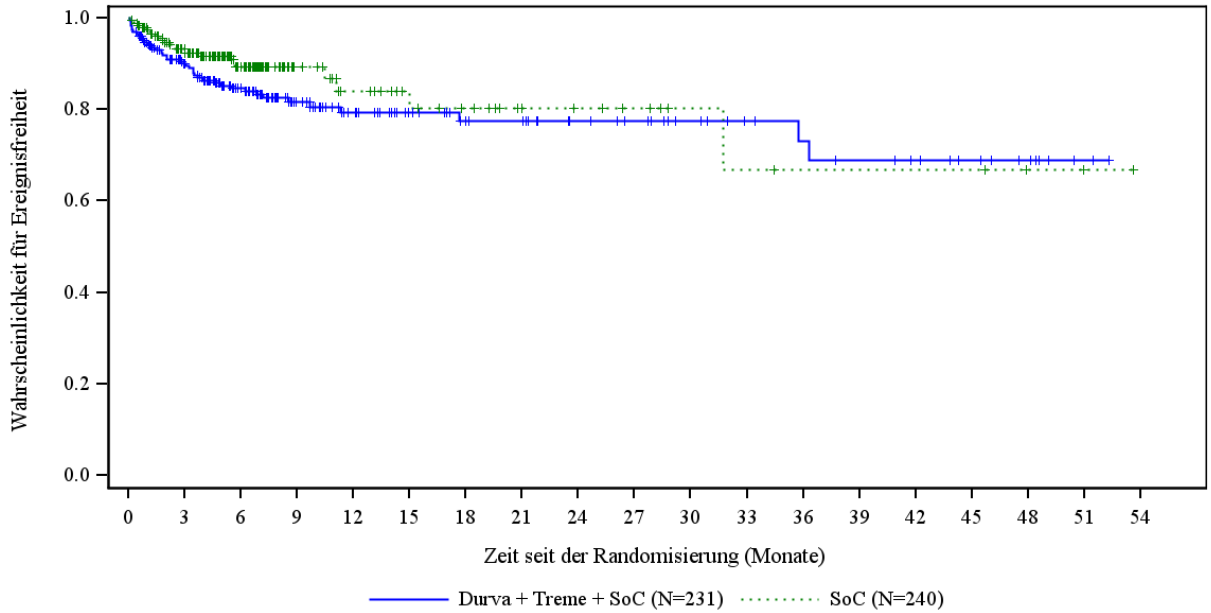
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae316g.sas Executed : 2022-11-22T125637

Anhang 4-G 1.2.1.4: Schwerwiegende unerwünschte Ereignisse nach SOC und PT

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 7

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE SOC : Infektionen und parasitaere Erkrankungen



Anzahl an Patienten unter Risiko

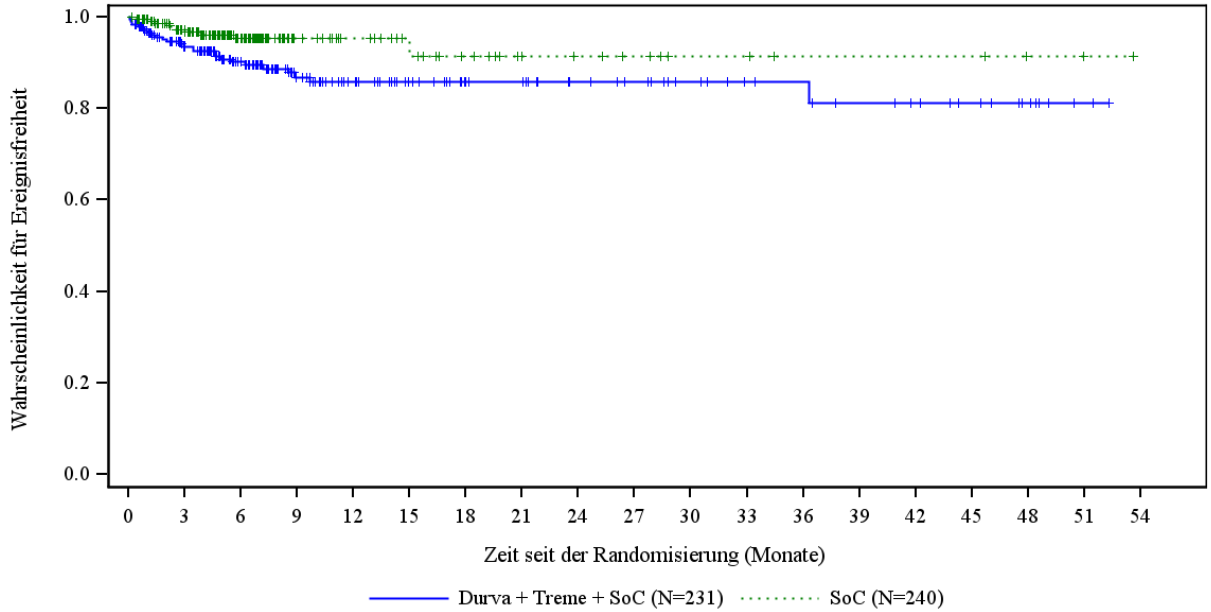
Durva + Treme + SoC	231	176	131	85	61	48	39	38	31	28	23	19	17	15	13	10	7	2	0
SoC	240	181	105	39	28	22	18	12	11	9	6	5	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE PT : Pneumonie



Anzahl an Patienten unter Risiko

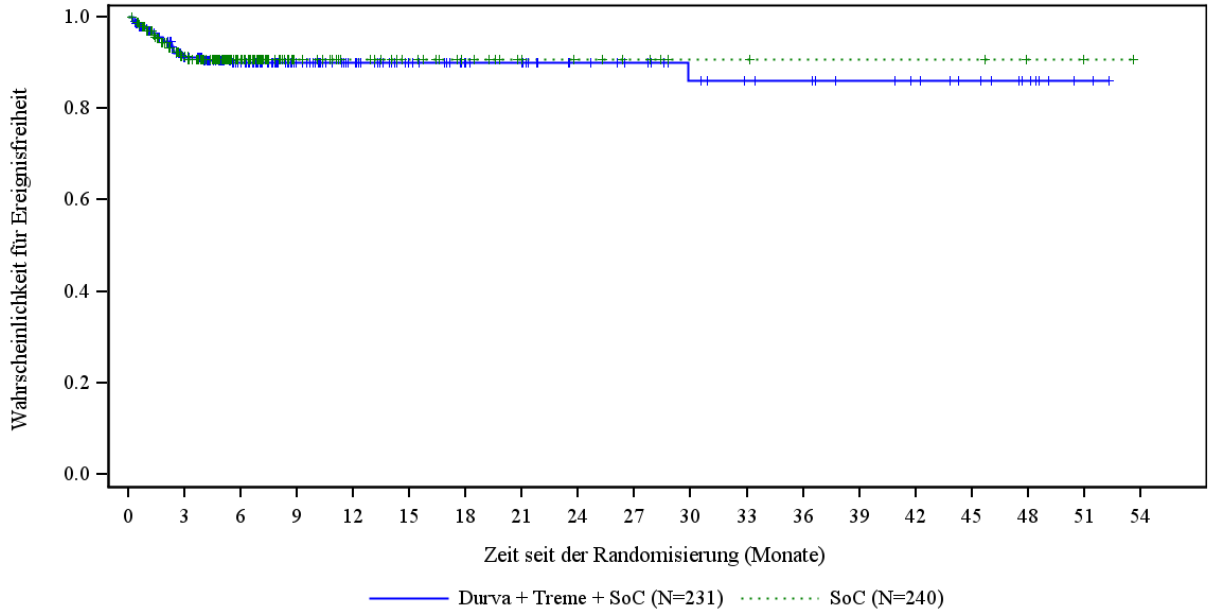
Durva + Treme + SoC	231	183	136	88	64	51	40	39	32	29	24	20	19	16	14	11	7	2	0
SoC	240	186	109	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE SOC : Erkrankungen des Blutes und des Lymphsystems



Anzahl an Patienten unter Risiko

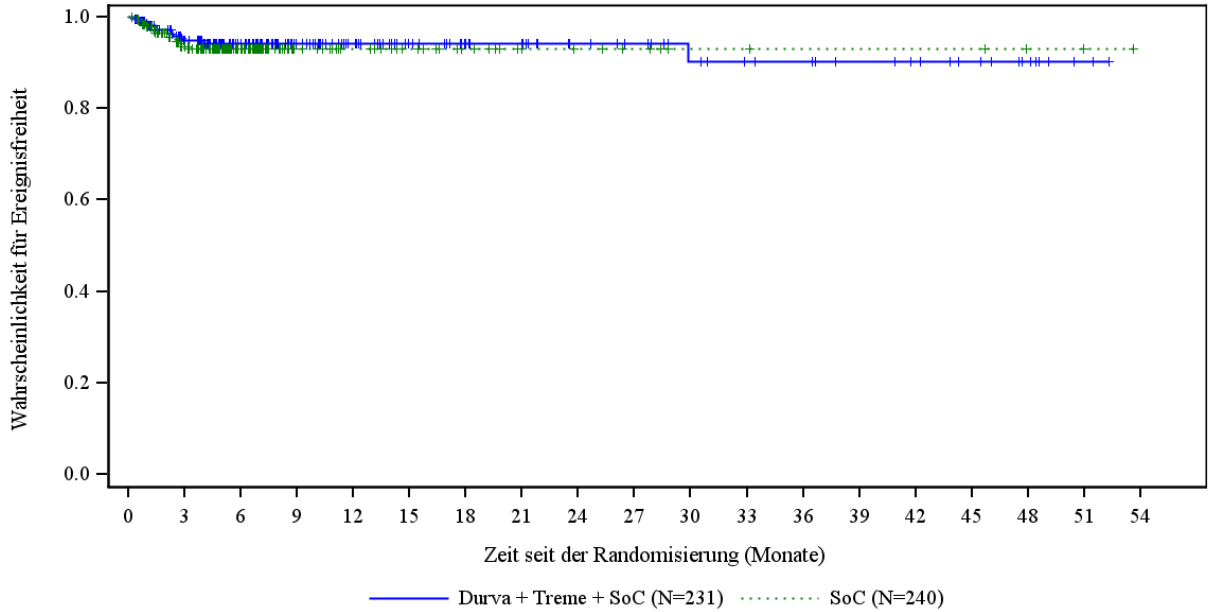
Durva + Treme + SoC	231	176	134	91	67	51	40	38	31	28	23	20	19	16	14	11	7	2	0
SoC	240	171	100	37	29	23	17	11	10	8	5	5	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE PT : Anaemie



Anzahl an Patienten unter Risiko

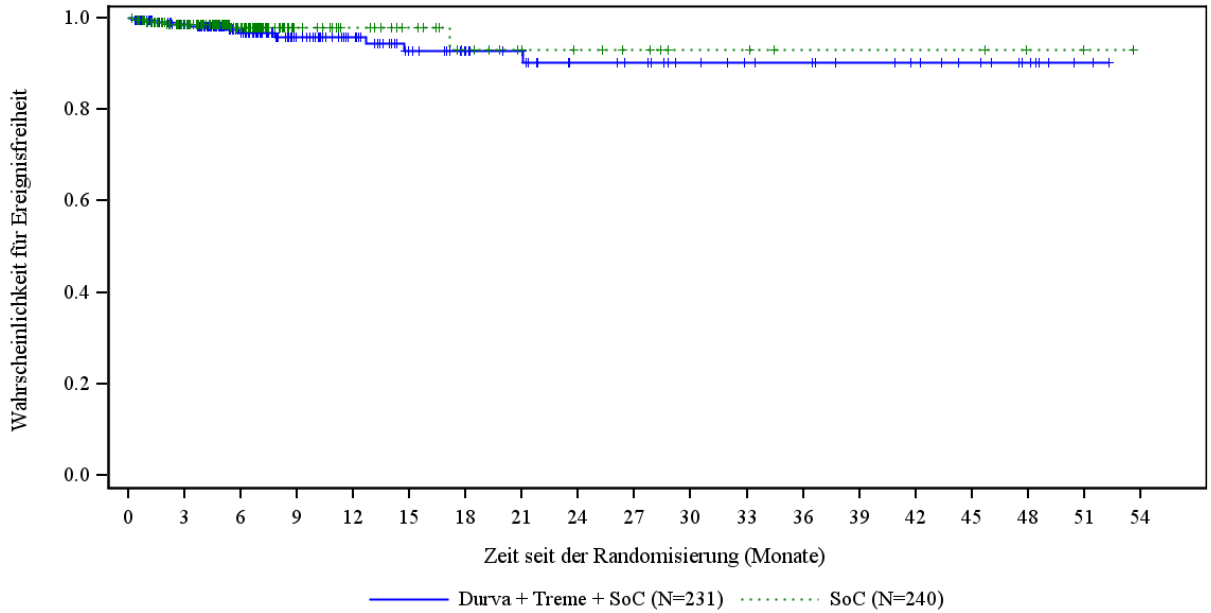
Durva + Treme + SoC	231	182	137	93	68	52	41	38	31	28	23	20	19	16	14	11	7	2	0
SoC	240	175	102	38	29	23	17	11	10	8	5	5	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE SOC : Erkrankungen des Nervensystems



Anzahl an Patienten unter Risiko

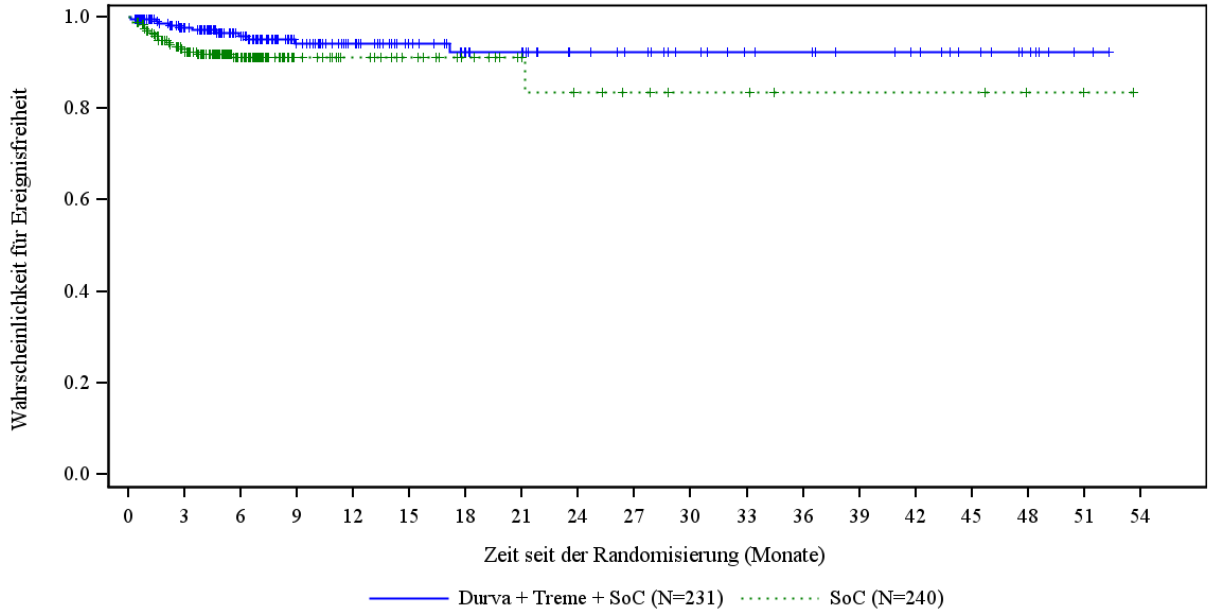
Durva + Treme + SoC	231	191	141	95	70	52	41	37	30	28	23	20	19	16	14	11	7	2	0
SoC	240	187	109	39	30	24	17	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE SOC : Erkrankungen der Atemwege, des Brustraums und Mediastinums



Anzahl an Patienten unter Risiko

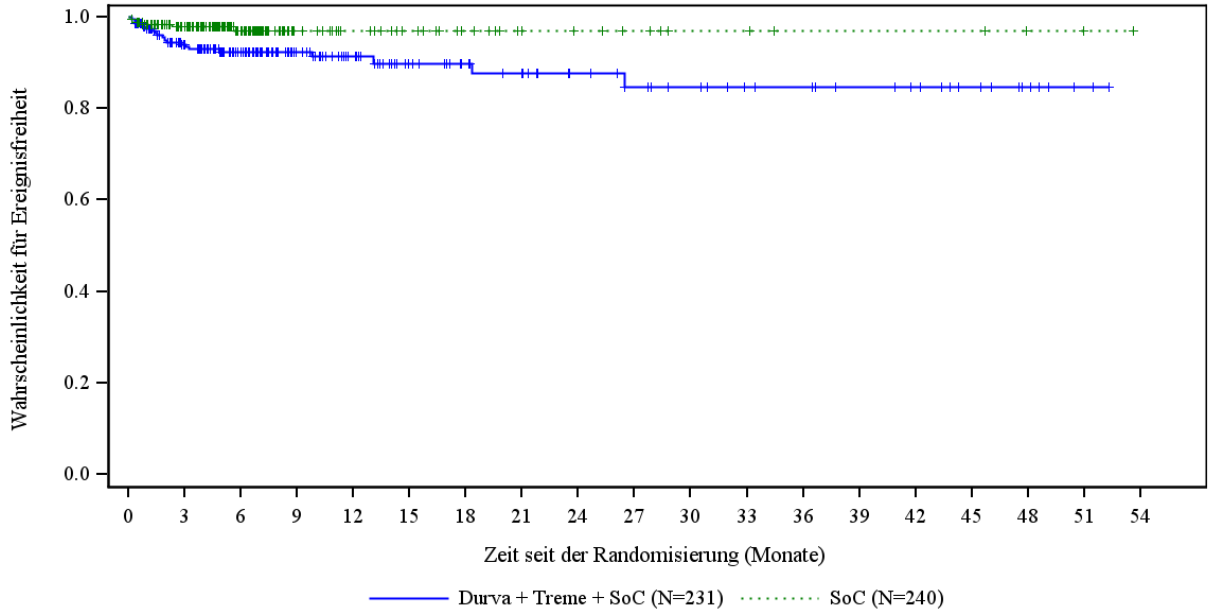
Durva + Treme + SoC	231	187	144	96	71	55	43	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	181	108	39	30	24	18	12	10	8	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

Figure 4.5.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events by SOC/PT
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUE SOC : Erkrankungen des Gastrointestinaltrakts



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	182	137	92	67	51	42	37	31	27	24	20	19	16	14	10	6	2	0
SoC	240	187	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (SOC, PT) categories.
Analysis is only performed if that event occurs in at least 10 patients with at least 1% in one study arm.
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05. + indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae336g.sas Executed : 2022-11-22T130714

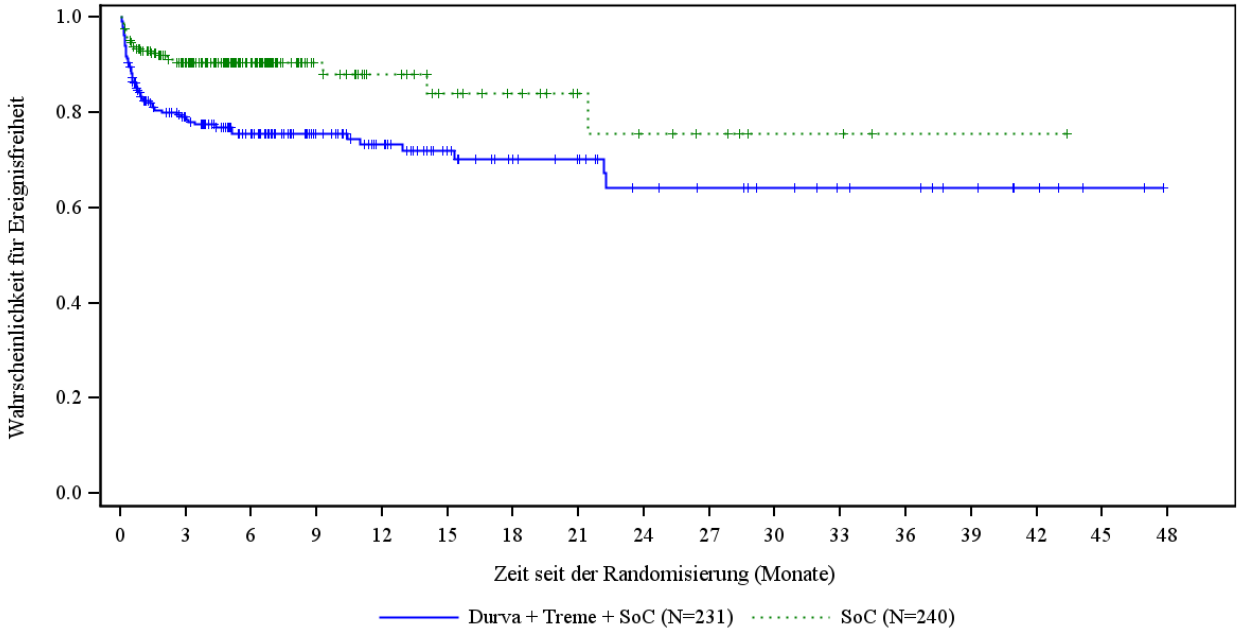
Anhang 4-G 1.2.2: Kaplan-Meier-Kurven für unerwünschte Ereignisse von speziellem Interesse nach Kategorie und PT

Anhang 4-G 1.2.2.1: Unerwünschte Ereignisse von speziellem Interesse nach Kategorie und PT

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 66

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Kategorie : Dermatitis / Hautausschlag



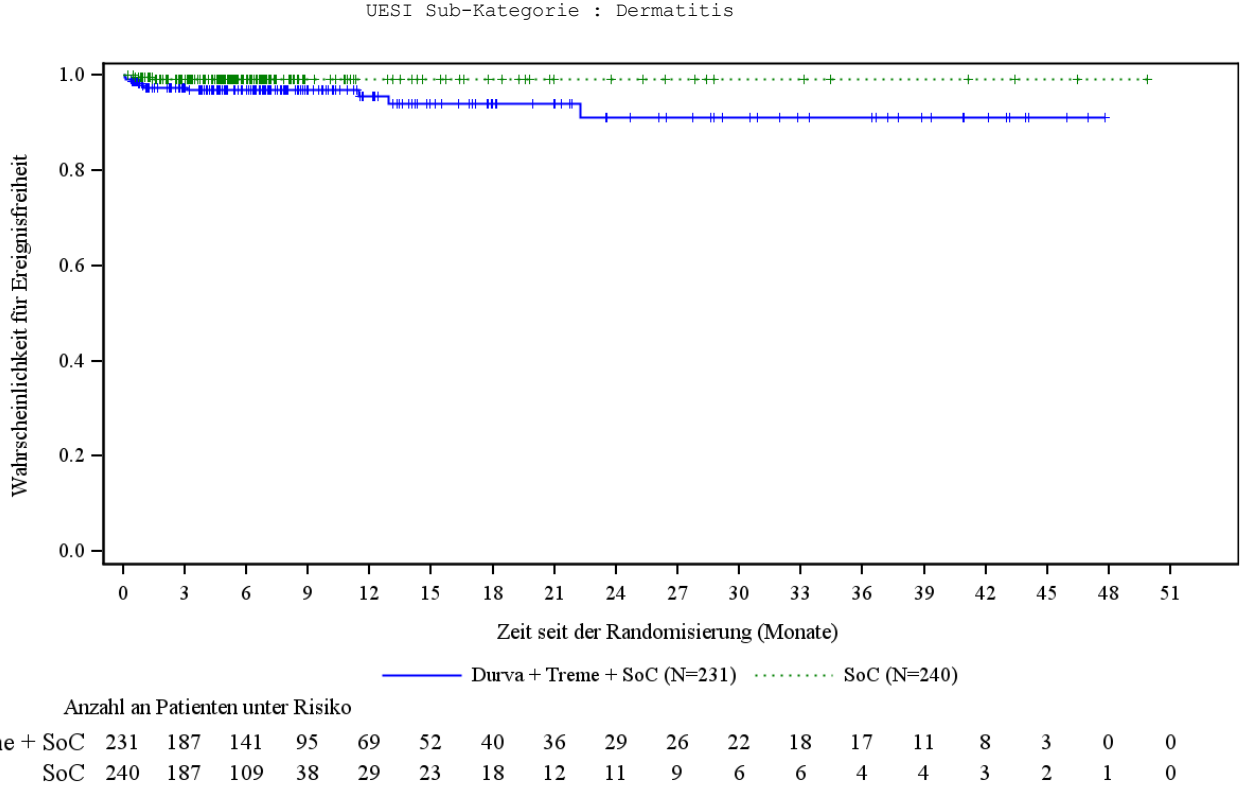
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	151	111	78	57	41	31	28	21	19	16	13	12	8	5	2	0
SoC	240	171	100	36	26	19	15	10	8	6	3	3	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

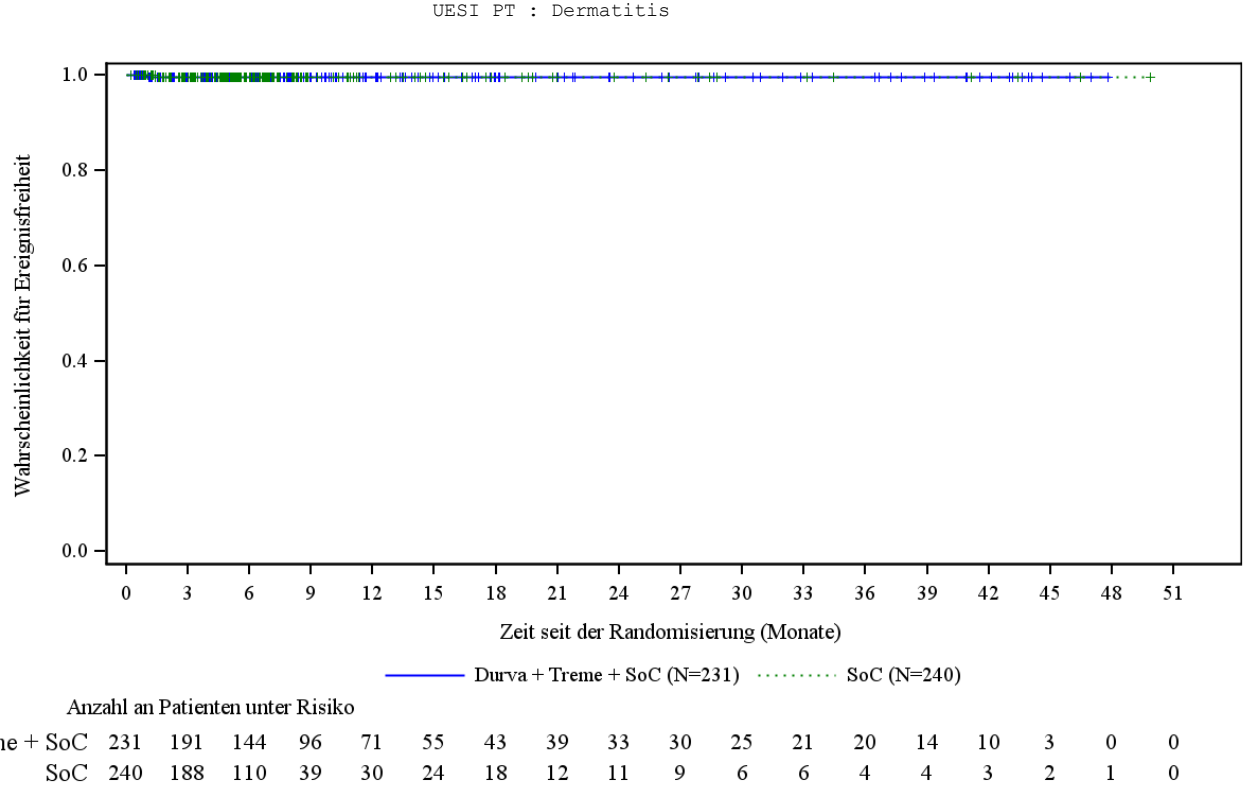
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

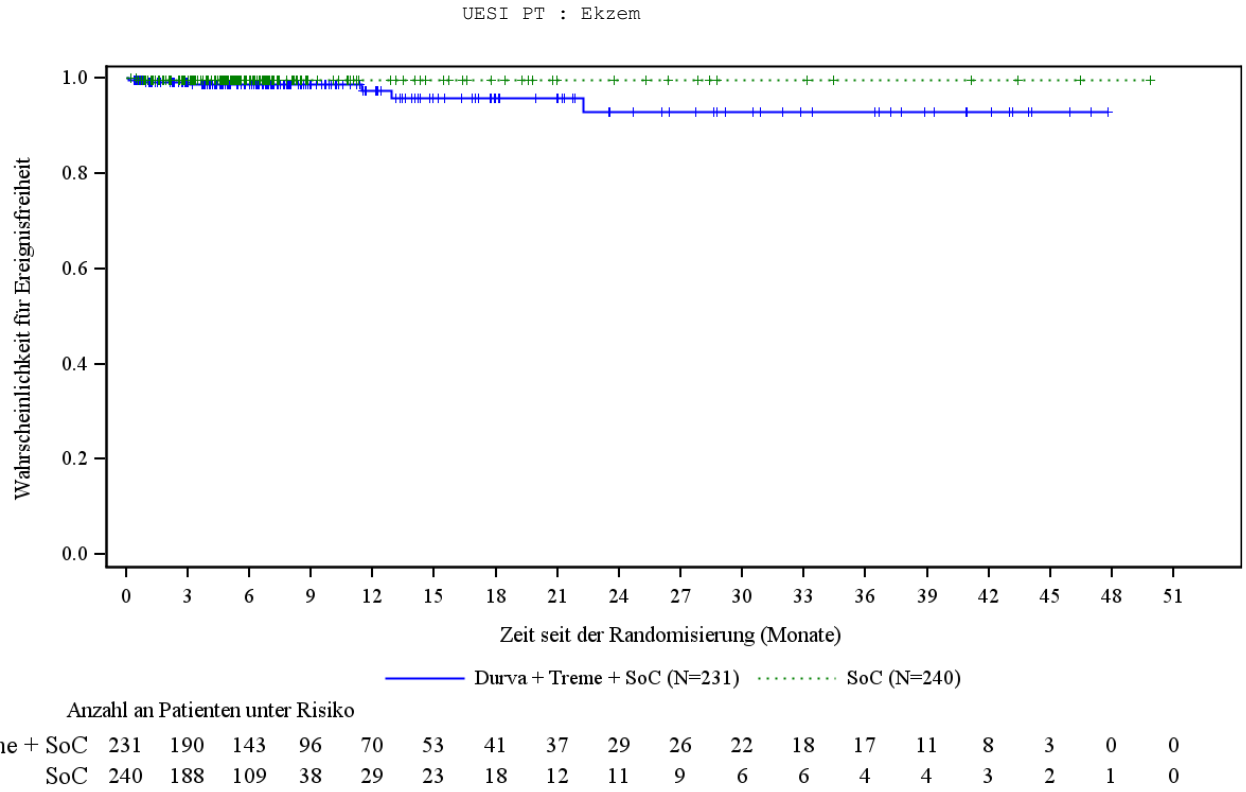
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

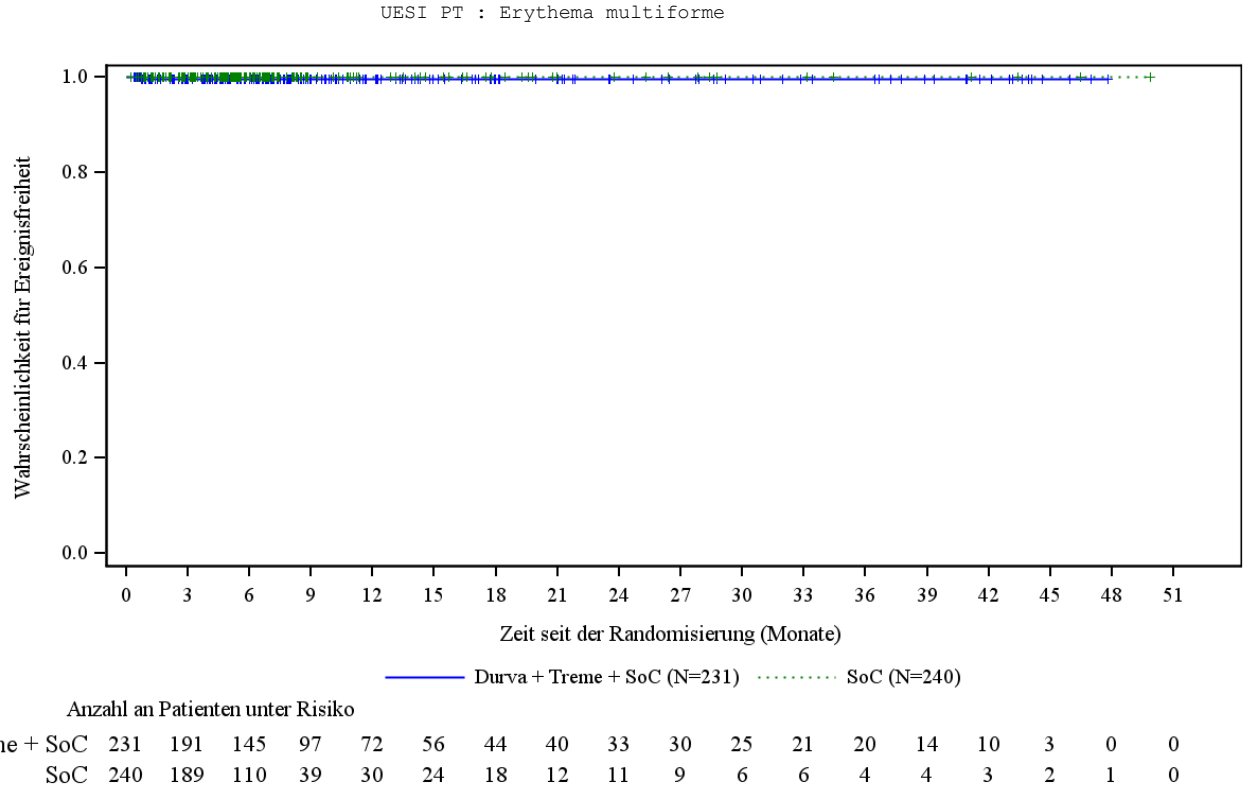
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

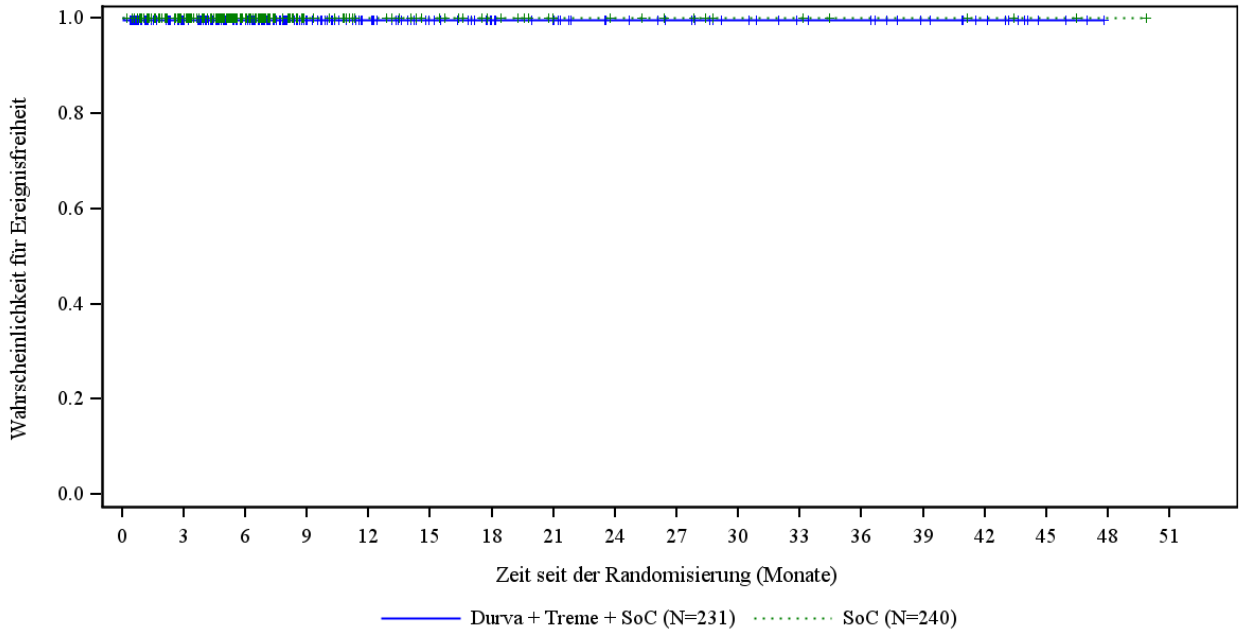


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Psoriasis



Anzahl an Patienten unter Risiko

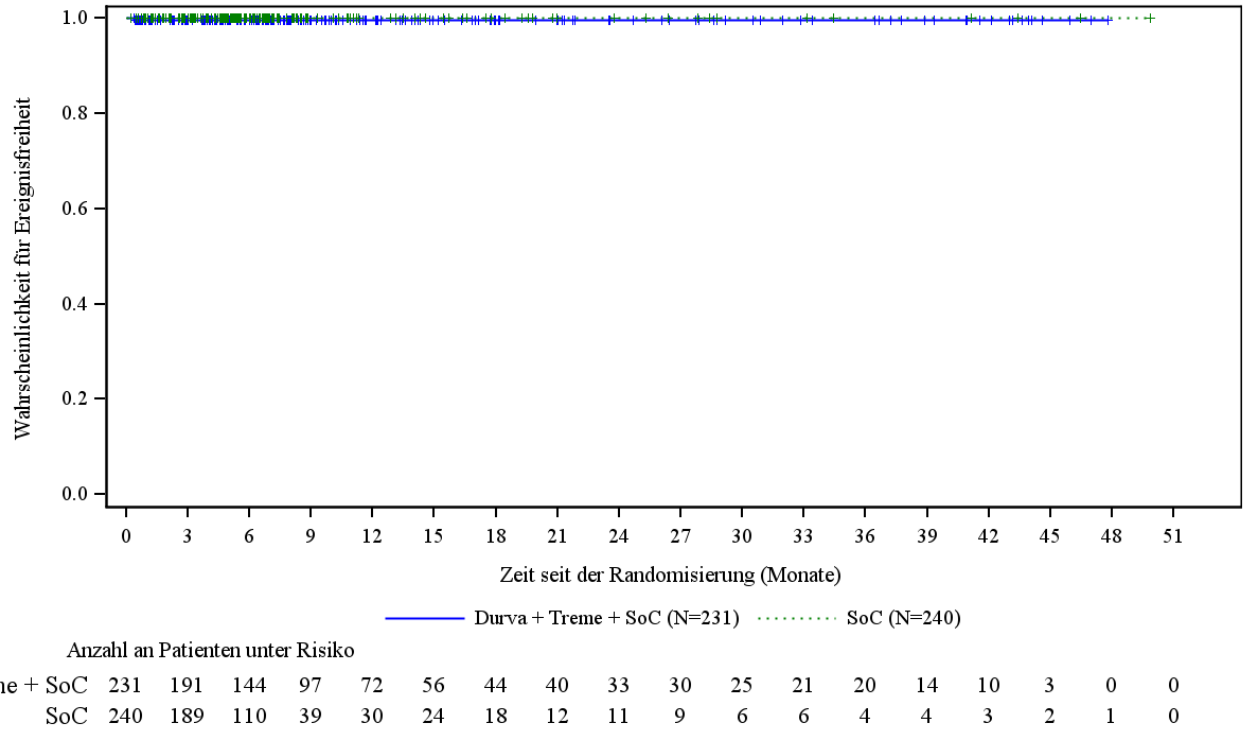
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Toxischer Hautausschlag



Anzahl an Patienten unter Risiko

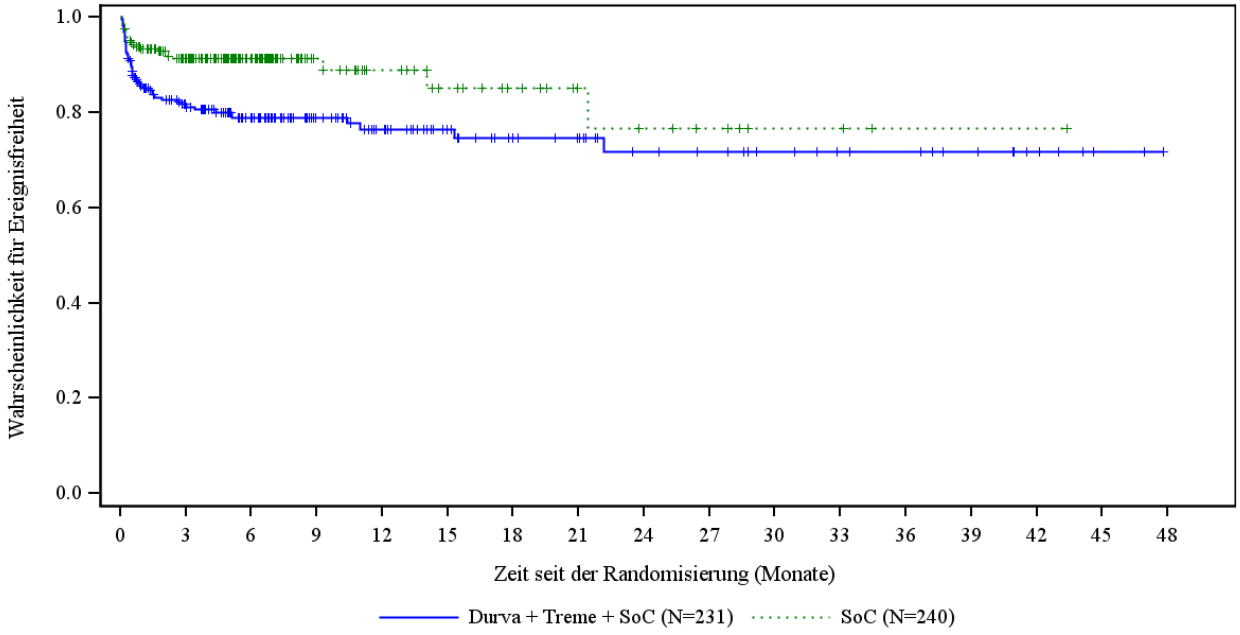
Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Sub-Kategorie : Hautausschlag



Anzahl an Patienten unter Risiko

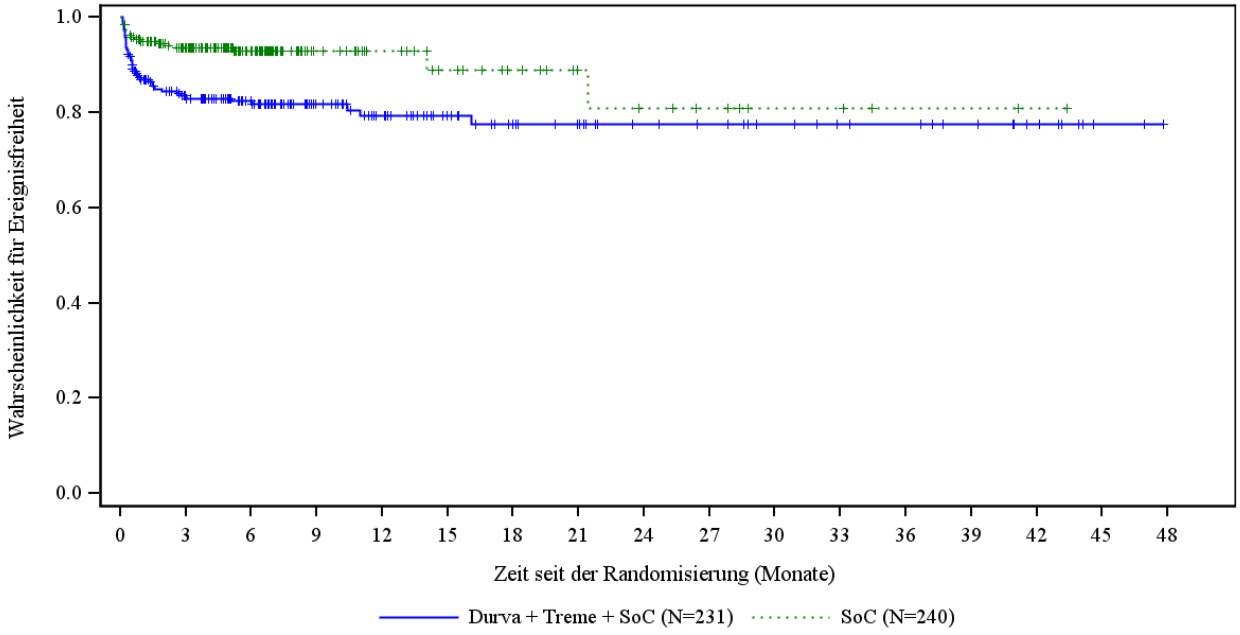
Durva + Treme + SoC	231	156	115	80	59	44	34	31	24	22	18	15	14	10	6	2	0
SoC	240	173	101	37	27	20	15	10	8	6	3	3	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Ausschlag



Anzahl an Patienten unter Risiko

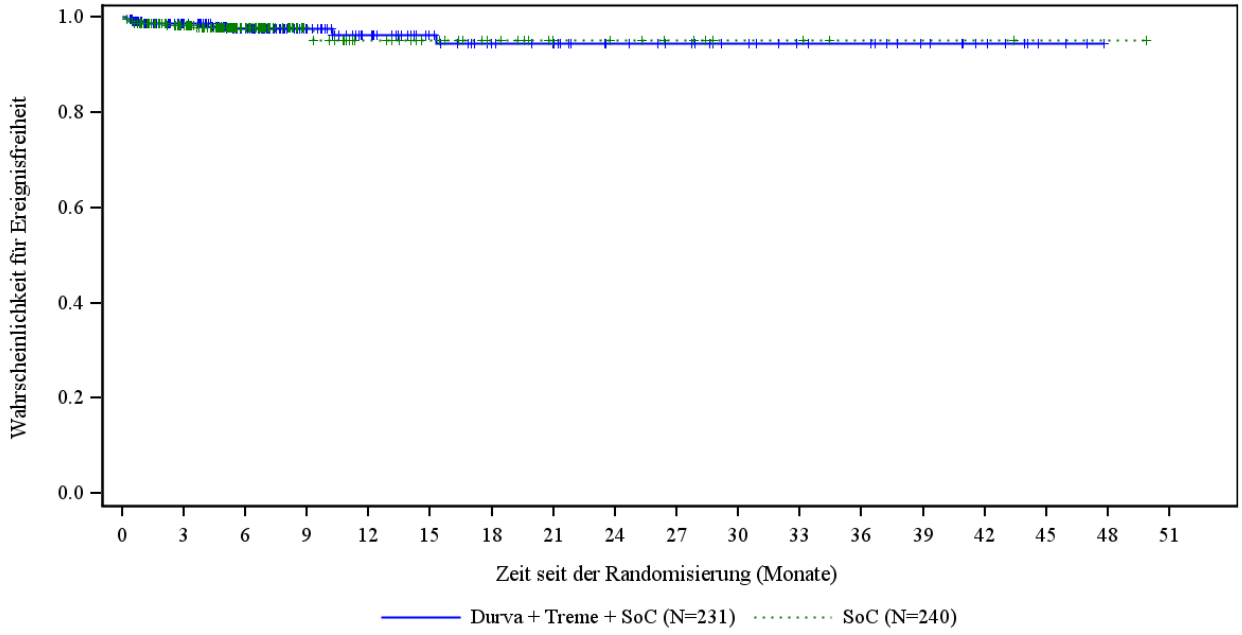
Durva + Treme + SoC	231	160	122	84	61	46	36	32	26	24	20	17	16	12	8	2	0
SoC	240	178	104	37	28	21	16	11	9	7	4	4	2	2	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Ausschlag makulo-papuloes



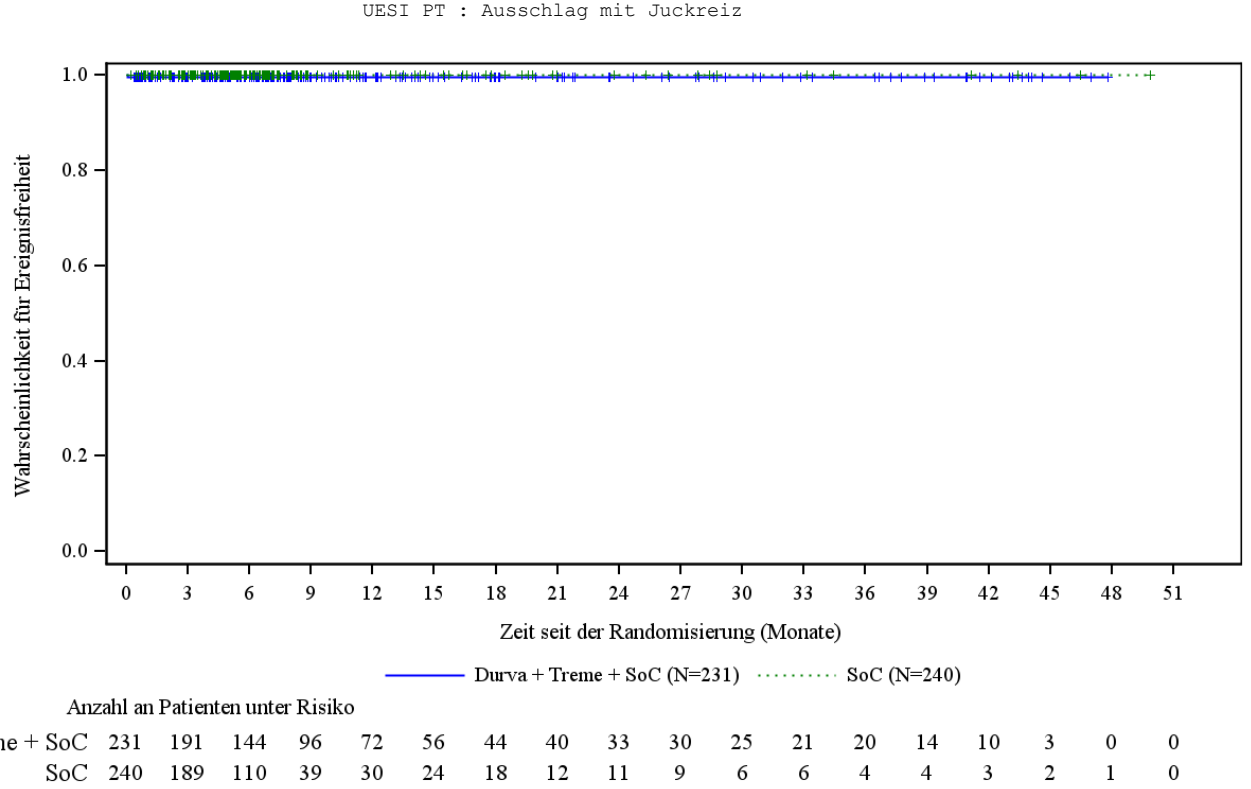
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	140	94	68	52	41	38	31	28	23	19	18	12	8	3	0	0
SoC	240	185	107	38	28	22	16	10	9	7	4	4	2	2	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



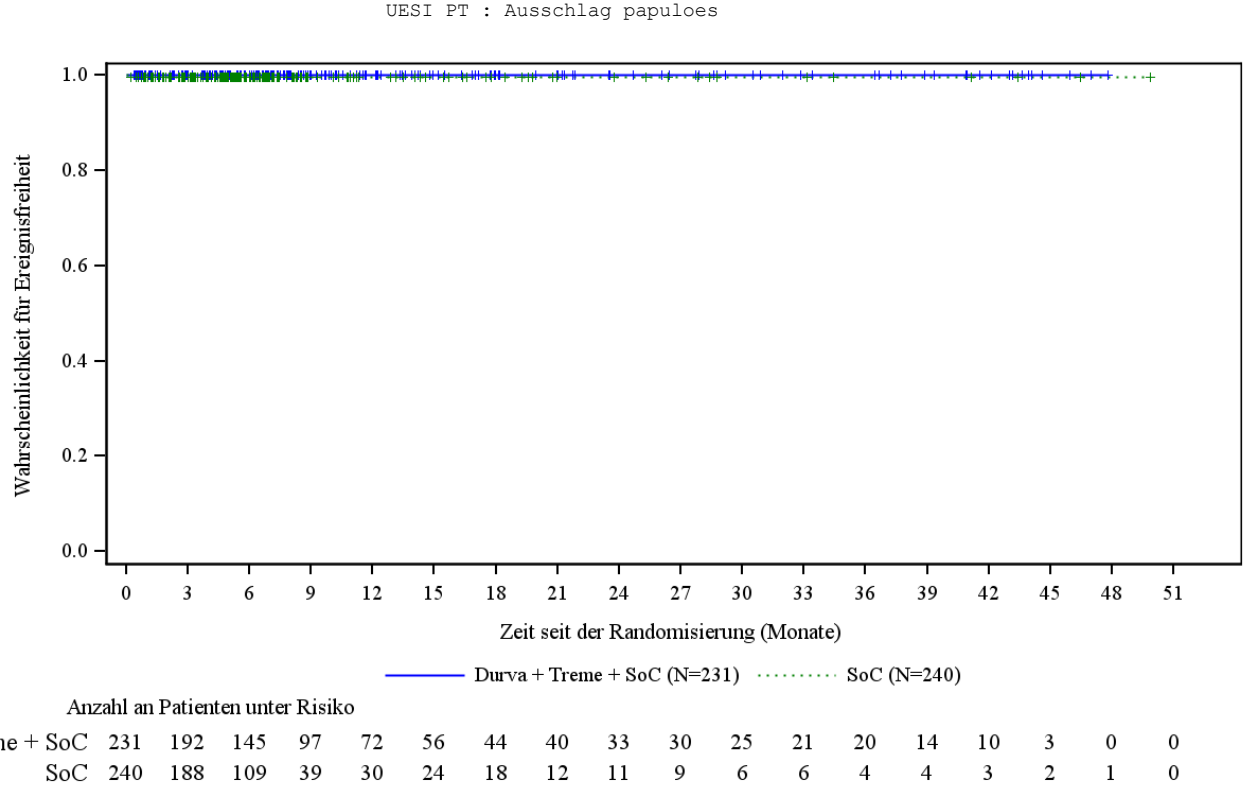
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

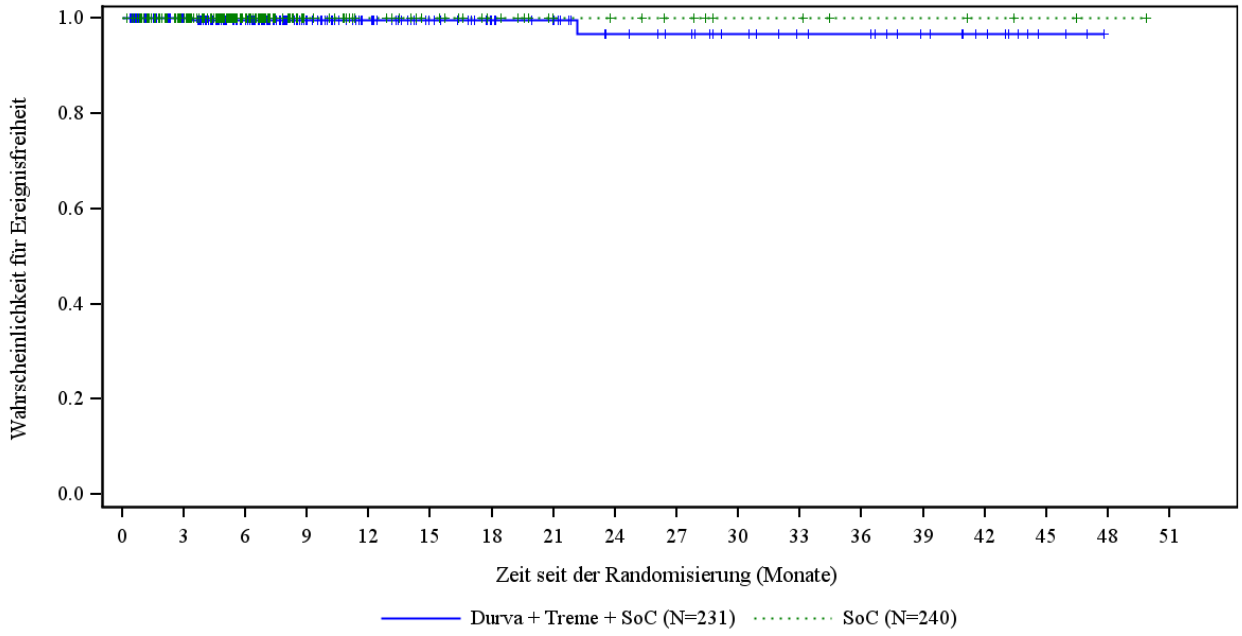
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Ausschlag pustuloes



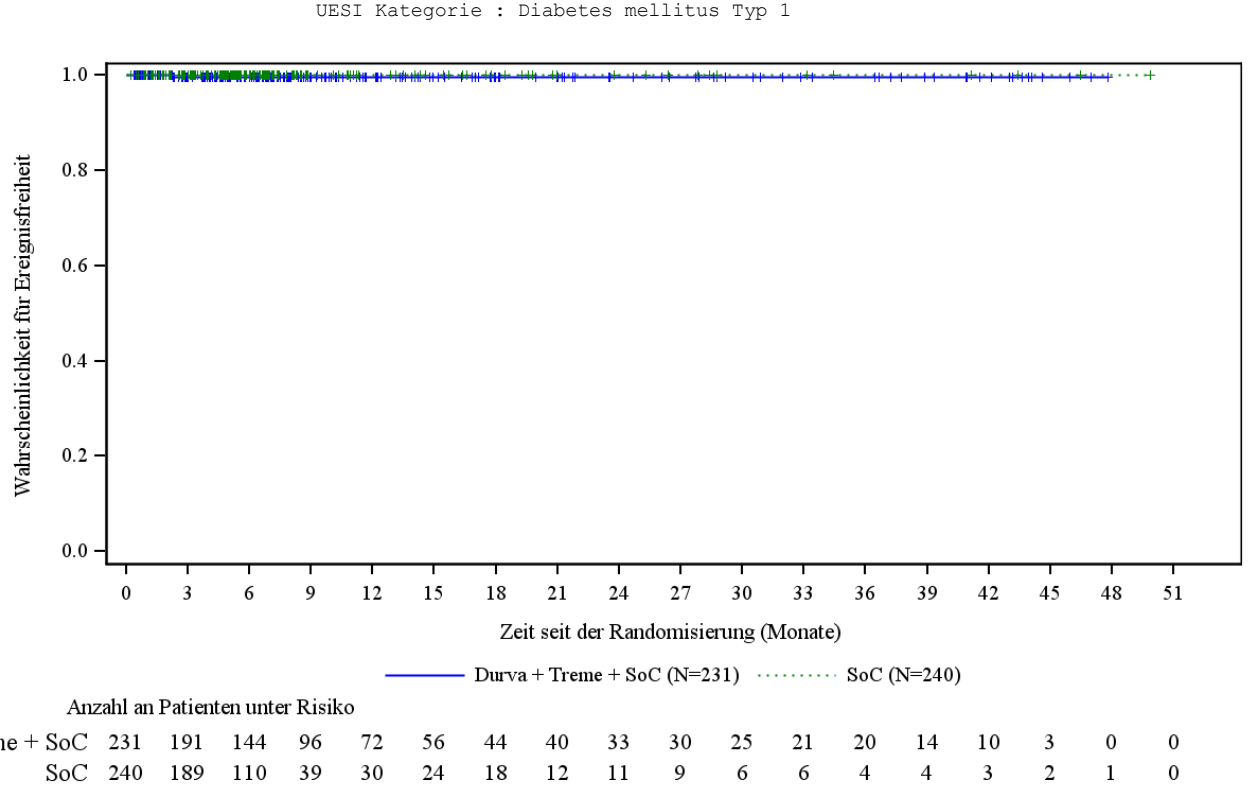
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	72	56	44	40	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

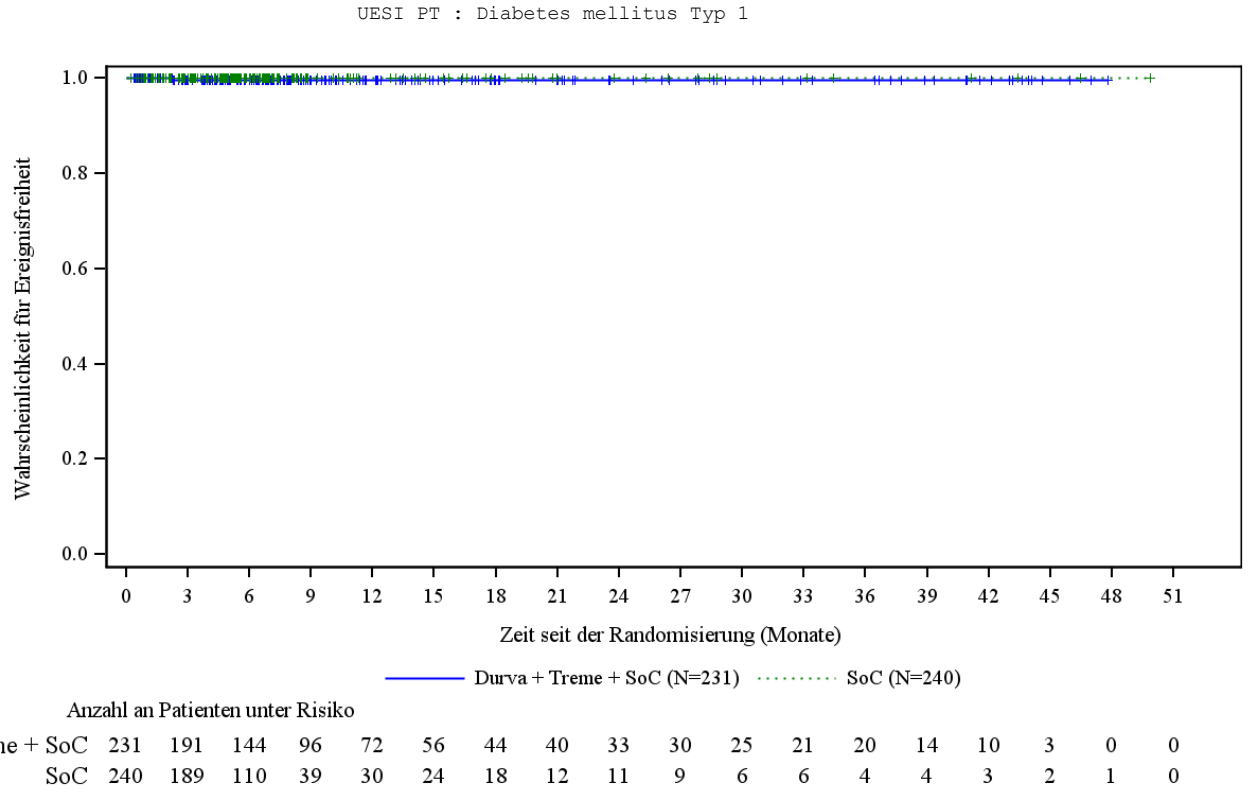
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

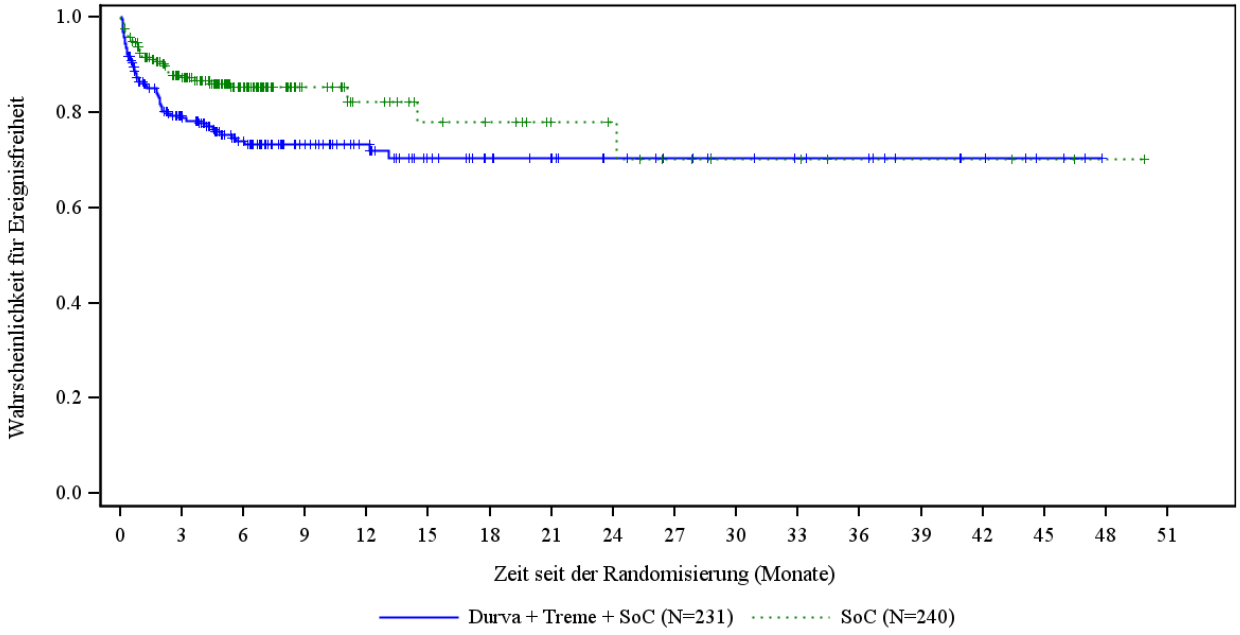


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Kategorie : Diarrhö / Kolitis



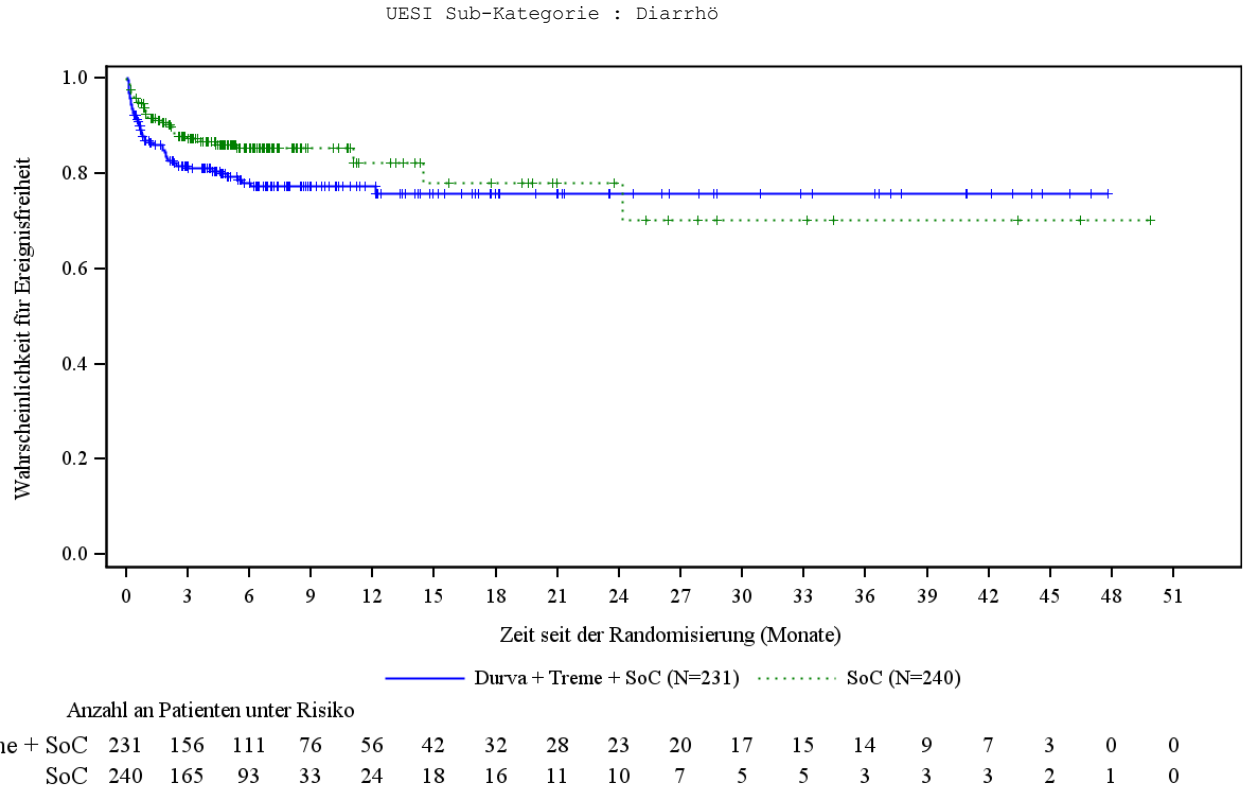
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	151	105	74	54	39	31	27	22	19	16	14	13	8	6	3	0	0
SoC	240	165	93	33	24	18	16	11	10	7	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

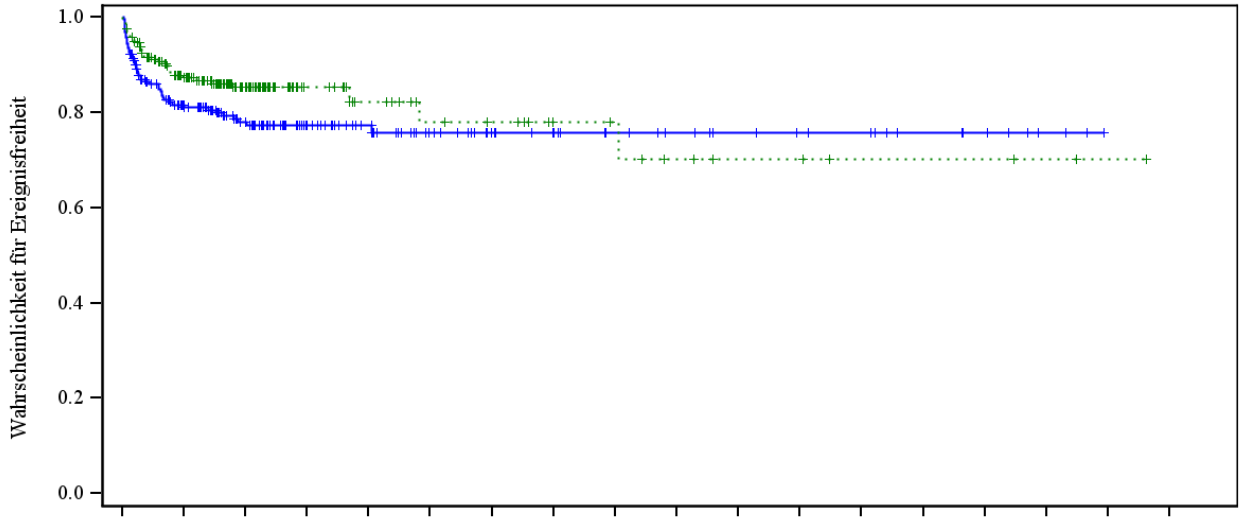


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Diarrhoe



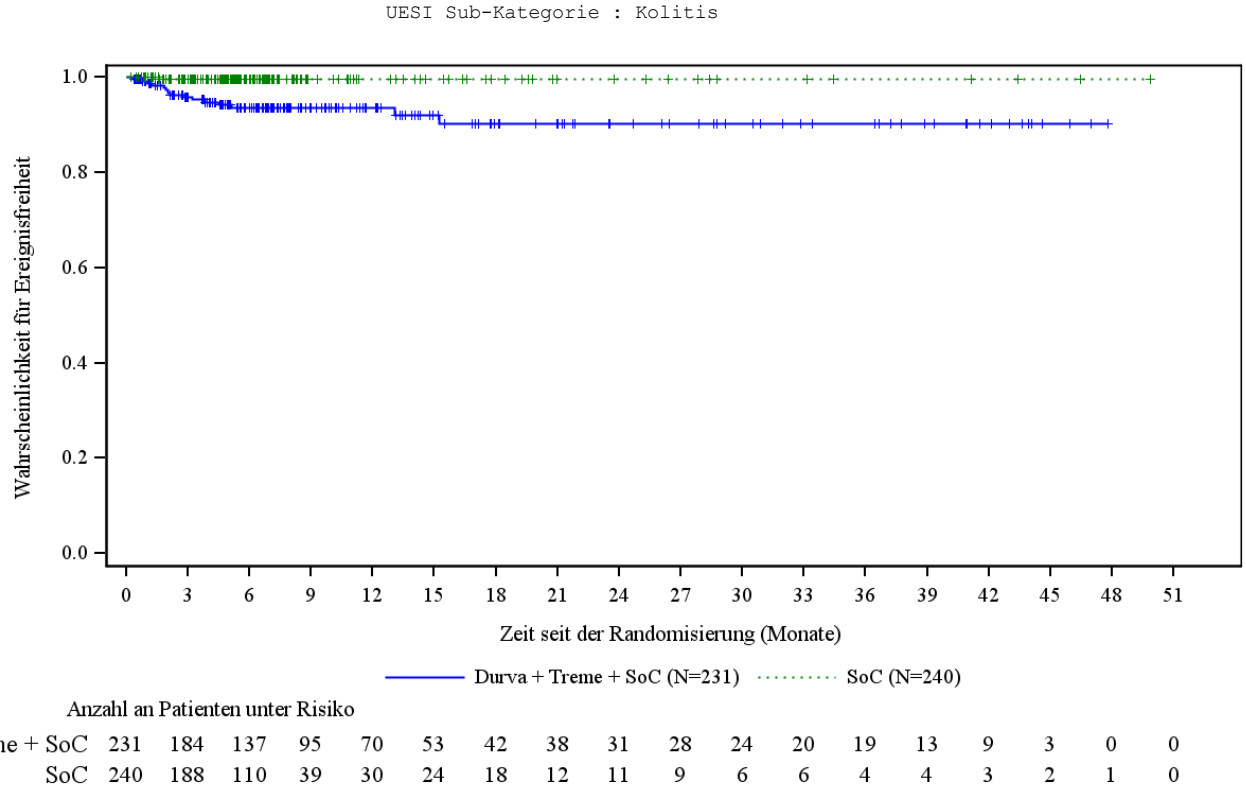
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	156	111	76	56	42	32	28	23	20	17	15	14	9	7	3	0	0
SoC	240	165	93	33	24	18	16	11	10	7	5	5	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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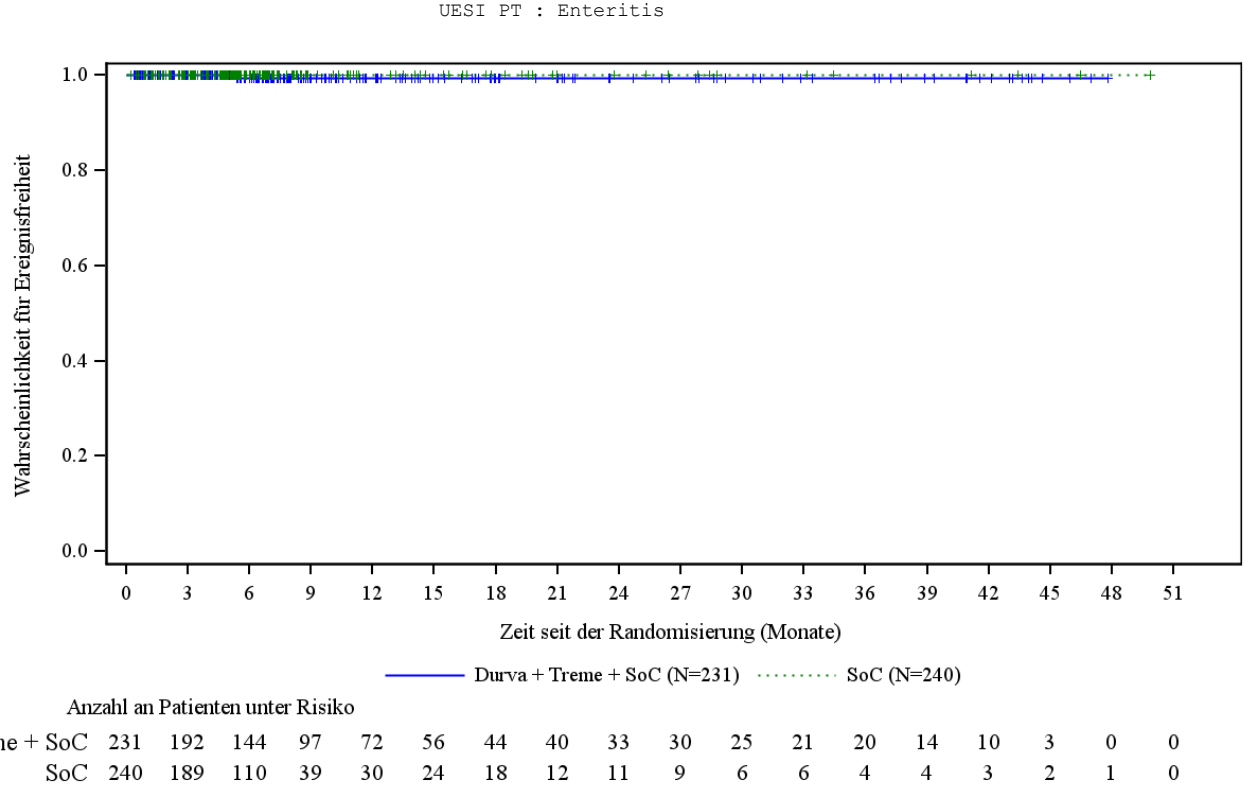
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



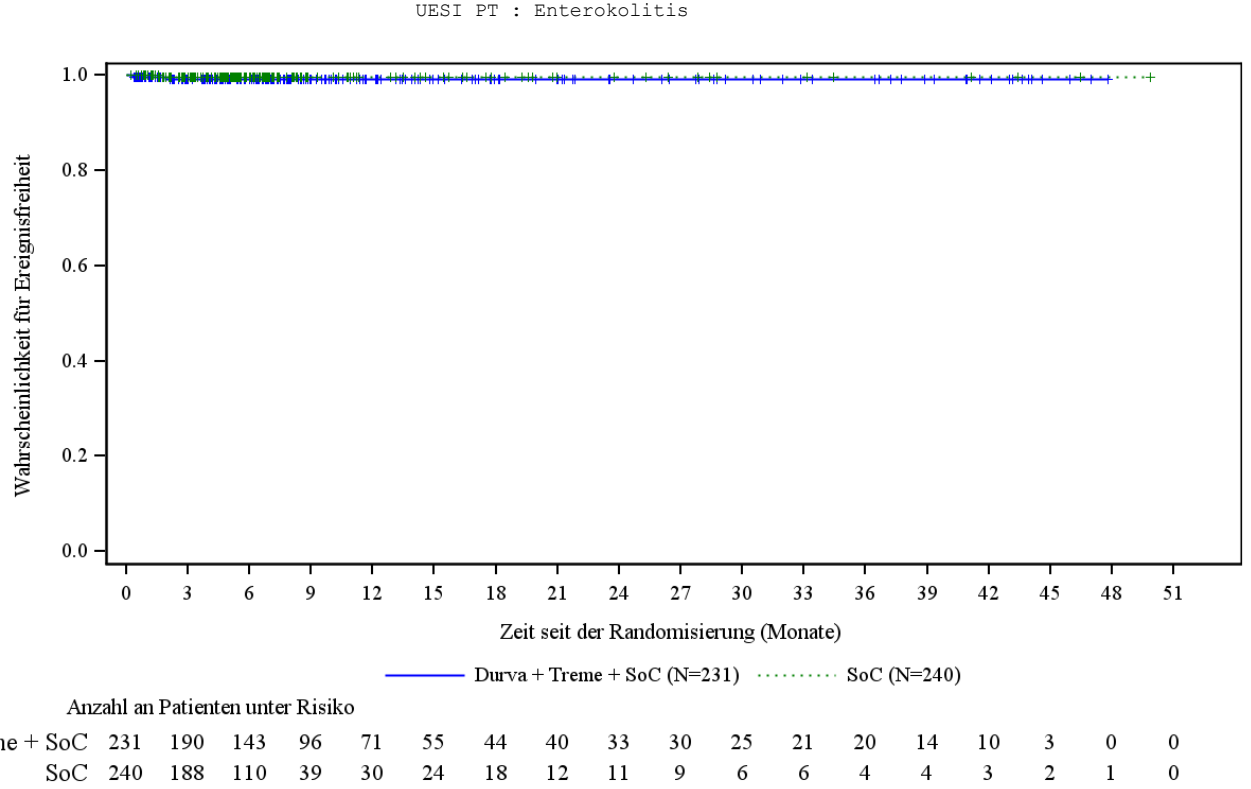
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
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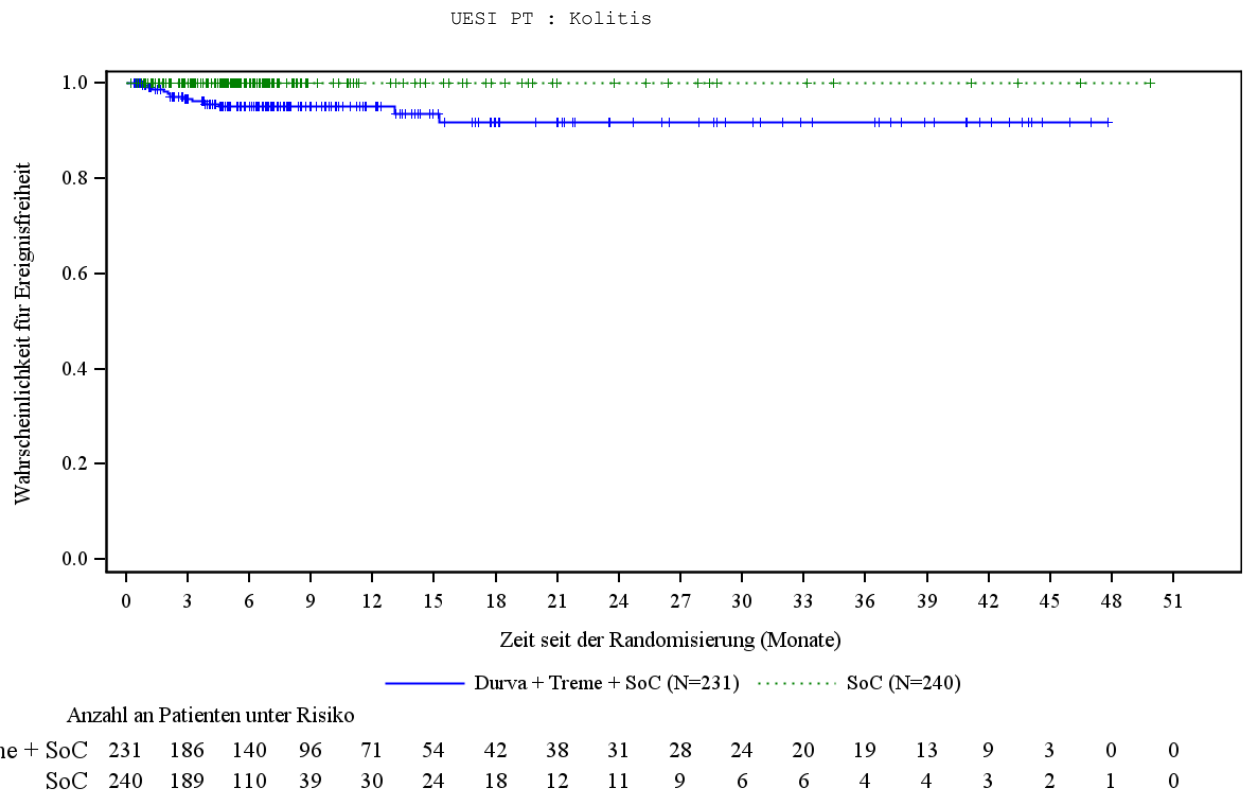
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



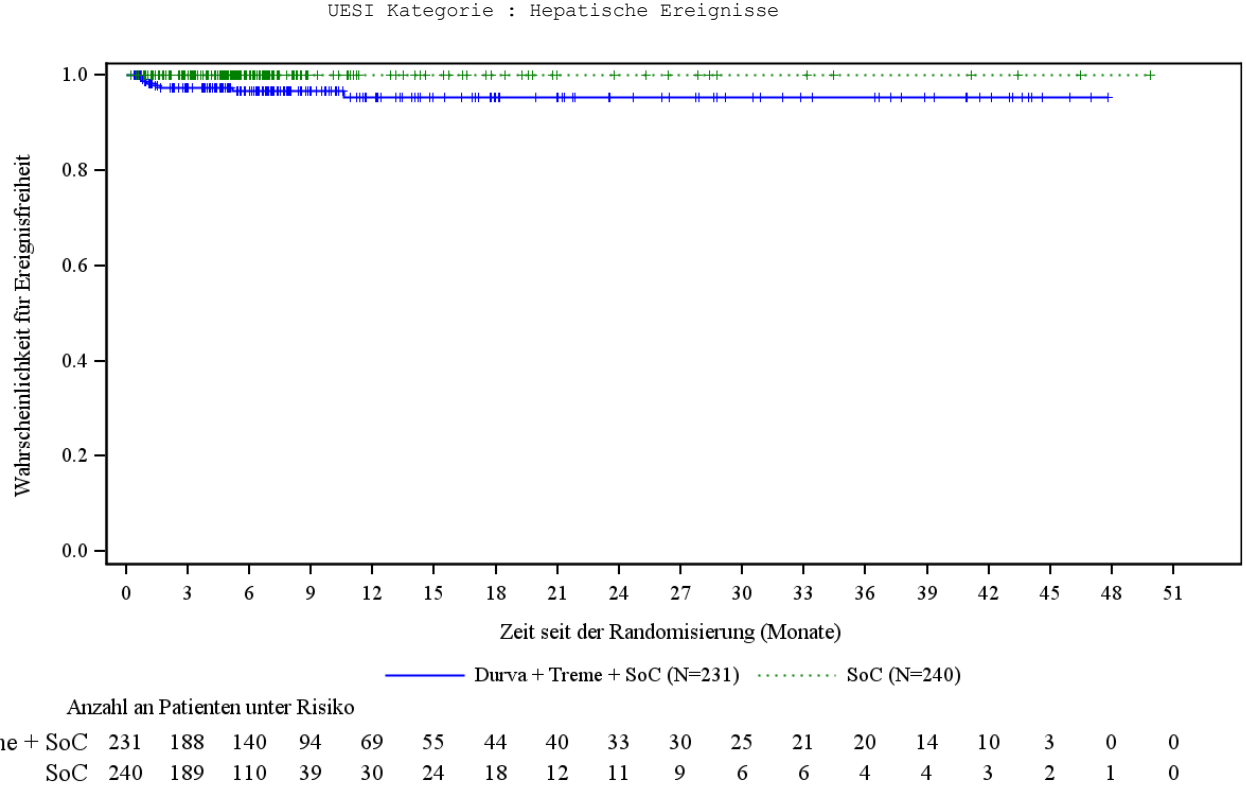
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	186	140	96	71	54	42	38	31	28	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

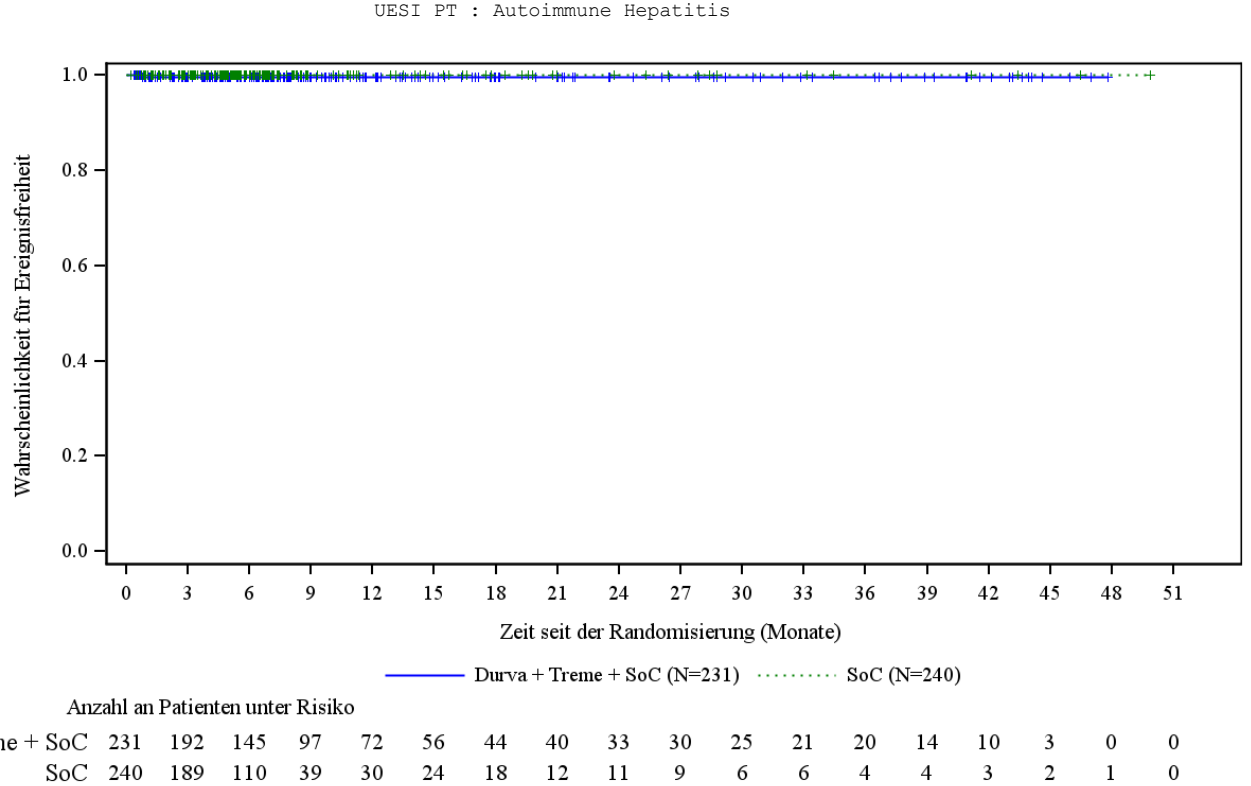
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

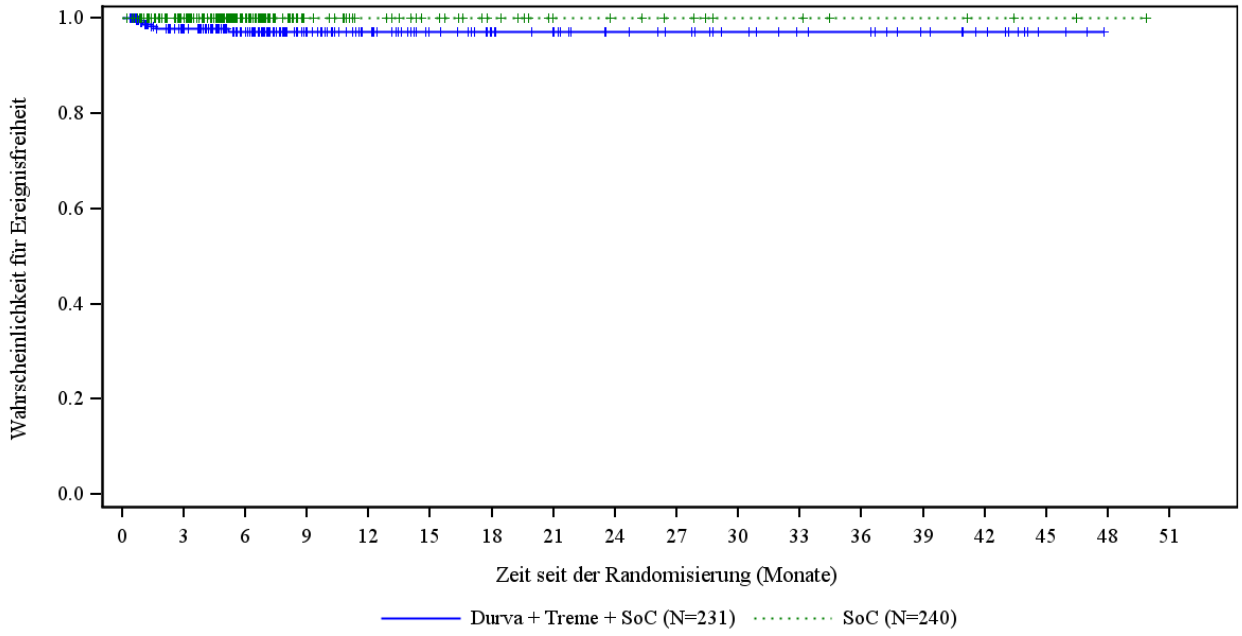


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Hepatitis



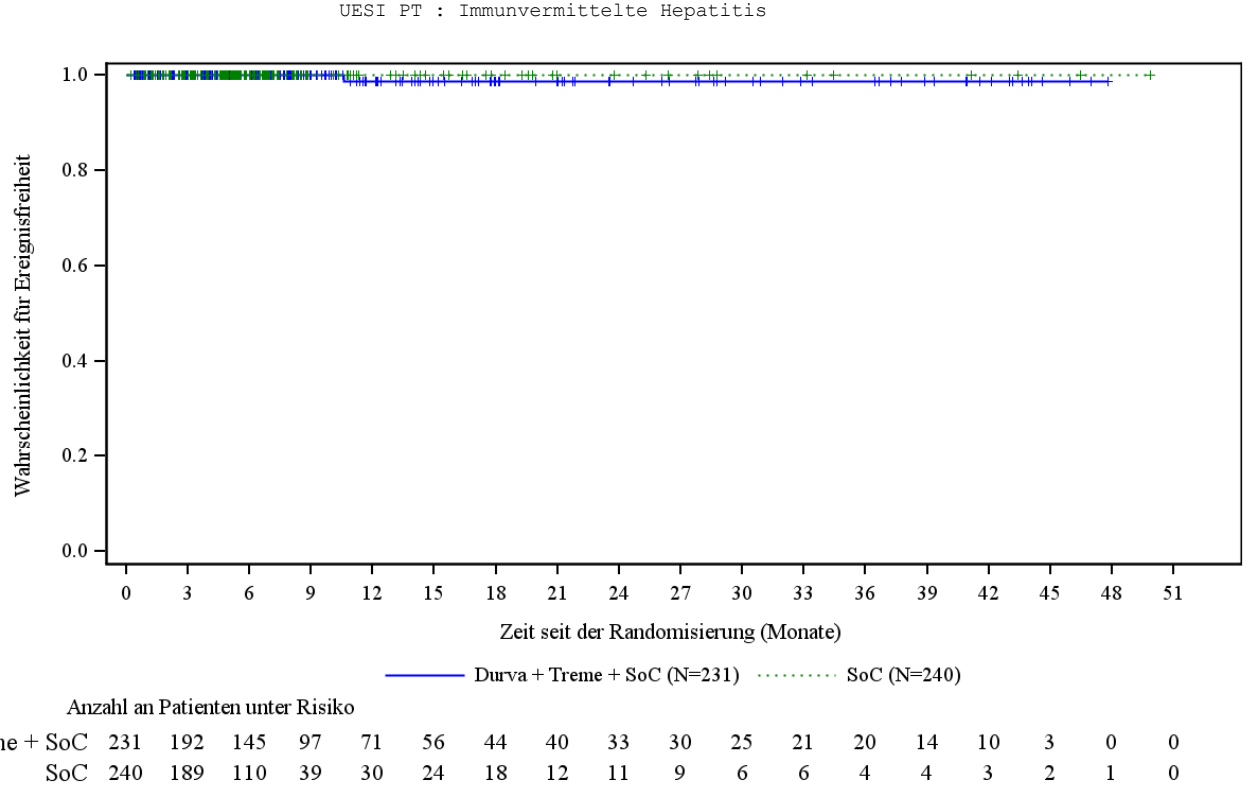
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	188	140	94	70	55	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



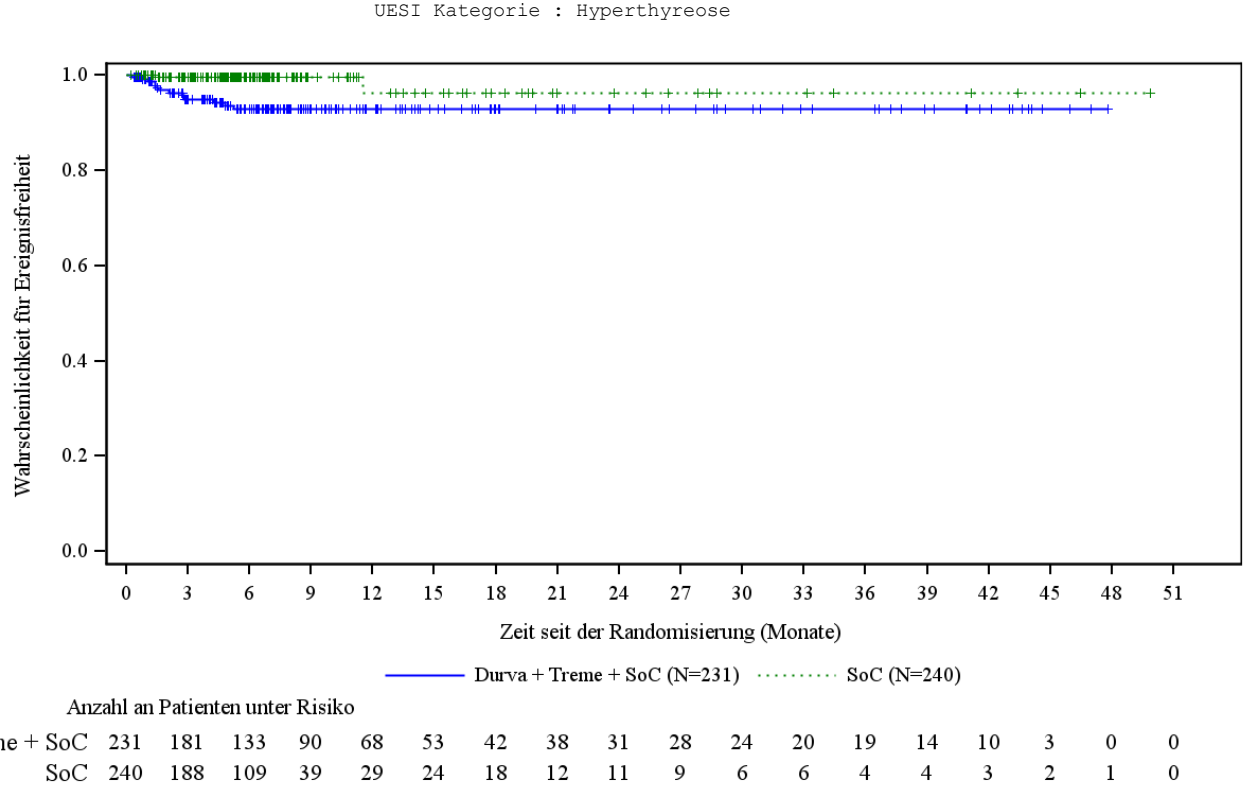
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	71	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

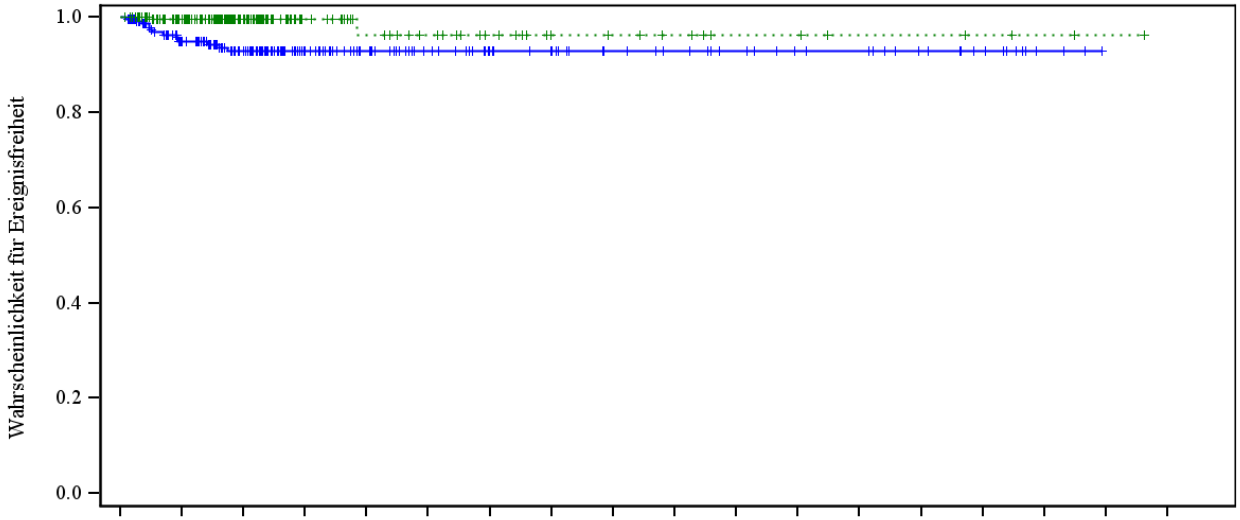


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Hyperthyroidismus



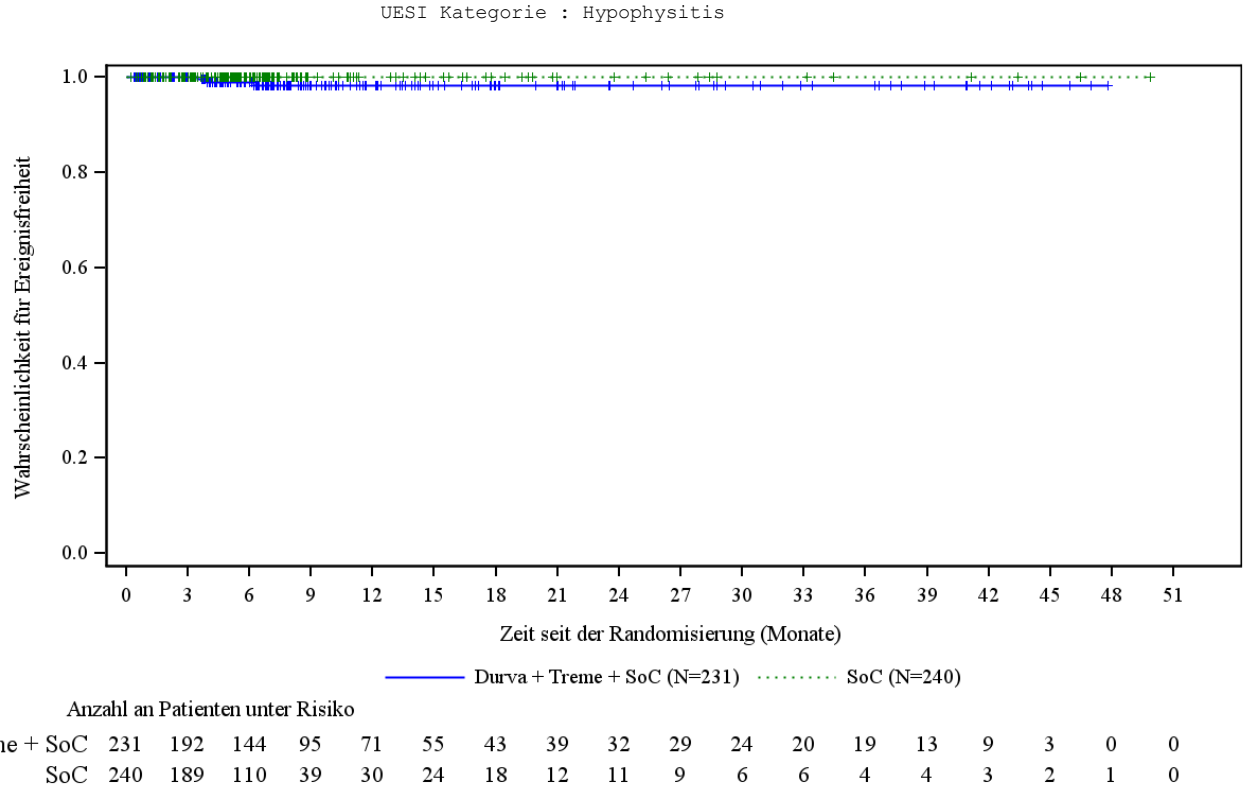
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	181	133	90	68	53	42	38	31	28	24	20	19	14	10	3	0	0
SoC	240	188	109	39	29	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

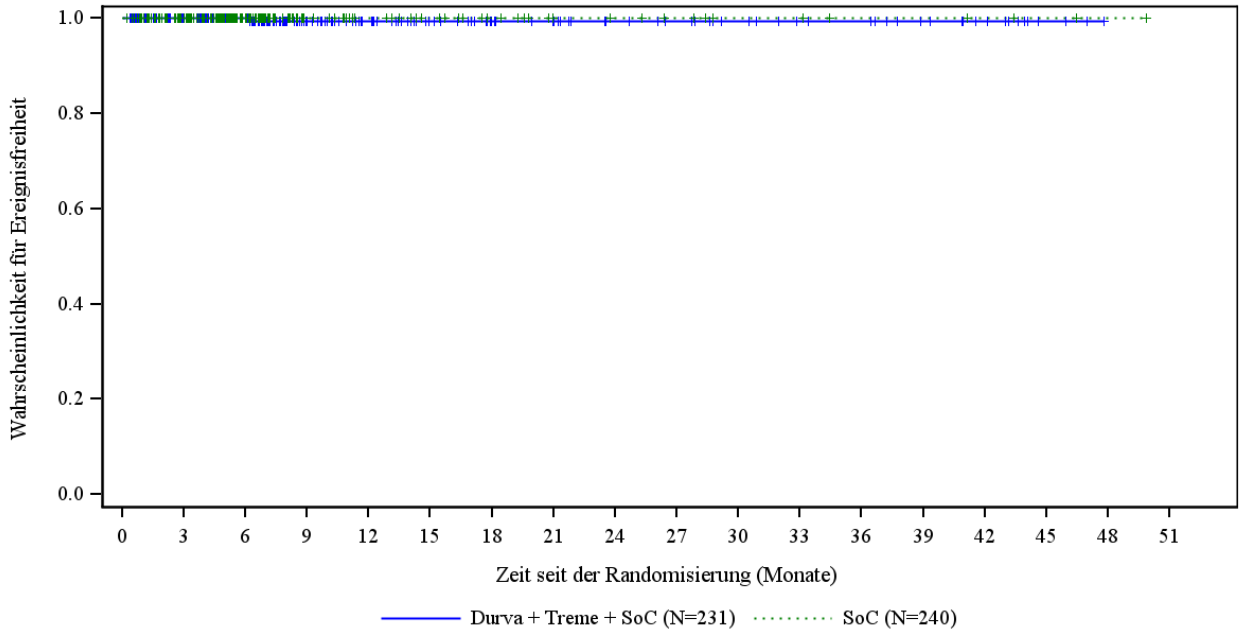
Durva + Treme + SoC	231	192	144	95	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Diabetes insipidus



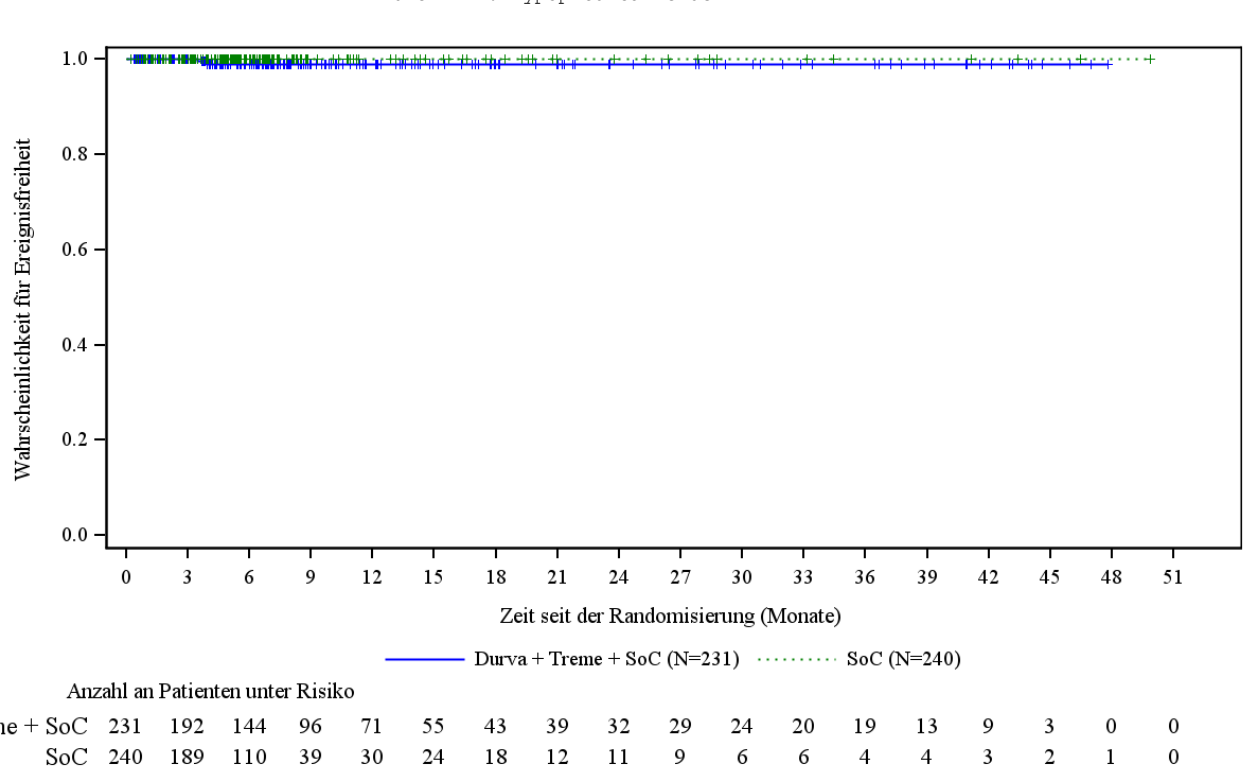
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

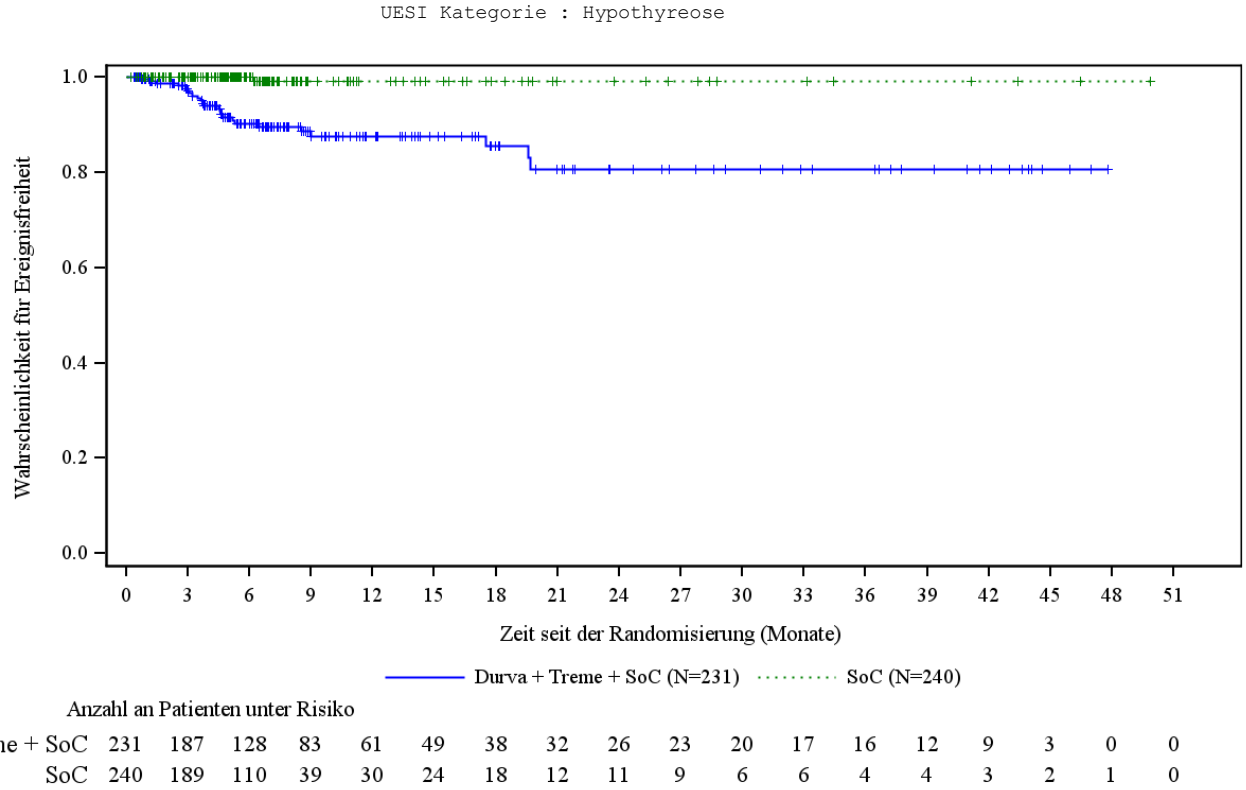
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

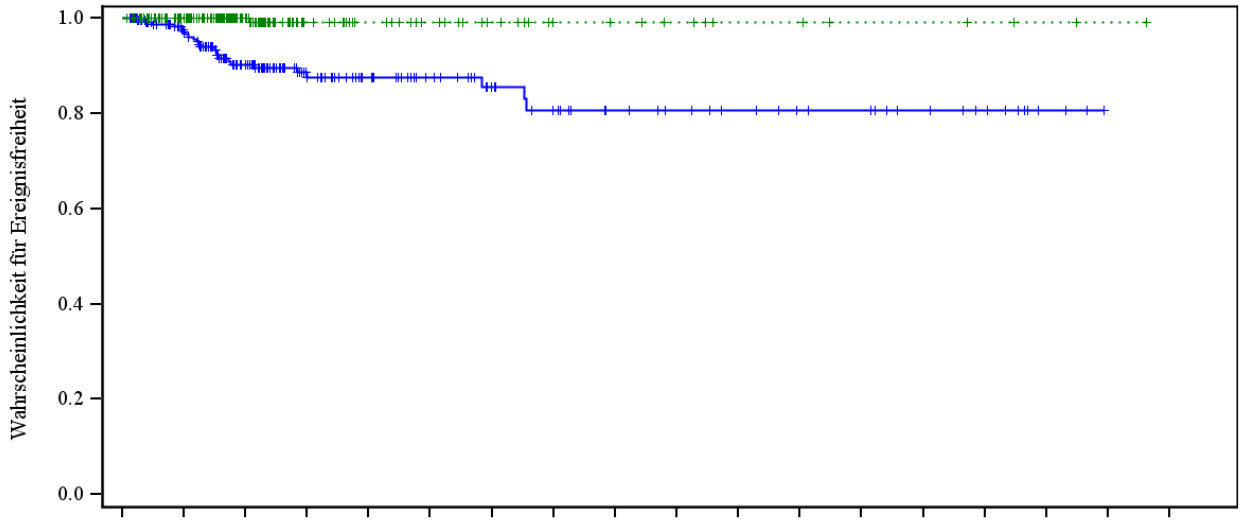


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Hypothyreose



Anzahl an Patienten unter Risiko

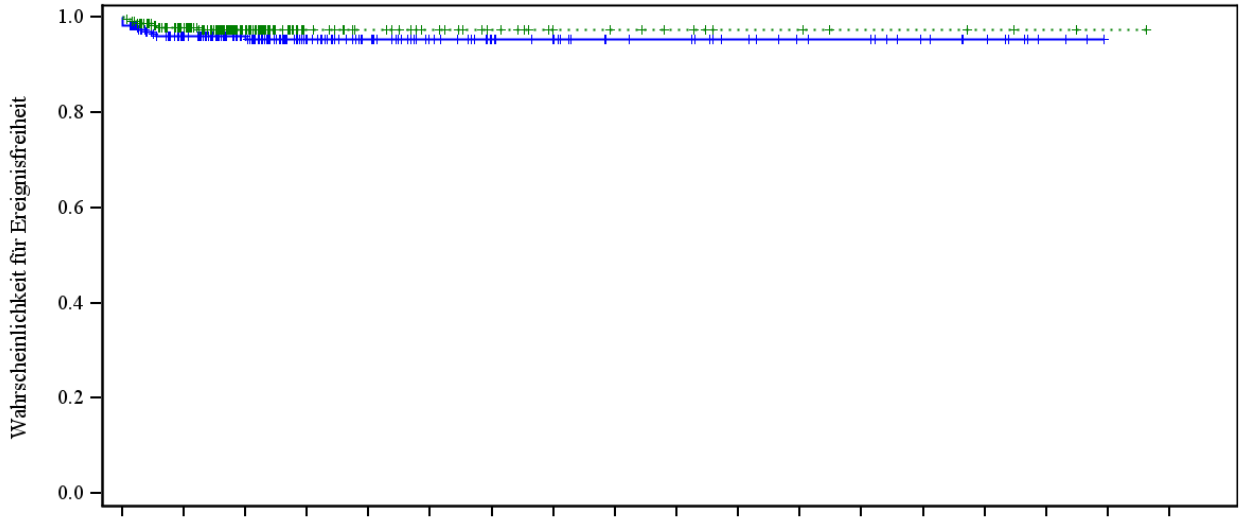
Durva + Treme + SoC	231	187	128	83	61	49	38	32	26	23	20	17	16	12	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Kategorie : Infusions- und Überempfindlichkeitsreaktion



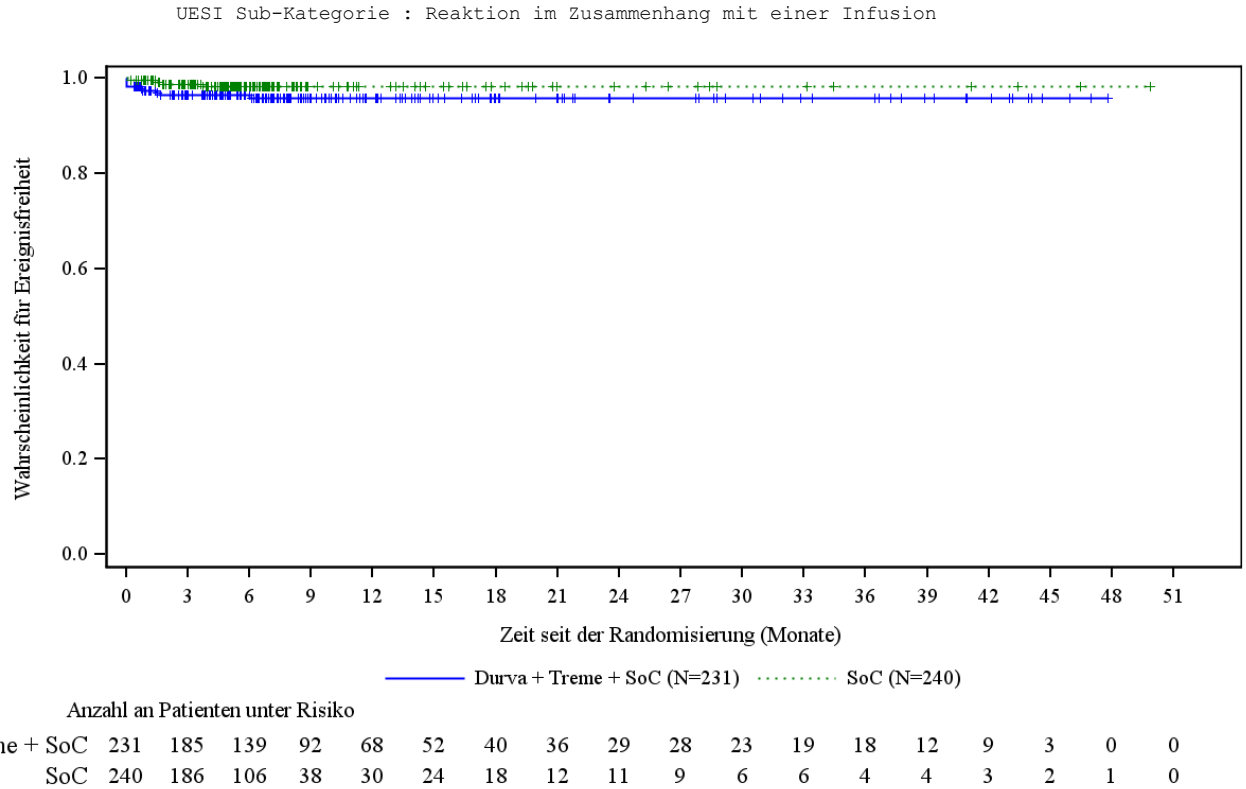
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	184	138	92	68	52	40	36	29	28	23	19	18	12	9	3	0	0
SoC	240	184	105	37	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

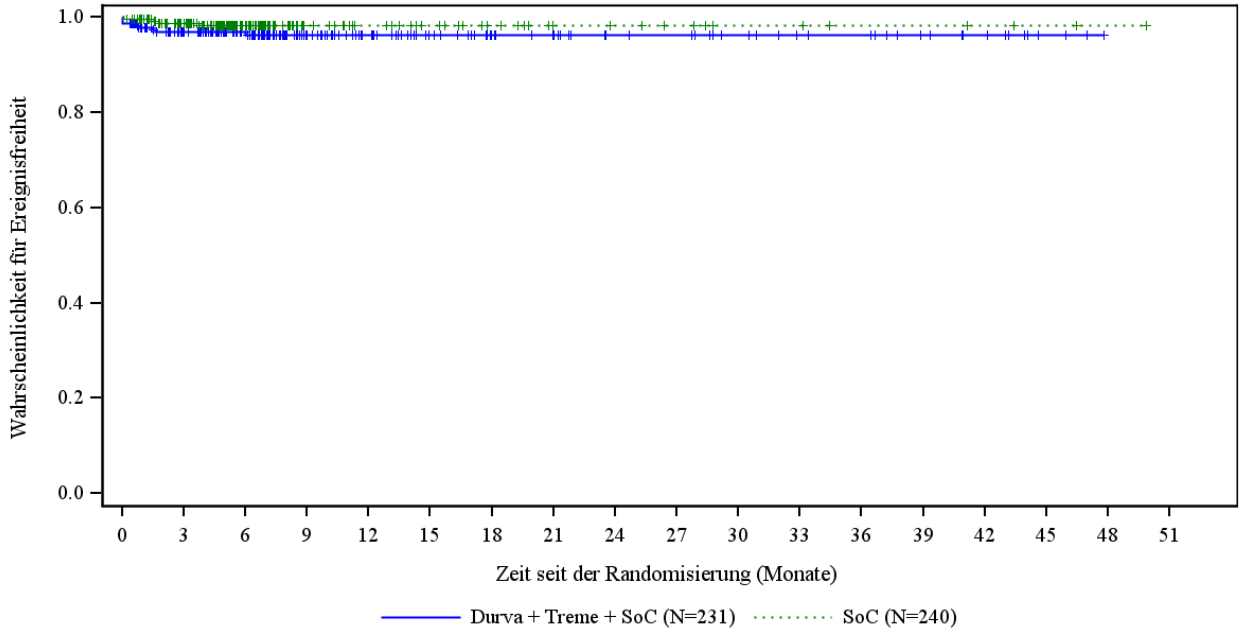


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Reaktion im Zusammenhang mit einer Infusion



Anzahl an Patienten unter Risiko

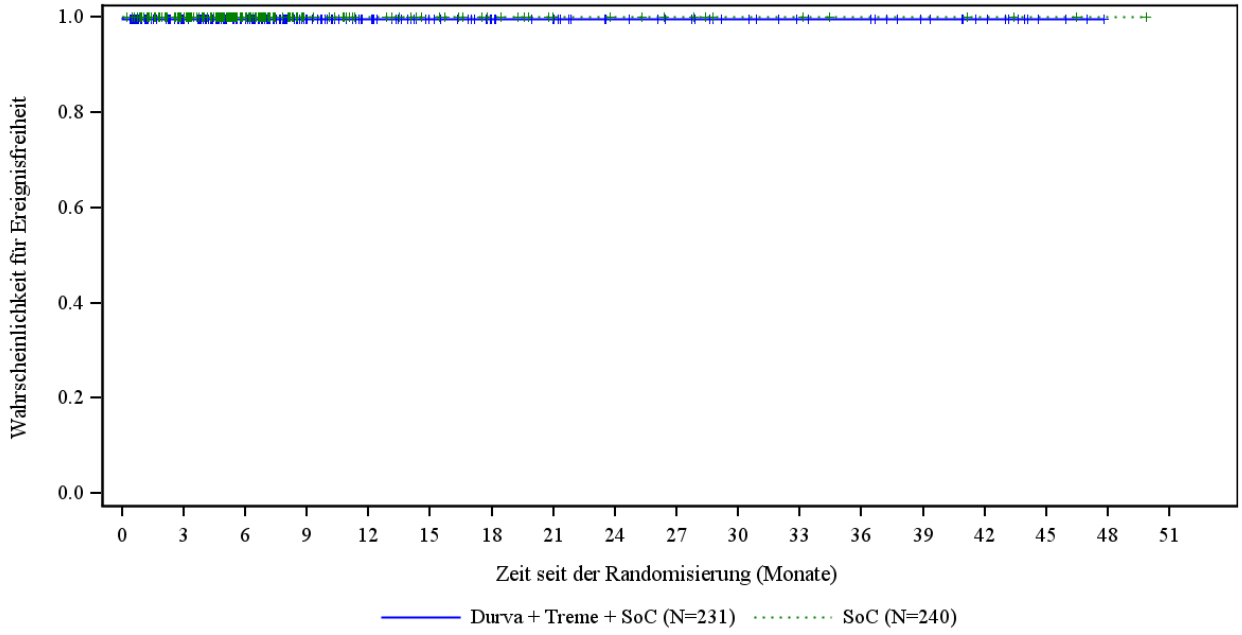
Durva + Treme + SoC	231	186	140	92	68	52	40	36	29	28	23	19	18	12	9	3	0	0
SoC	240	186	106	38	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Urtikaria



Anzahl an Patienten unter Risiko

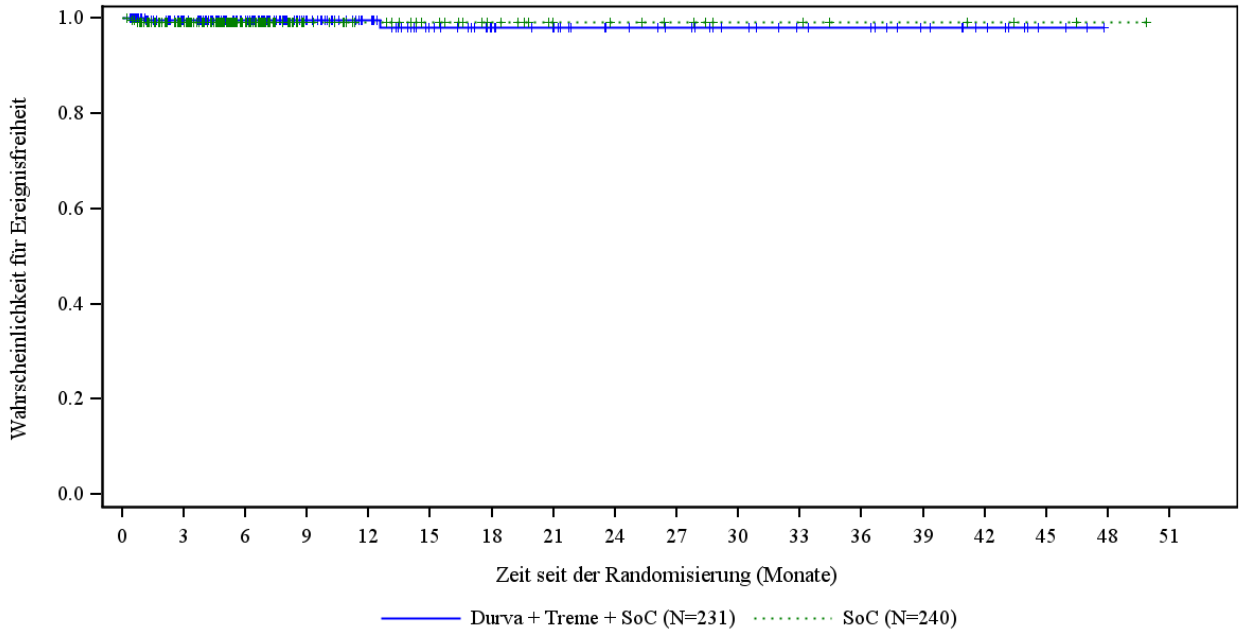
Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Sub-Kategorie : Überempfindlichkeitsreaktion / Anaphylaktische Reaktion



Anzahl an Patienten unter Risiko

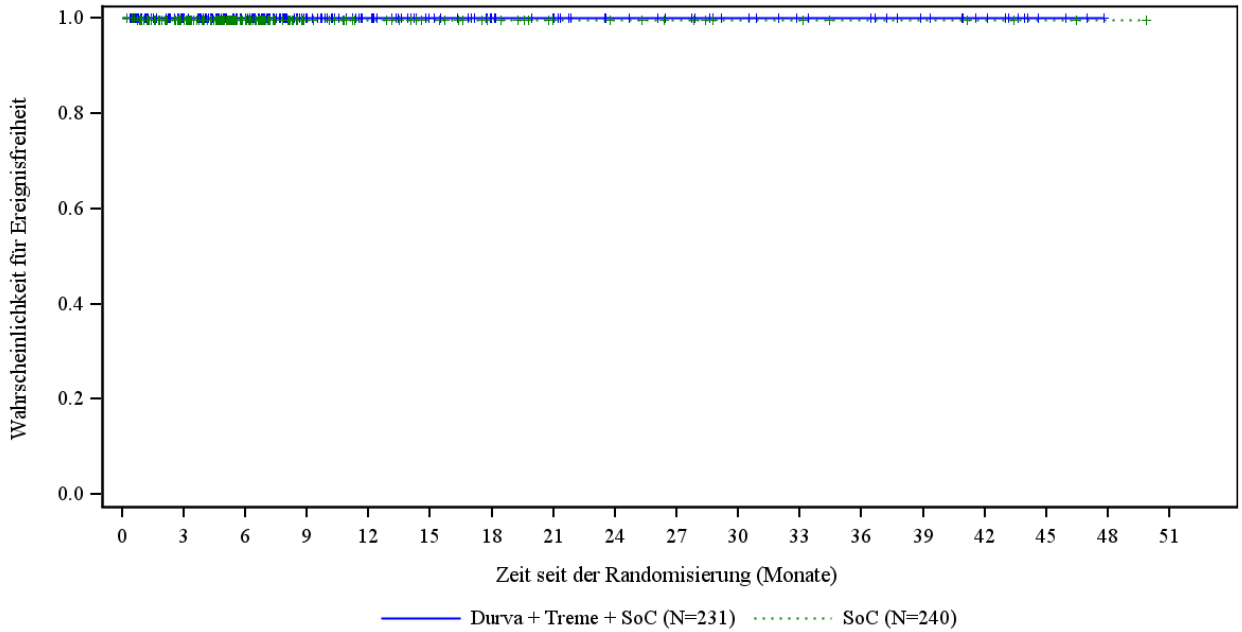
Durva + Treme + SoC	231	191	144	97	72	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	187	109	38	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Arzneimittelueberempfindlichkeit



Anzahl an Patienten unter Risiko

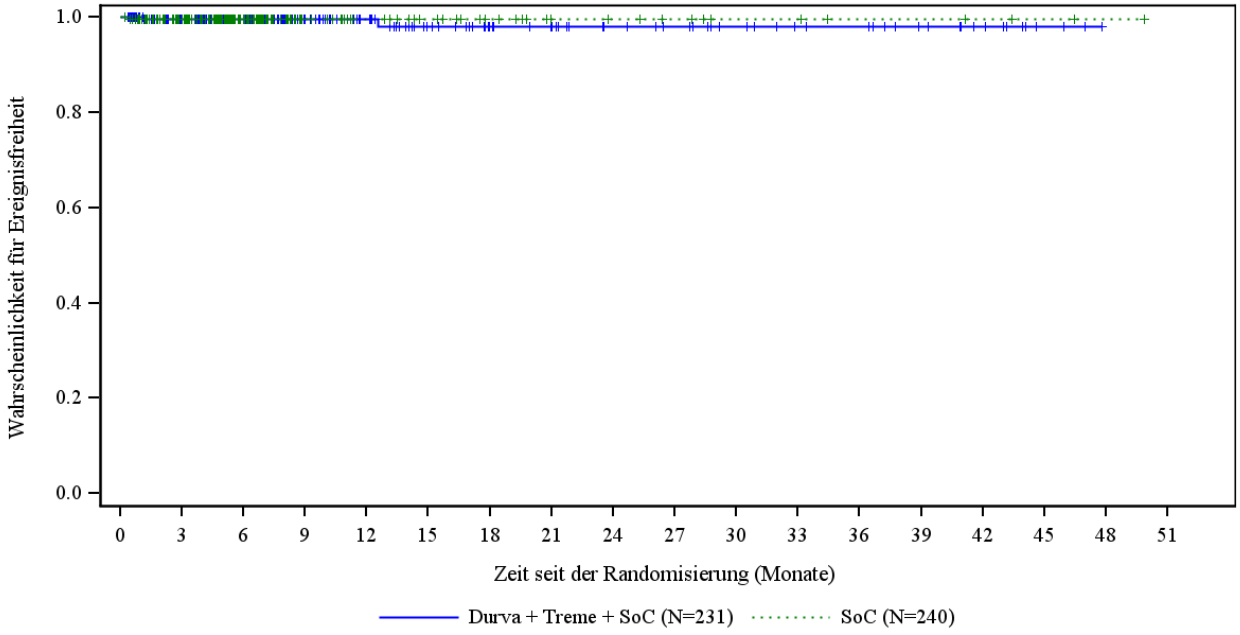
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	109	38	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Medikamentenausschlag



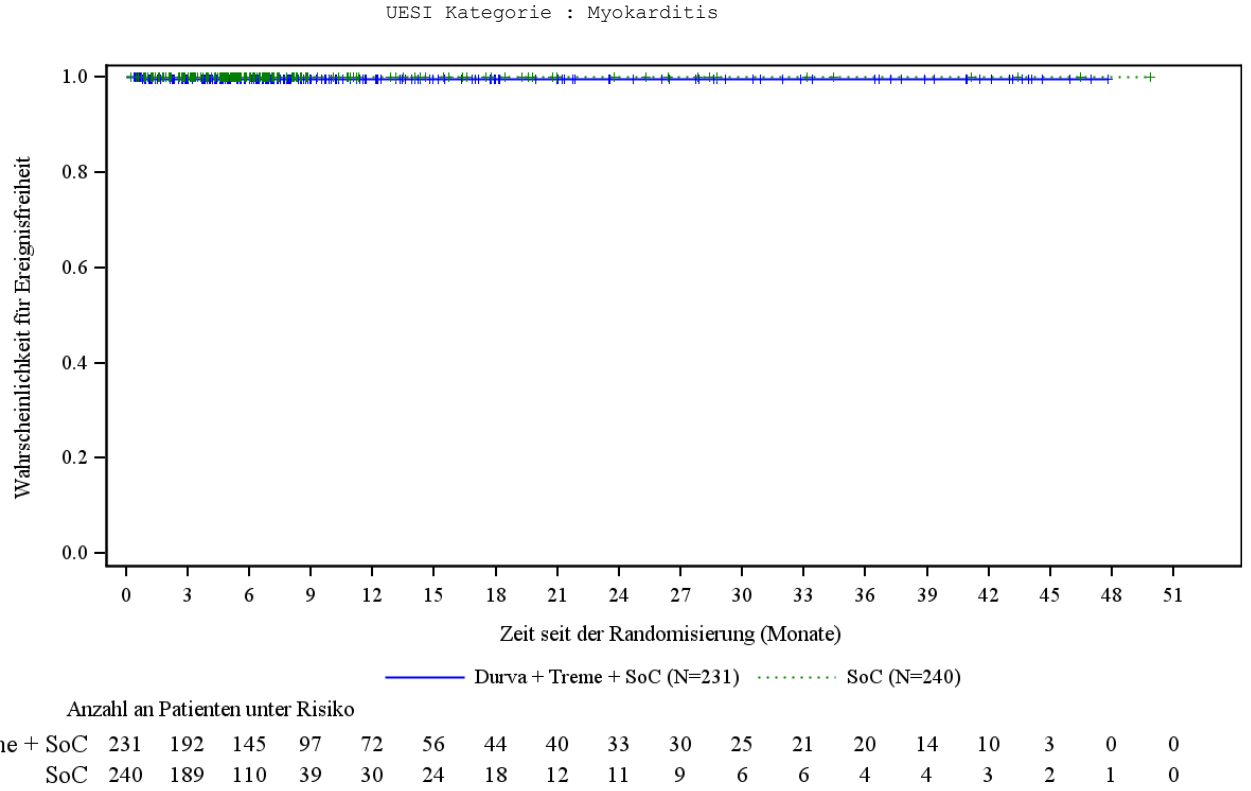
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	97	72	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

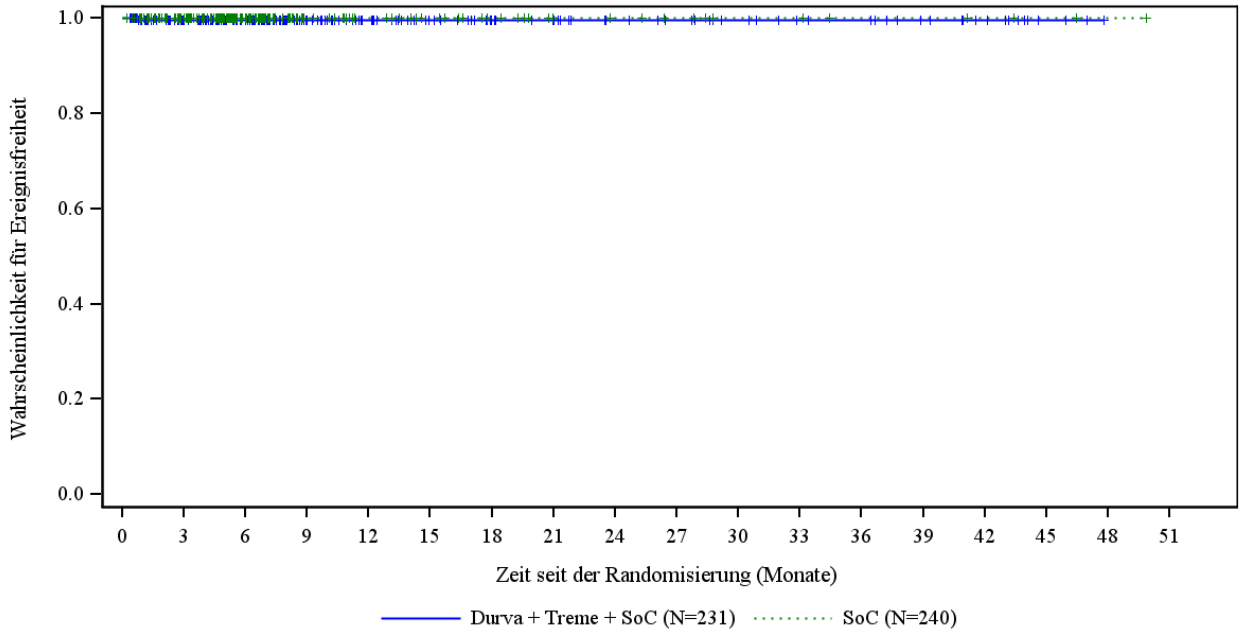


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Autoimmunmyokarditis



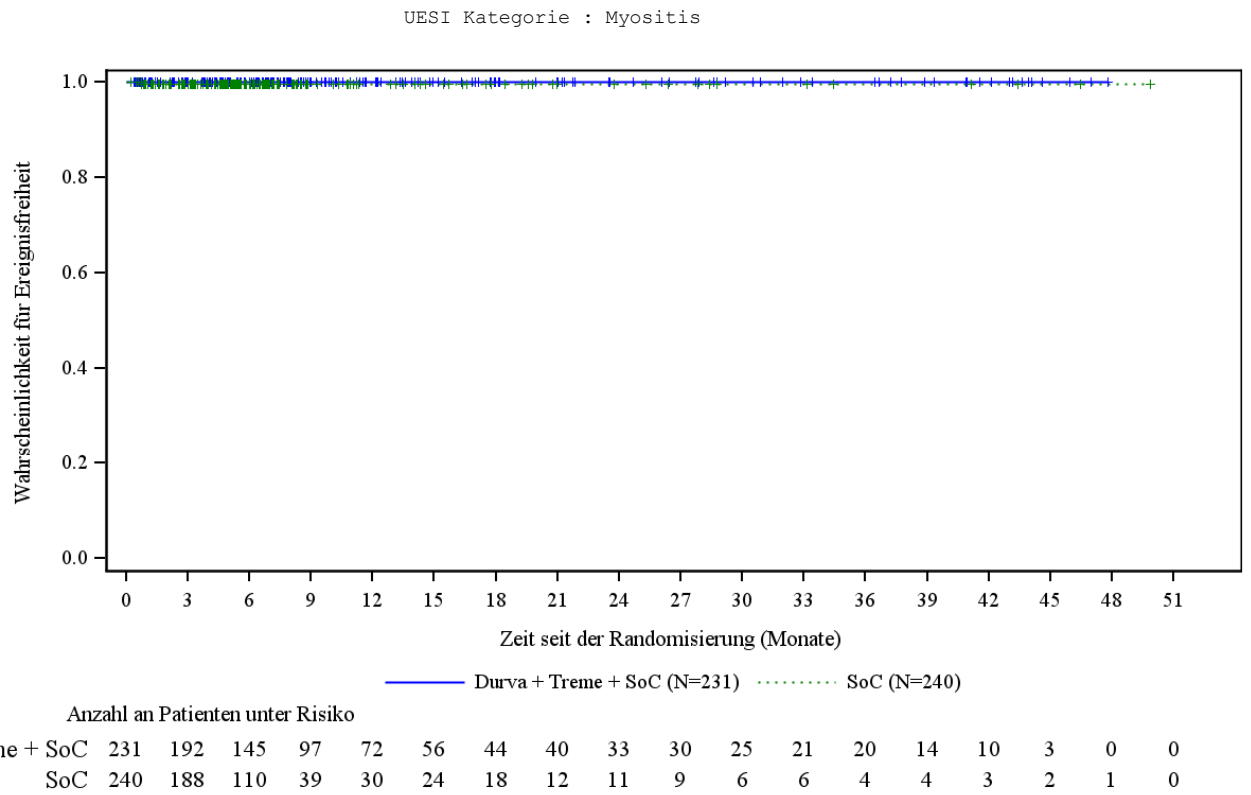
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

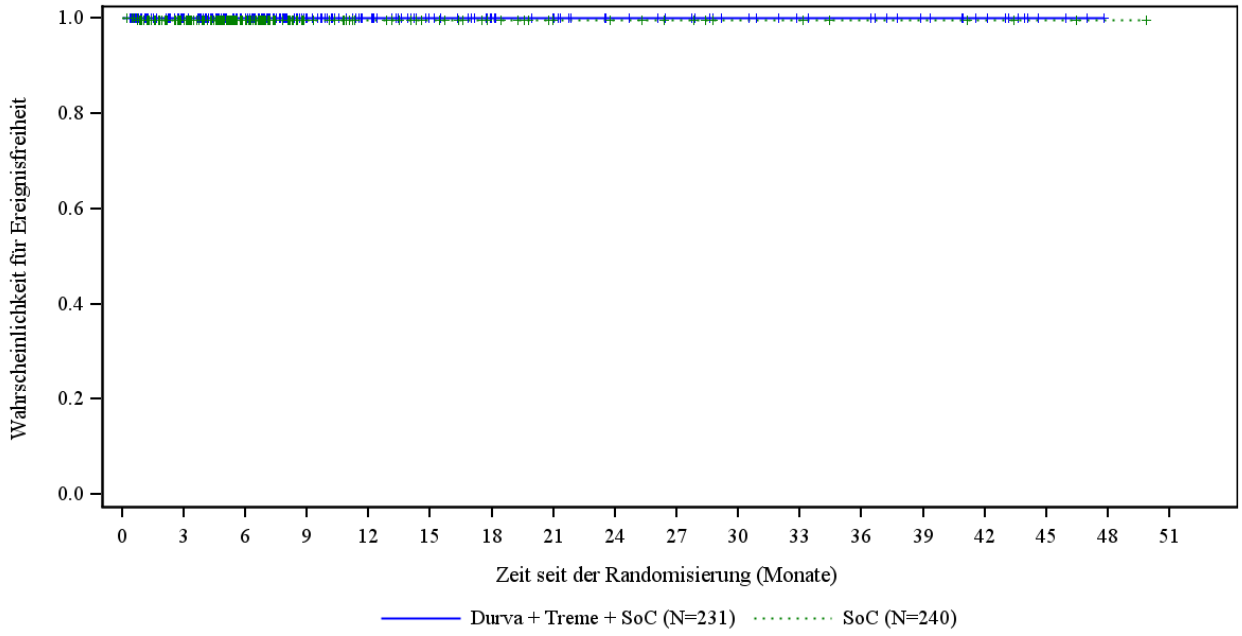


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Myositis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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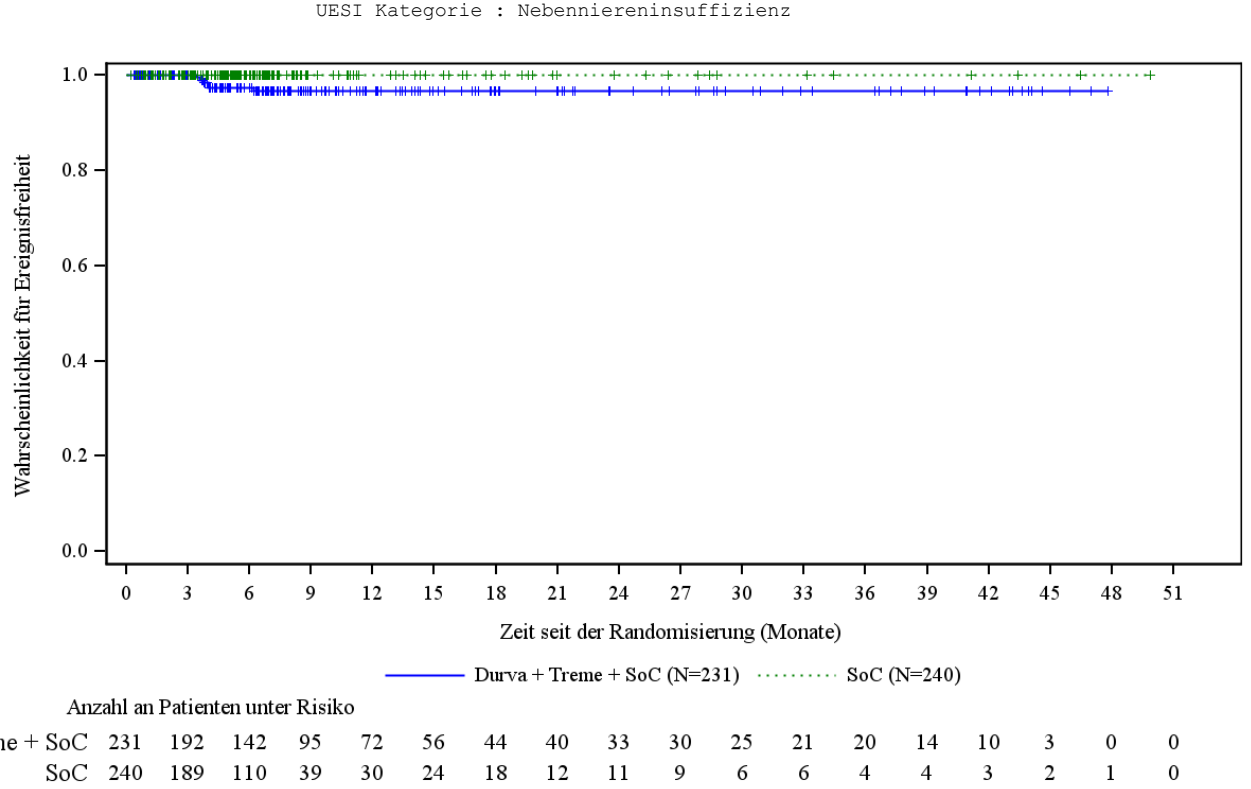
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



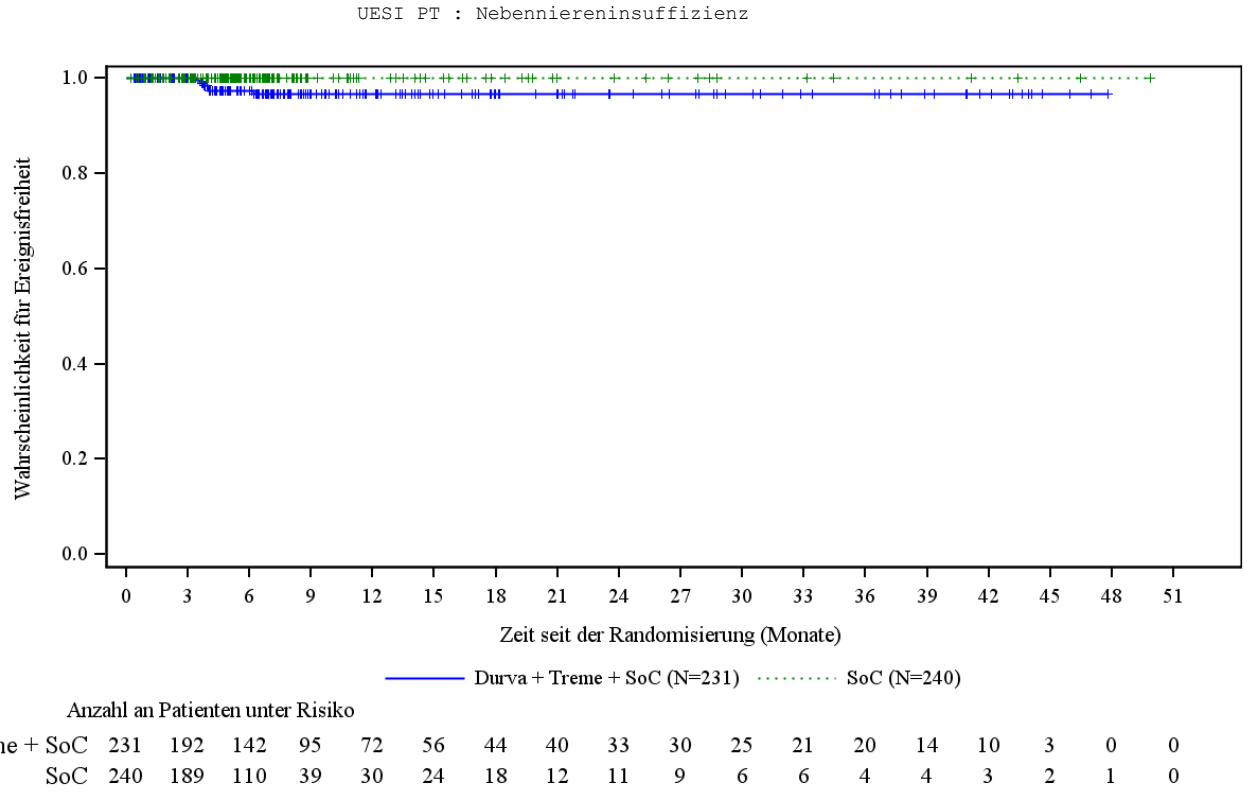
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	142	95	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

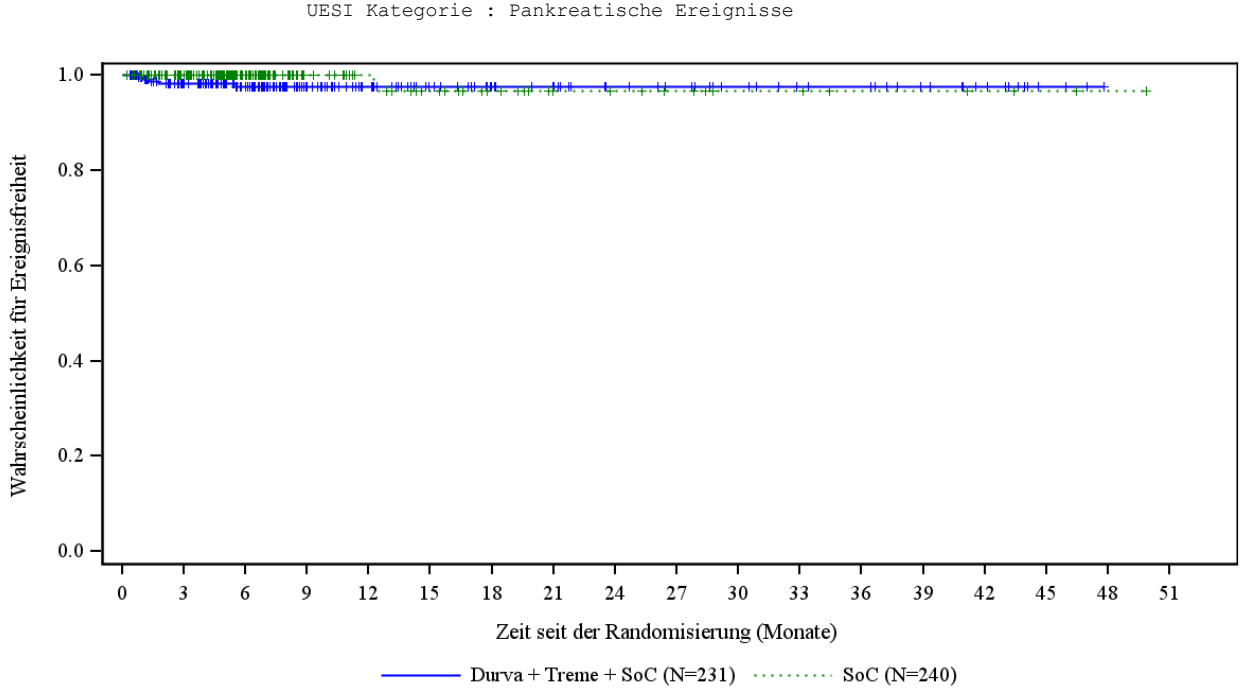
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

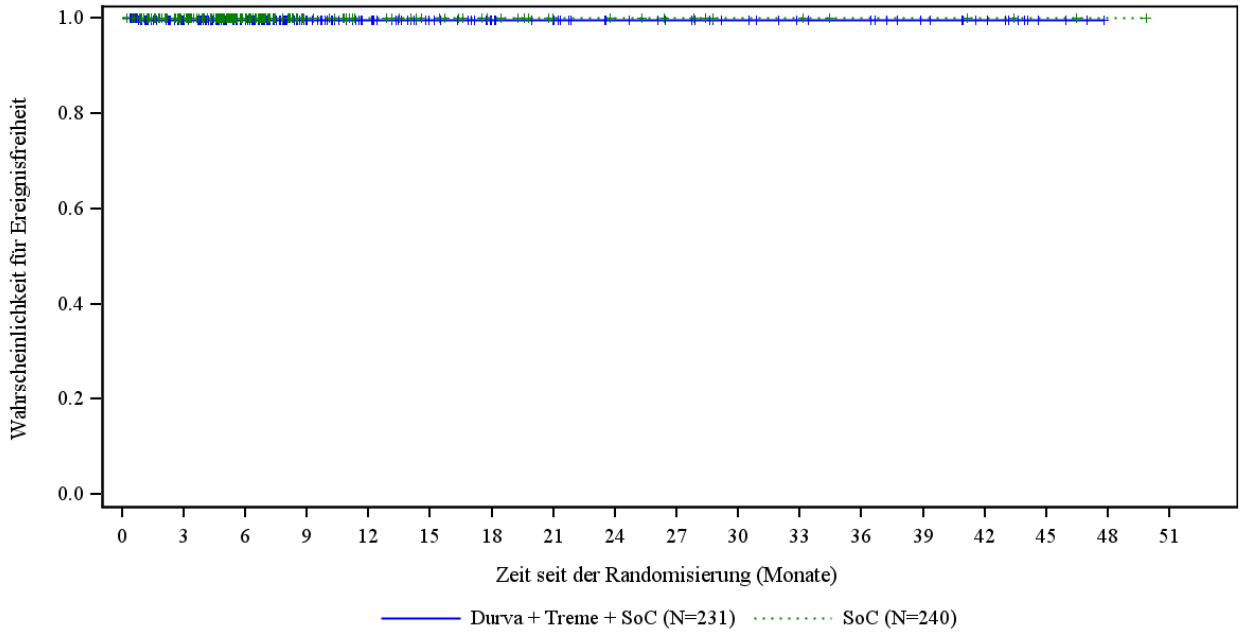
Durva + Treme + SoC	231	189	142	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Autoimmunpankreatitis



Anzahl an Patienten unter Risiko

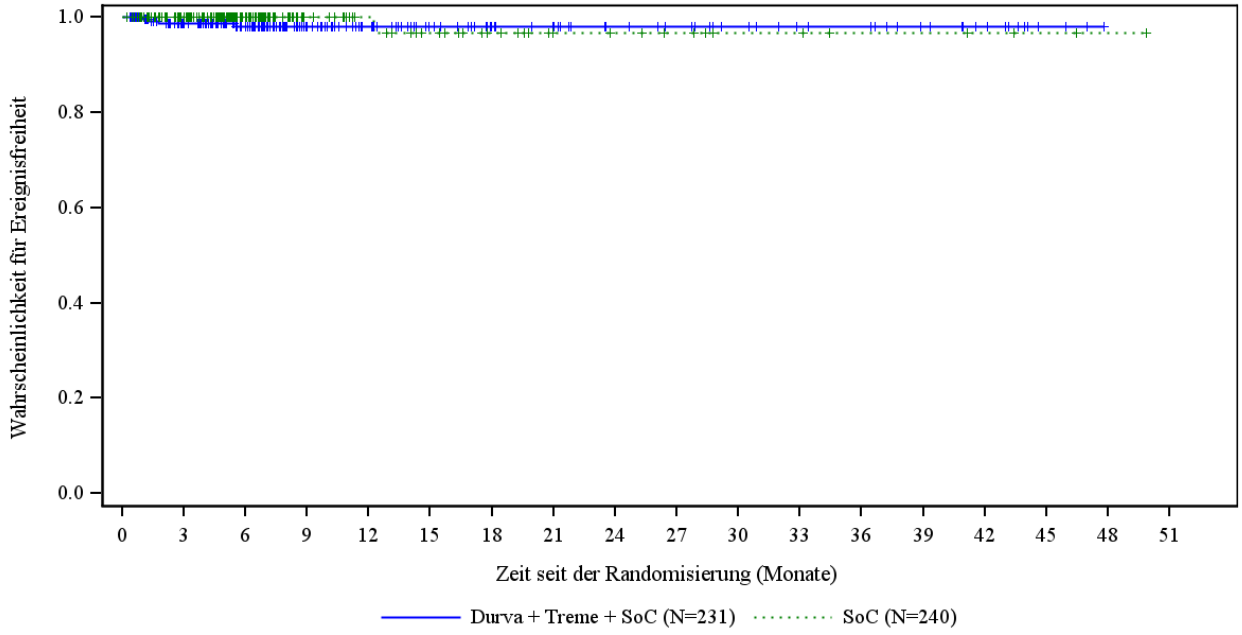
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Pankreatitis



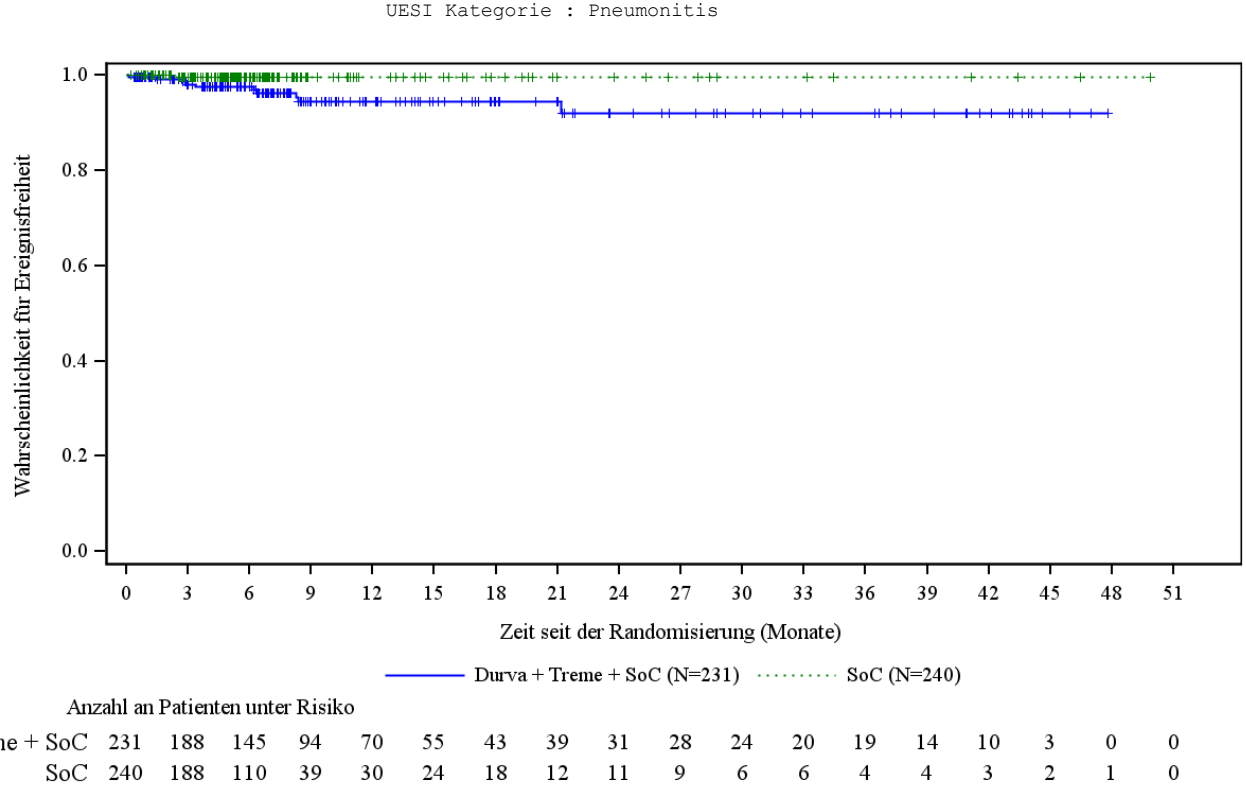
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	142	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

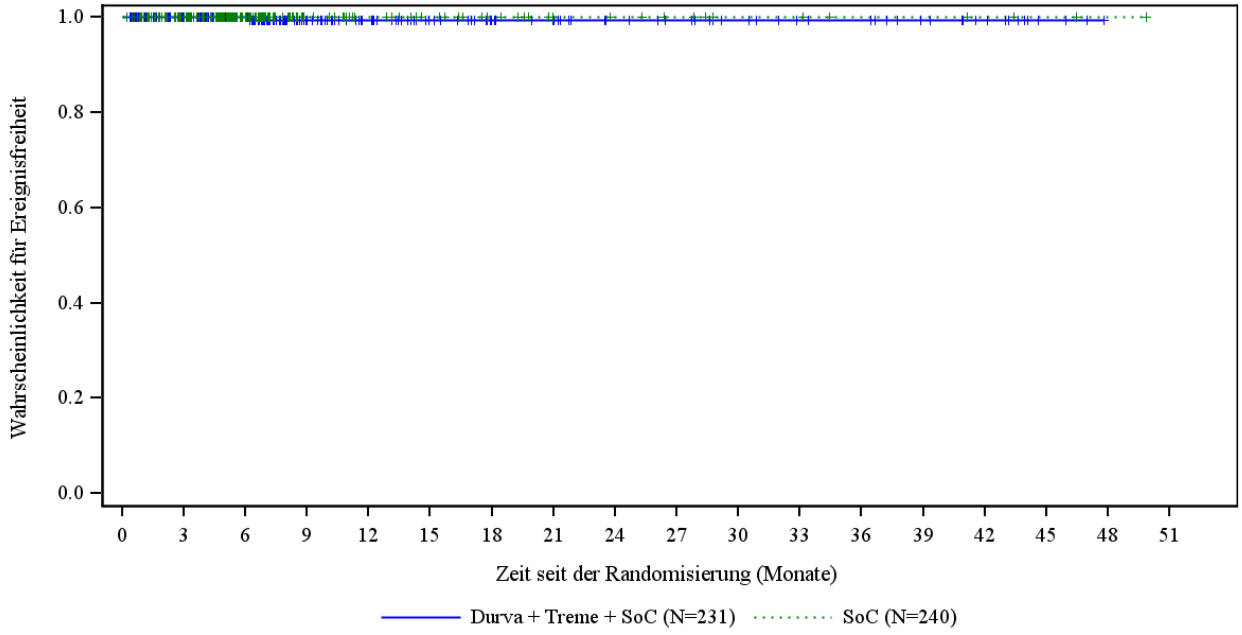


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Immunvermittelte Lungenerkrankung



Anzahl an Patienten unter Risiko

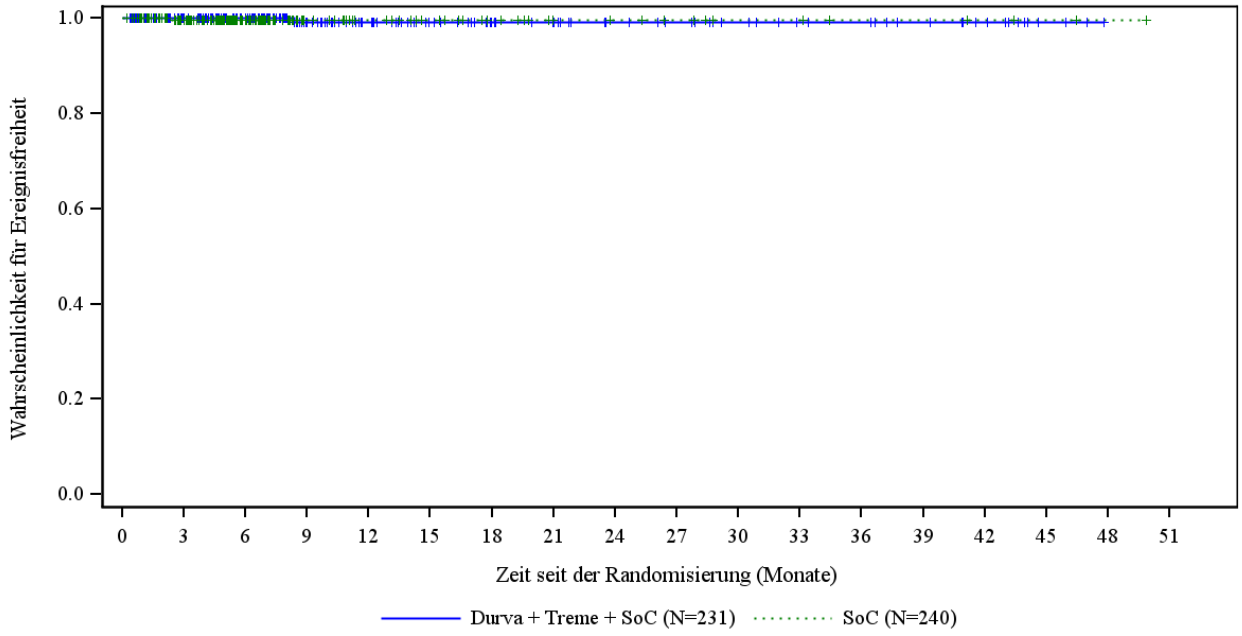
Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Interstitielle Lungenerkrankung



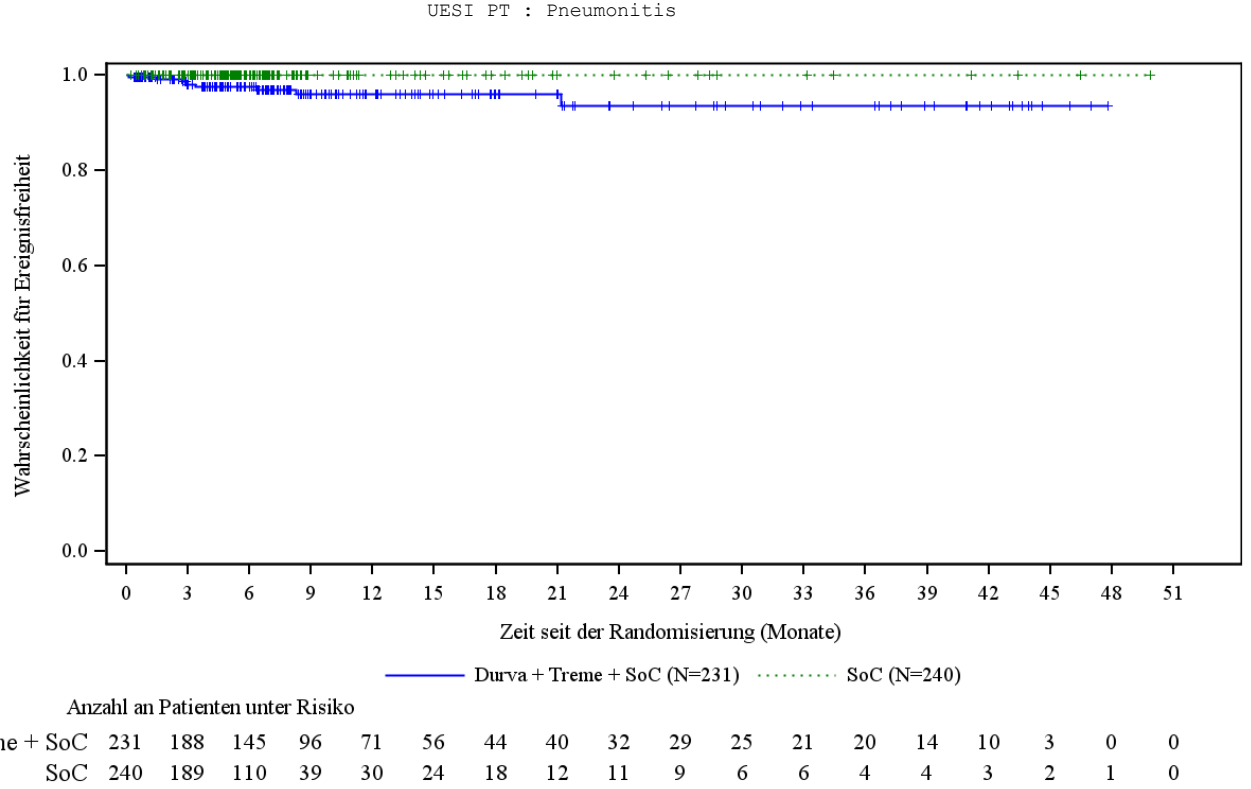
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	96	71	55	43	39	32	29	24	20	19	14	10	3	0	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

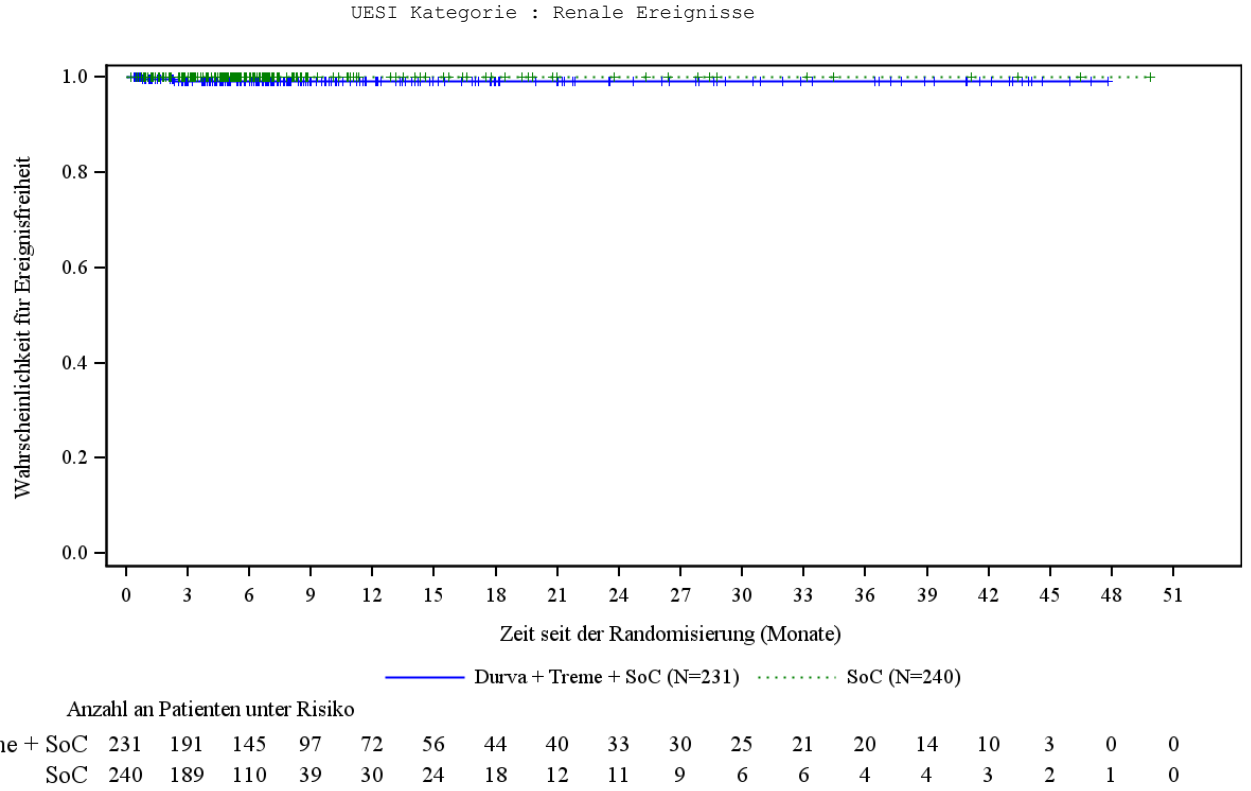
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

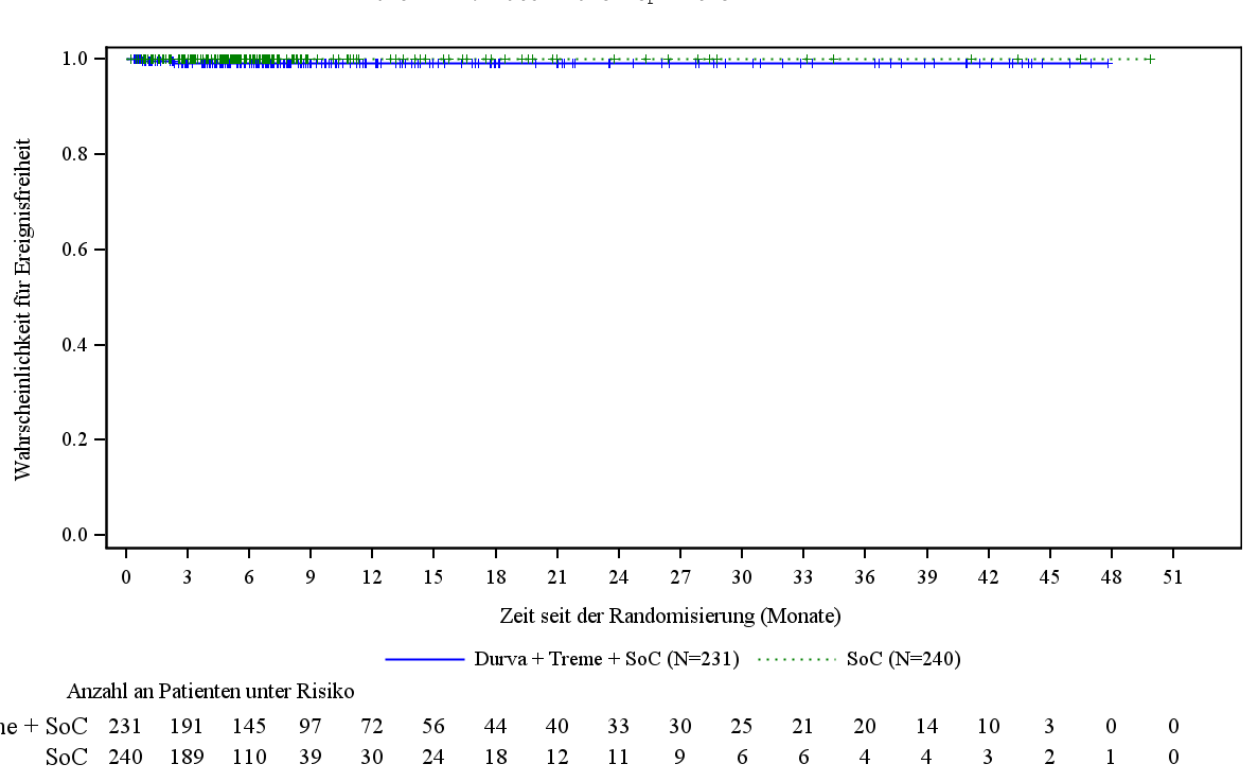
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

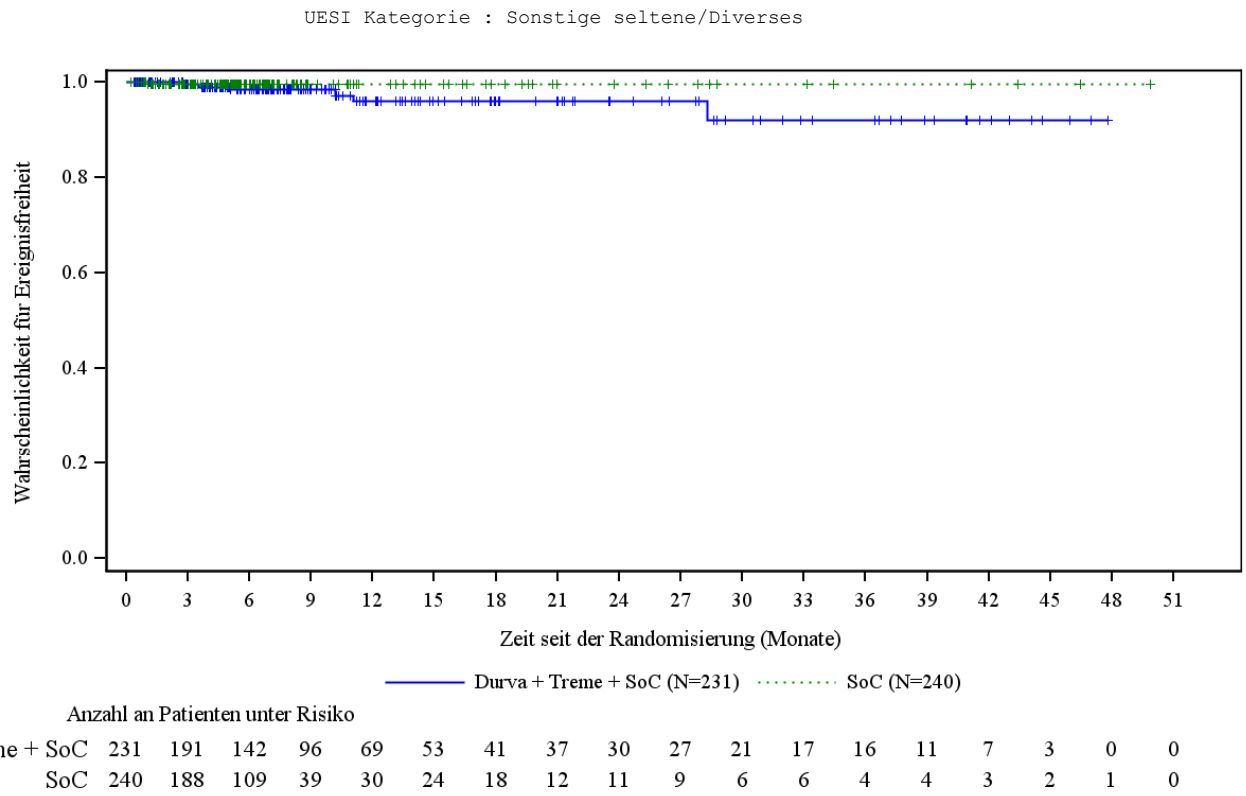
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

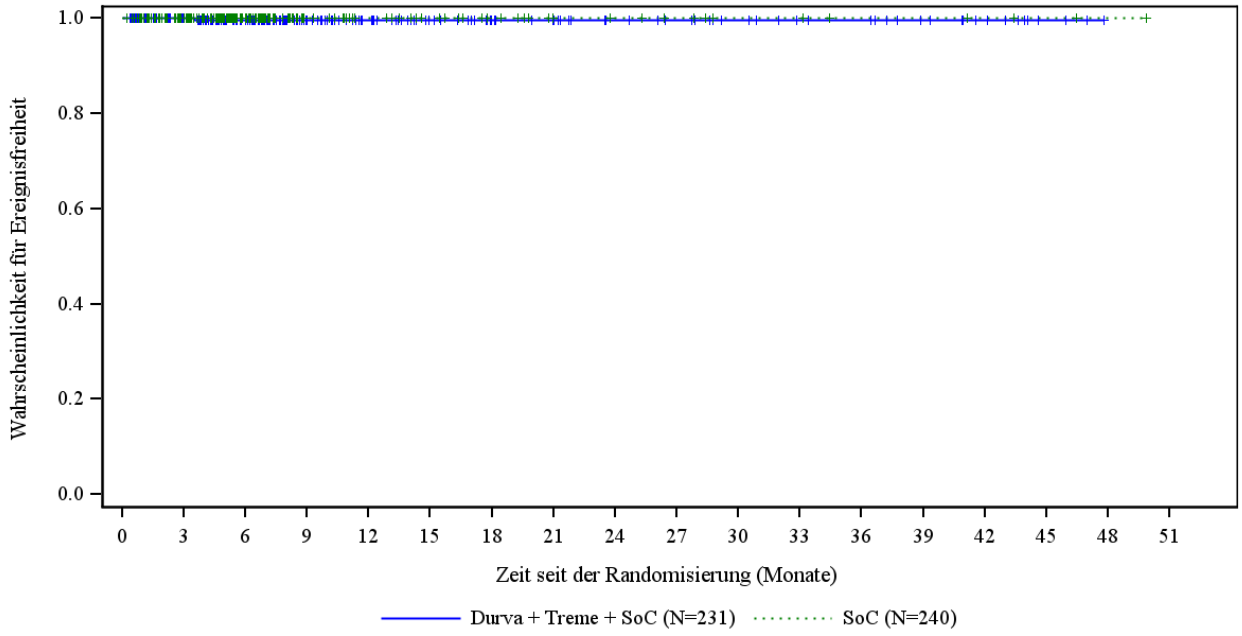
Durva + Treme + SoC	231	191	142	96	69	53	41	37	30	27	21	17	16	11	7	3	0	0
SoC	240	188	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Enzephalitis



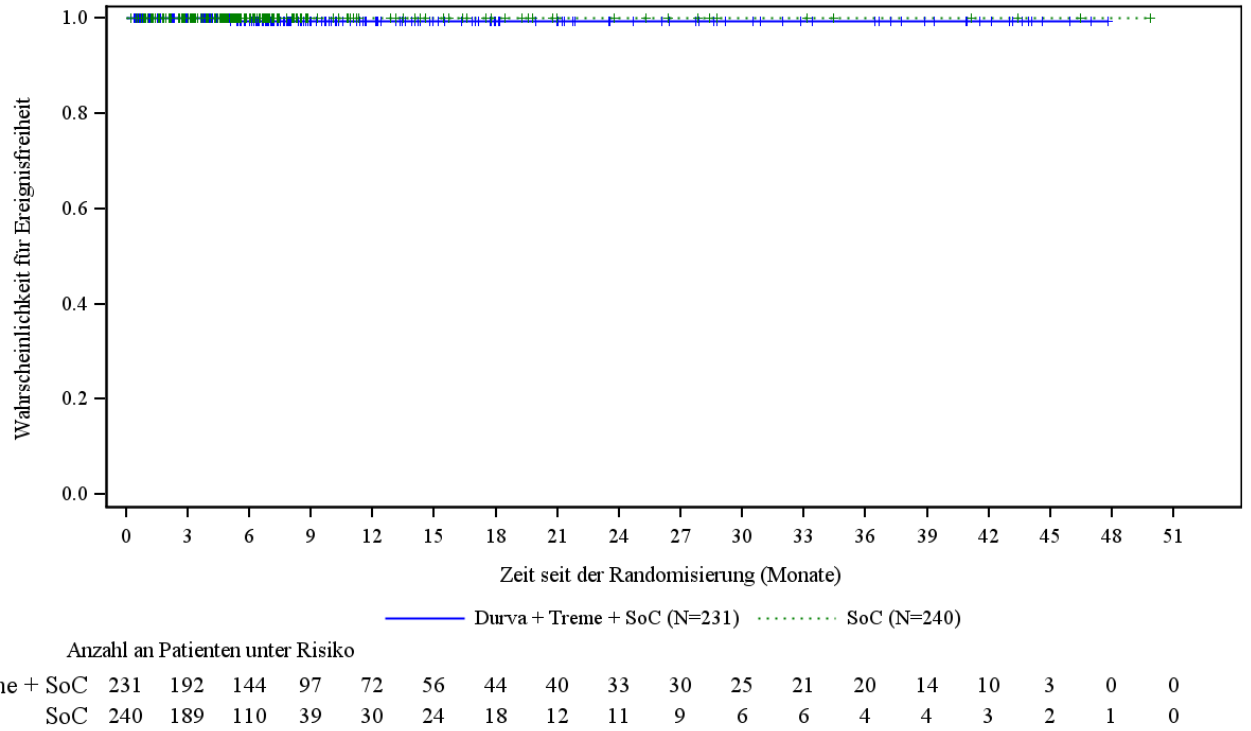
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

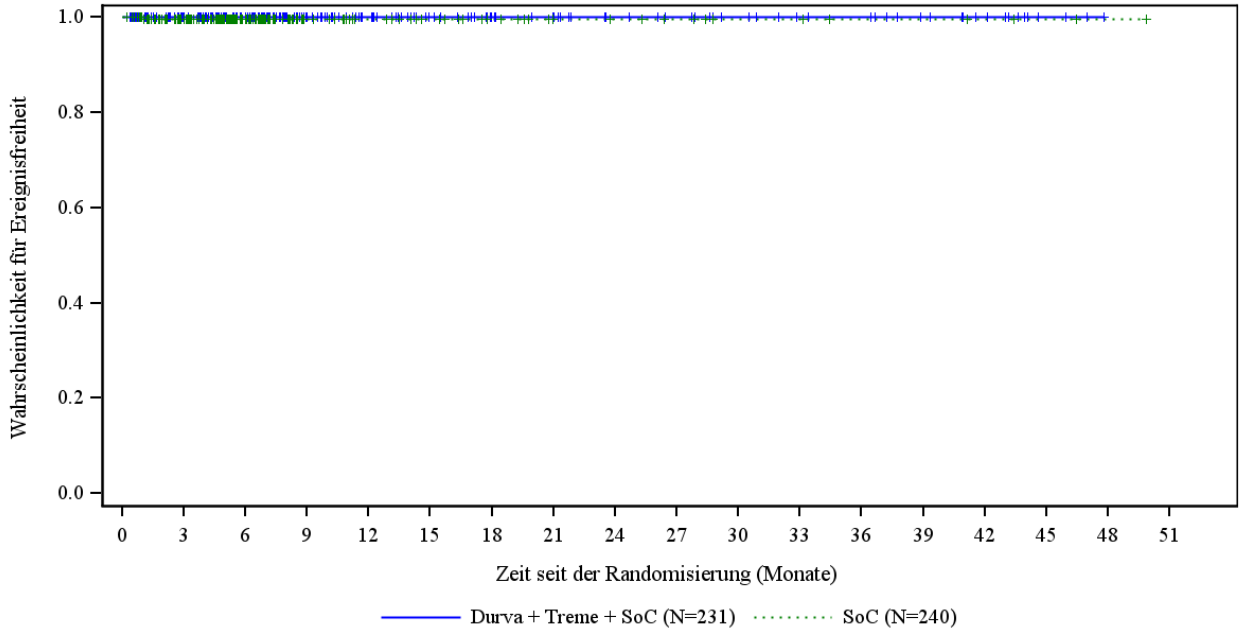


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Keratitis



Anzahl an Patienten unter Risiko

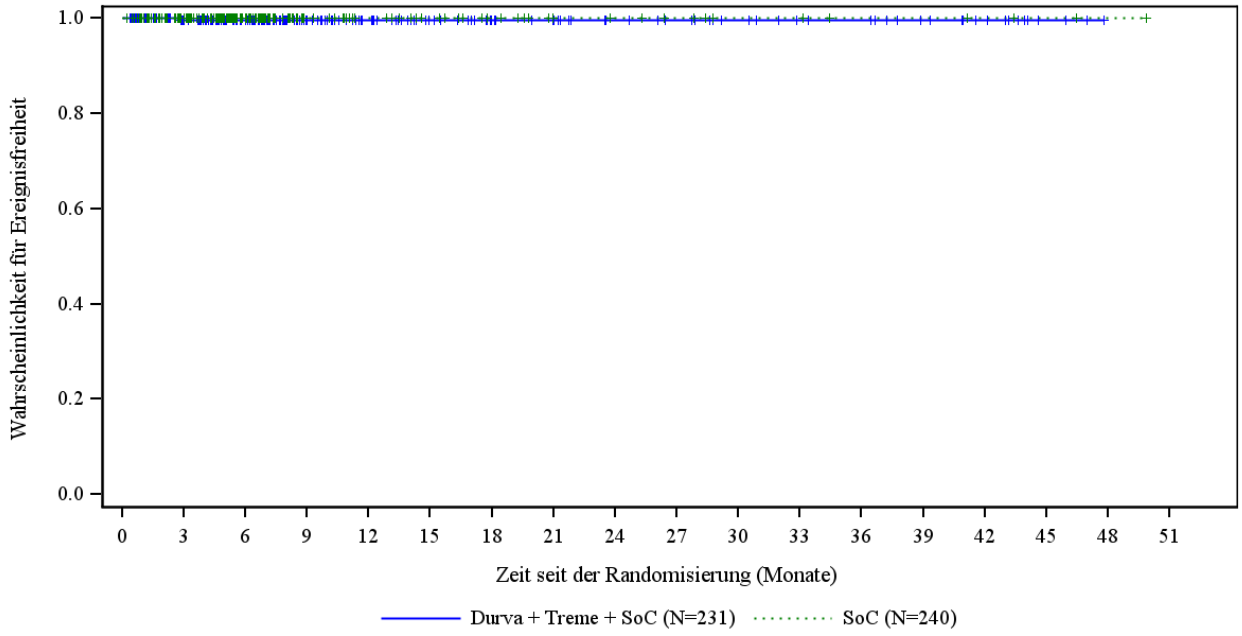
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Perikarditis



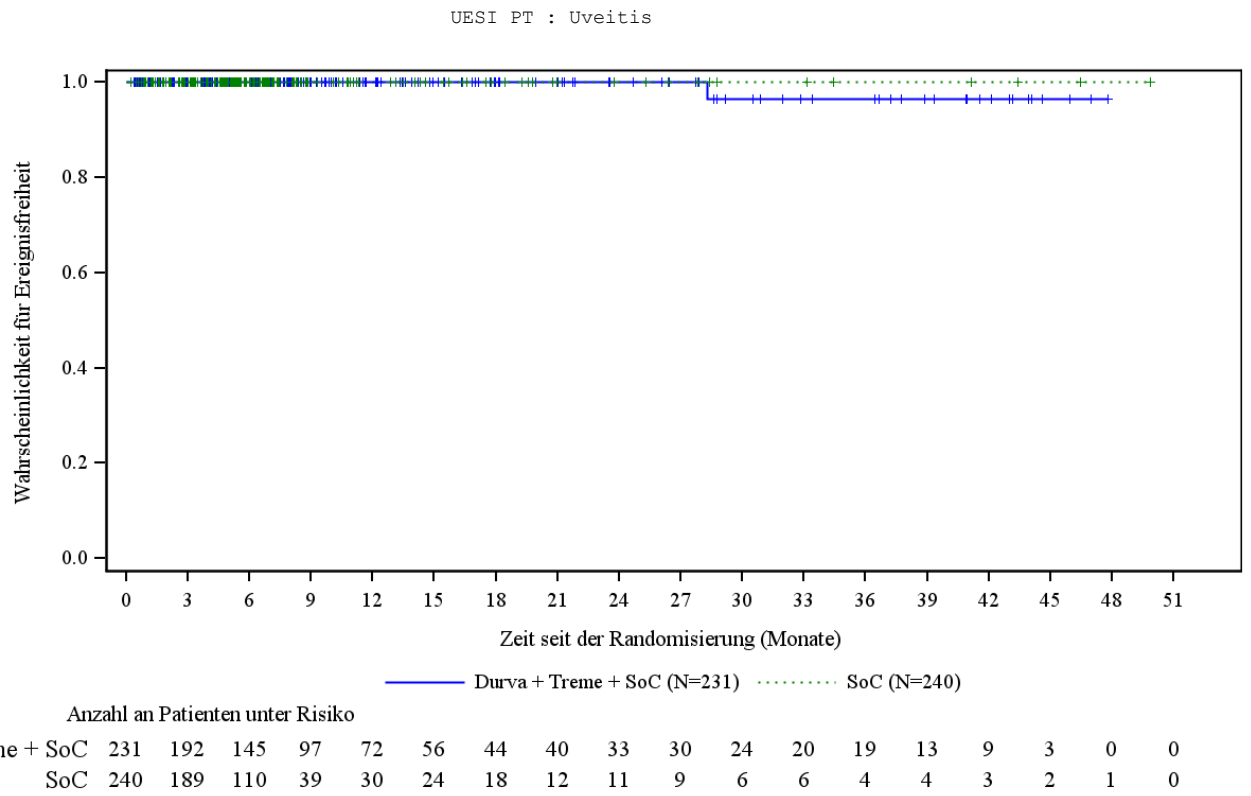
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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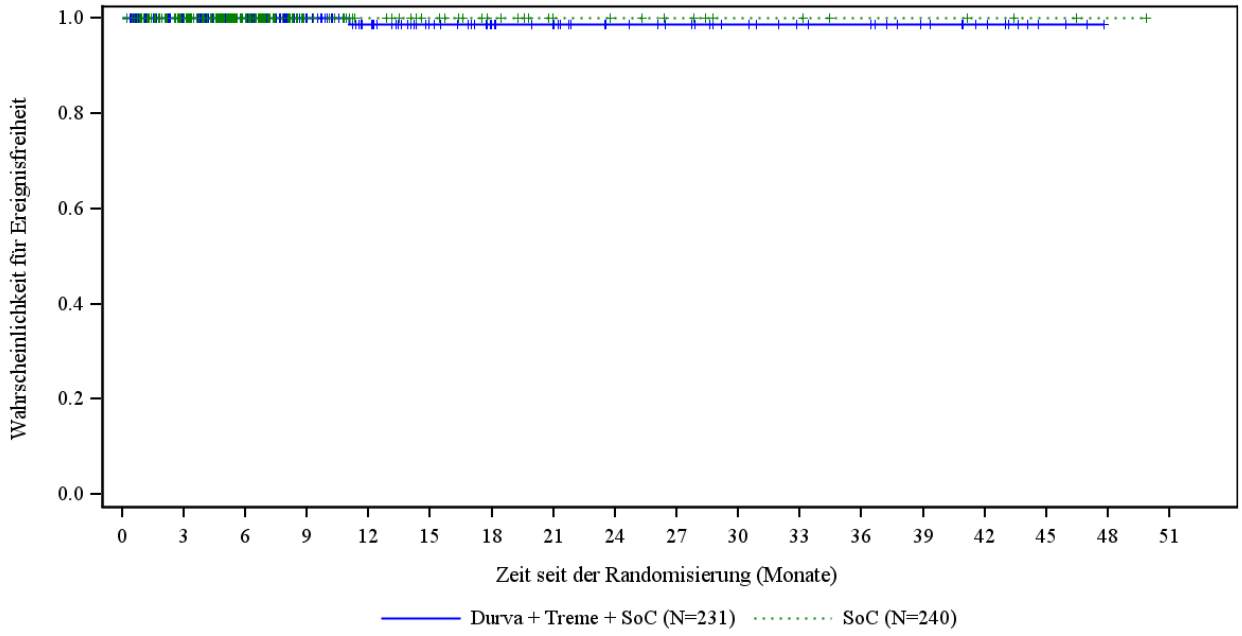
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Vaskulitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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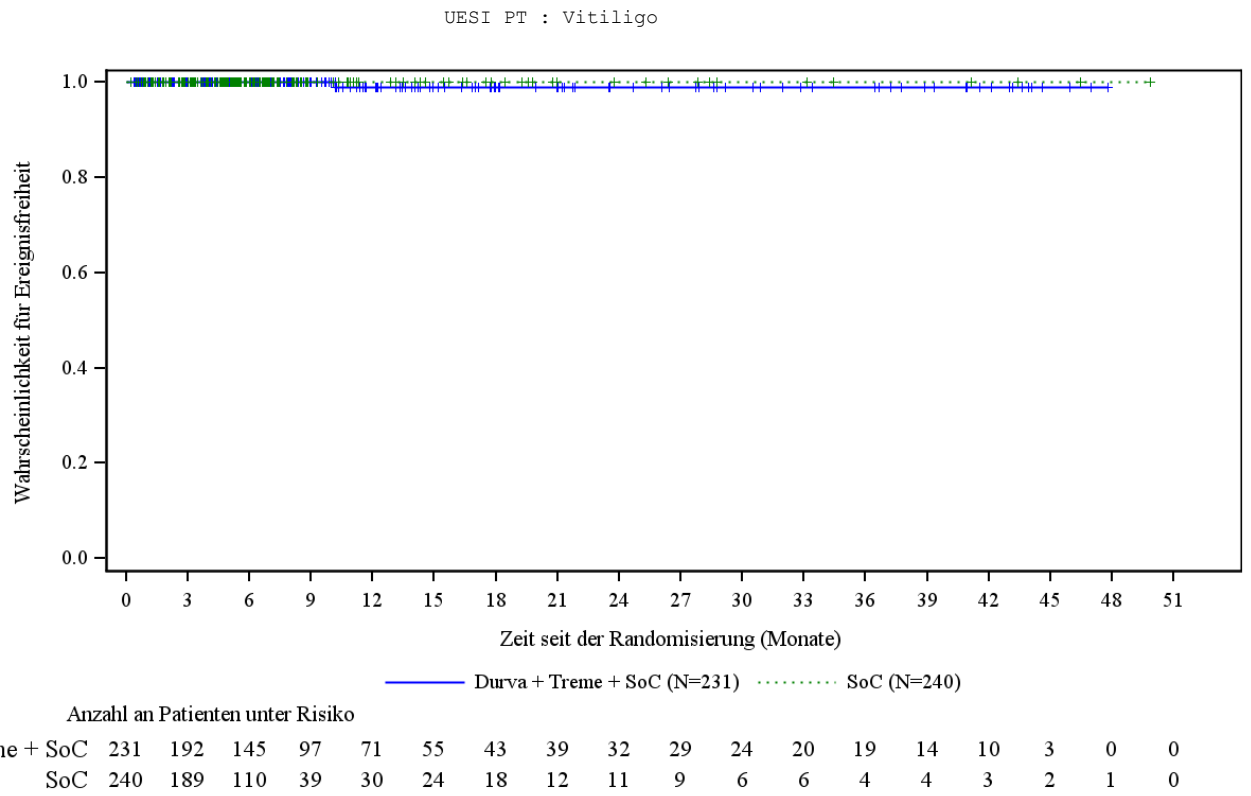
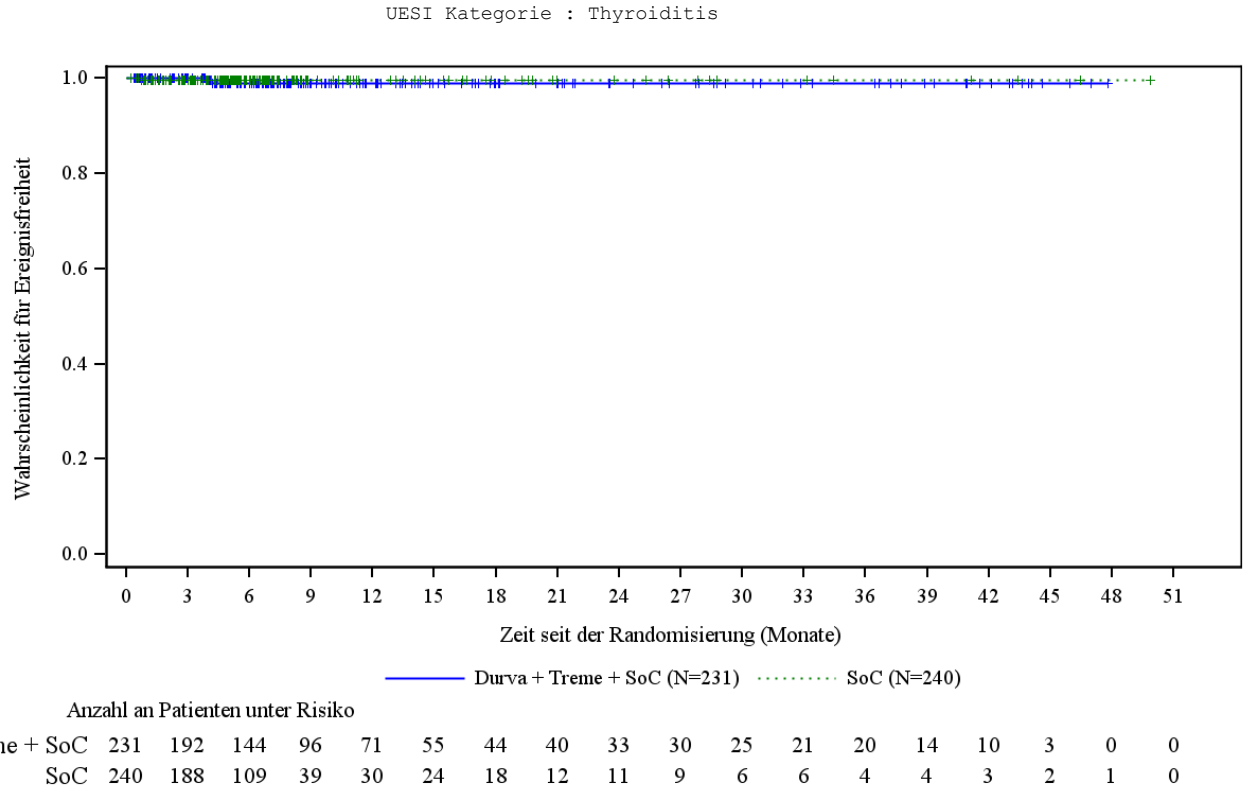
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

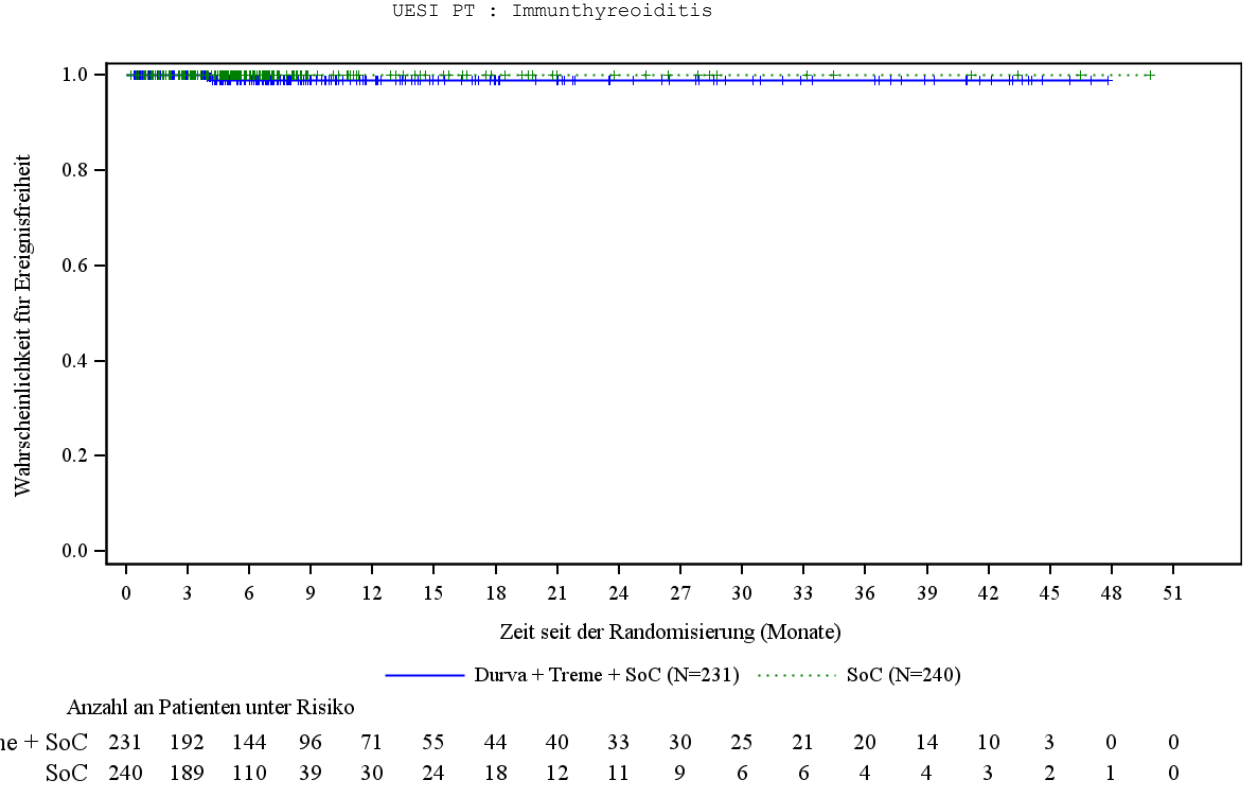
Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

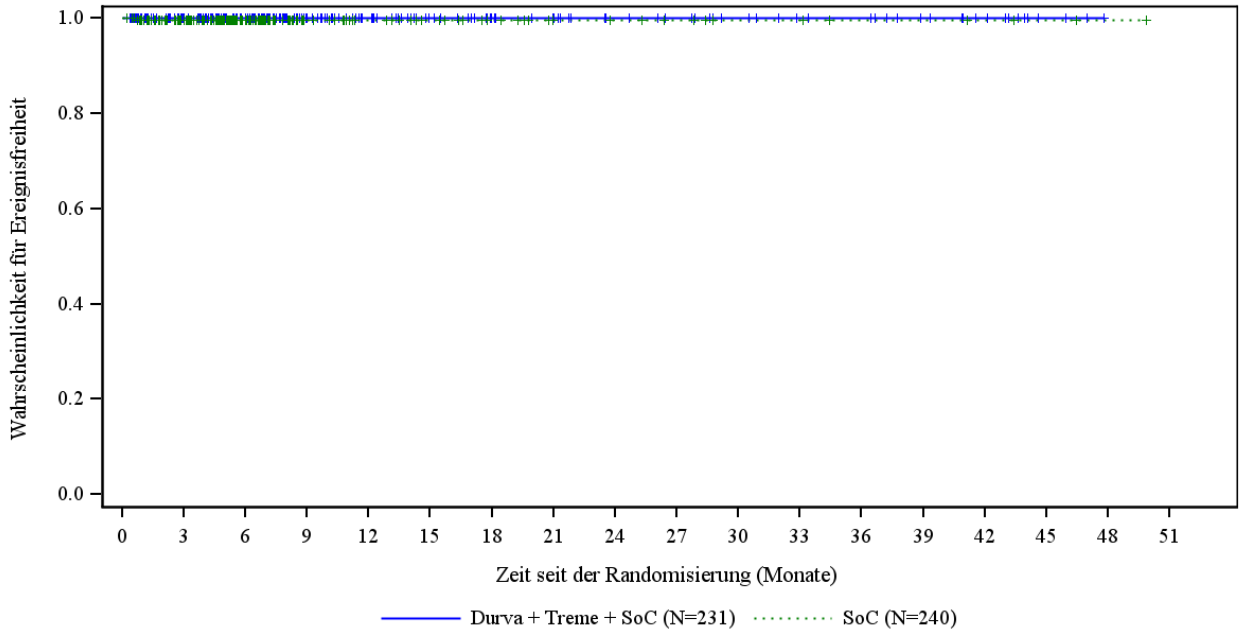


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Figure 4.6.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI PT : Thyroiditis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	188	109	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

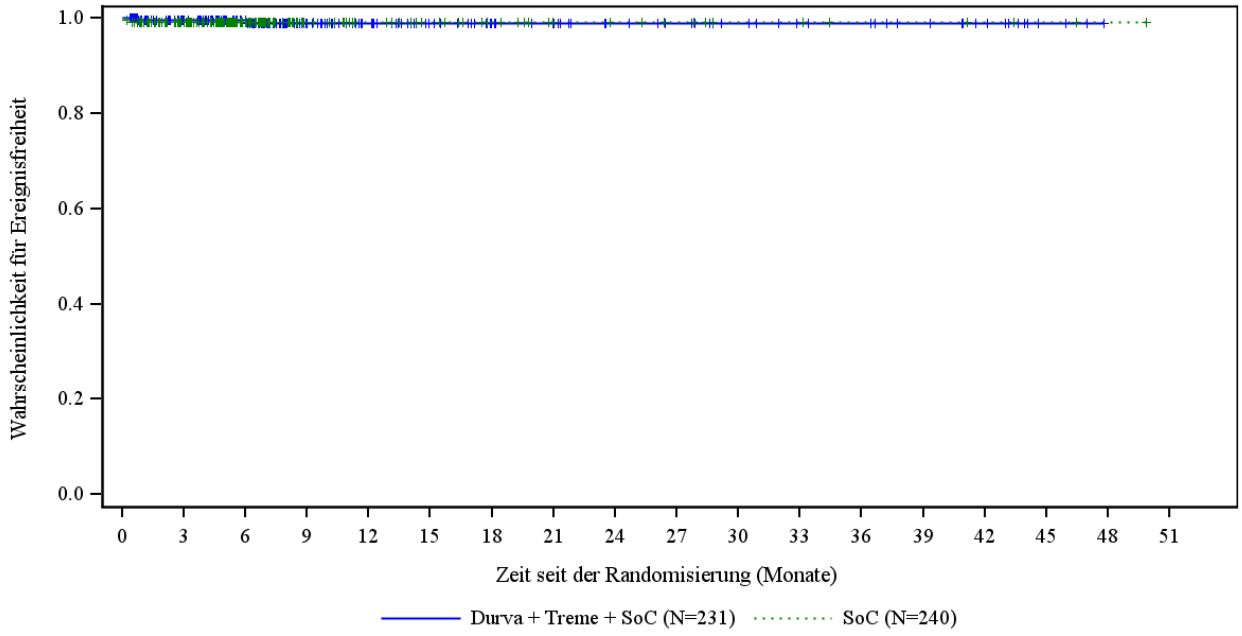
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae346g.sas Executed : 2022-11-22T131129

Anhang 4-G 1.2.2.2: Schwere unerwünschte Ereignisse von speziellem Interesse (CTCAE-Grad ≥ 3) nach Kategorie und PT

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 36

Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Grad >/=3 Kategorie : Dermatitis / Hautausschlag



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	145	96	71	55	43	39	32	29	24	20	19	14	10	3	0	0
SoC	240	187	108	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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+ indicates a censored observation.

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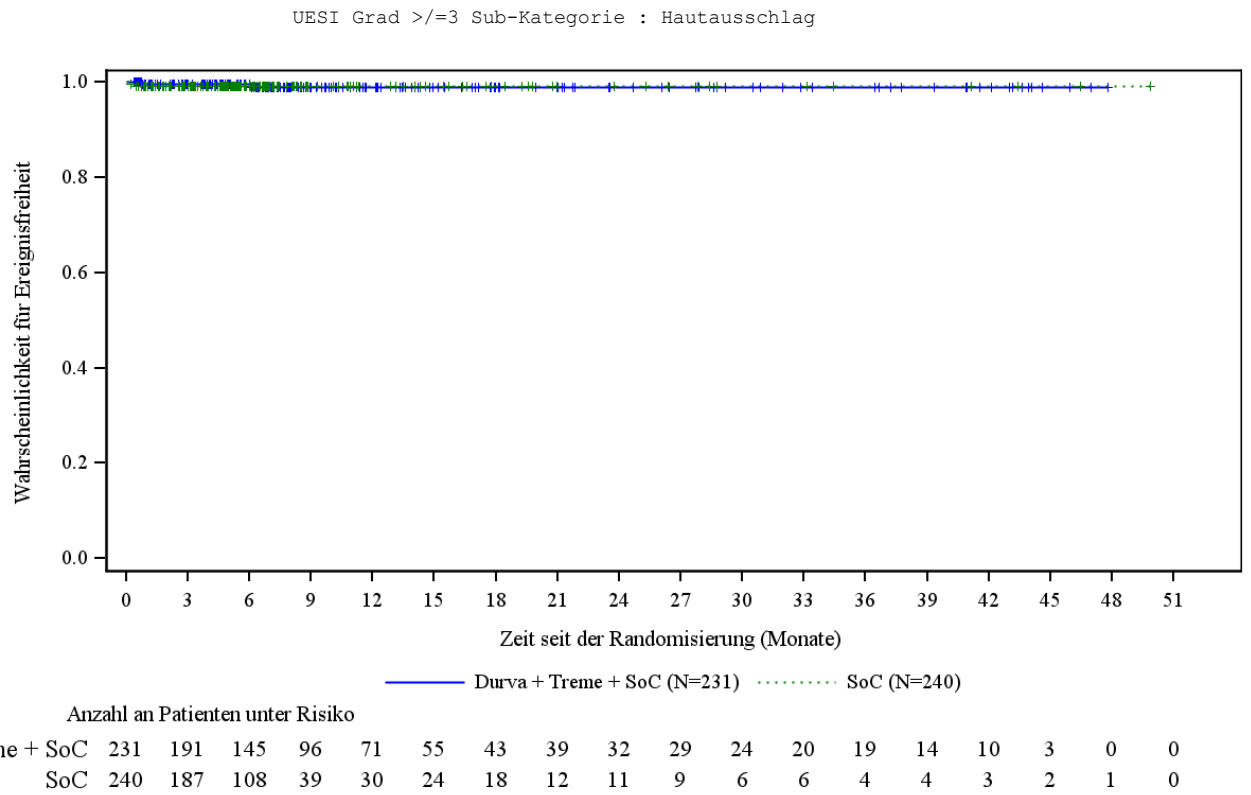
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



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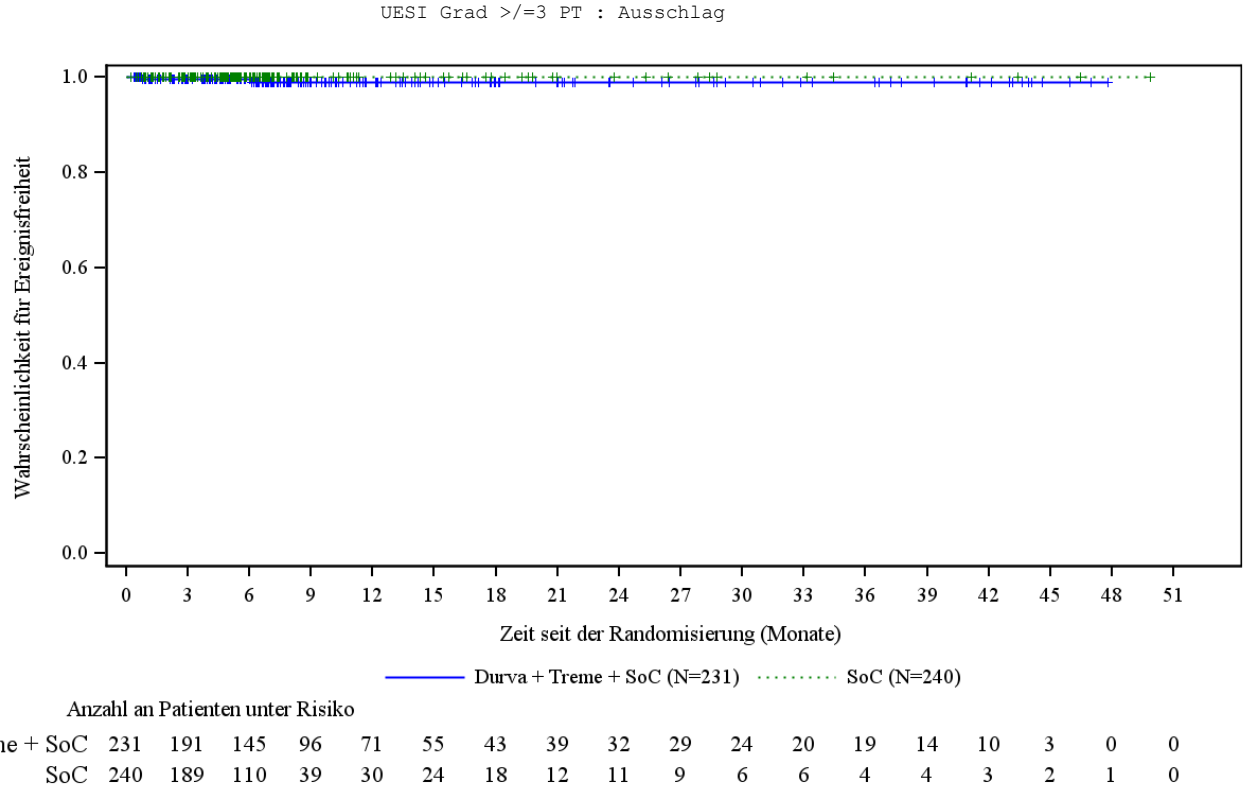

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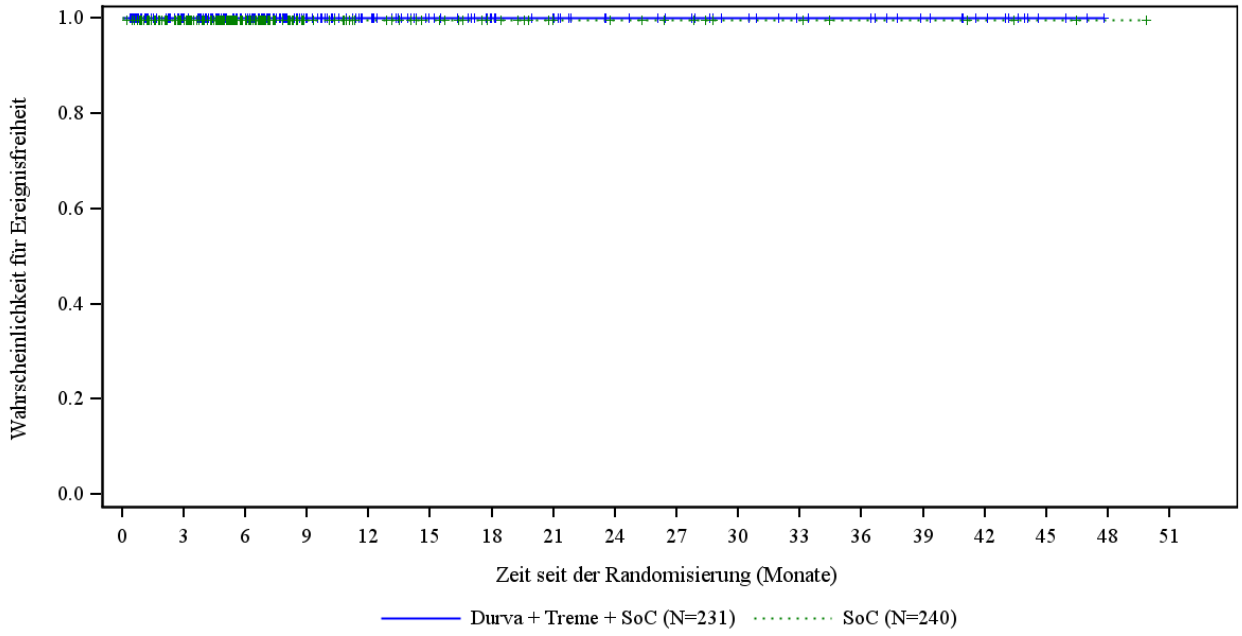
Data Cut-off: 25th October 2021

UESI Grad >/=3 PT : Ausschlag makulo-papuloes



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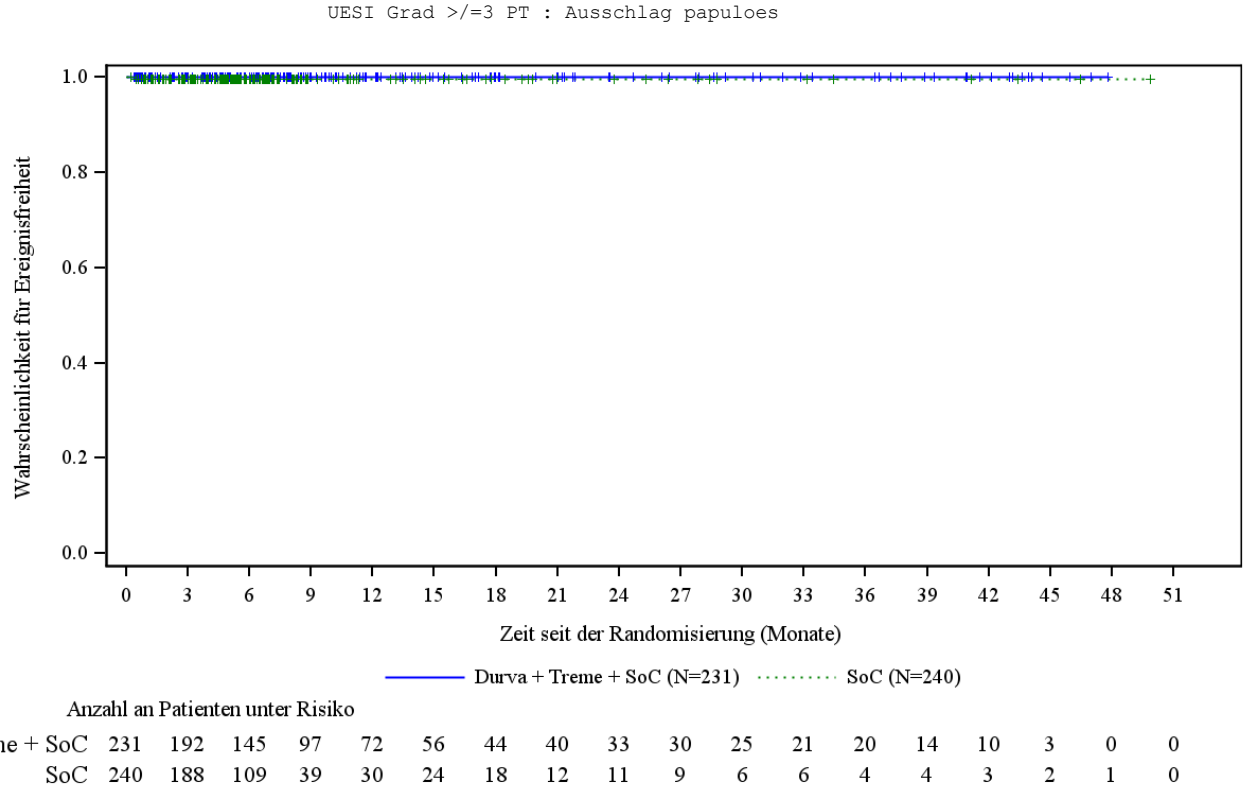

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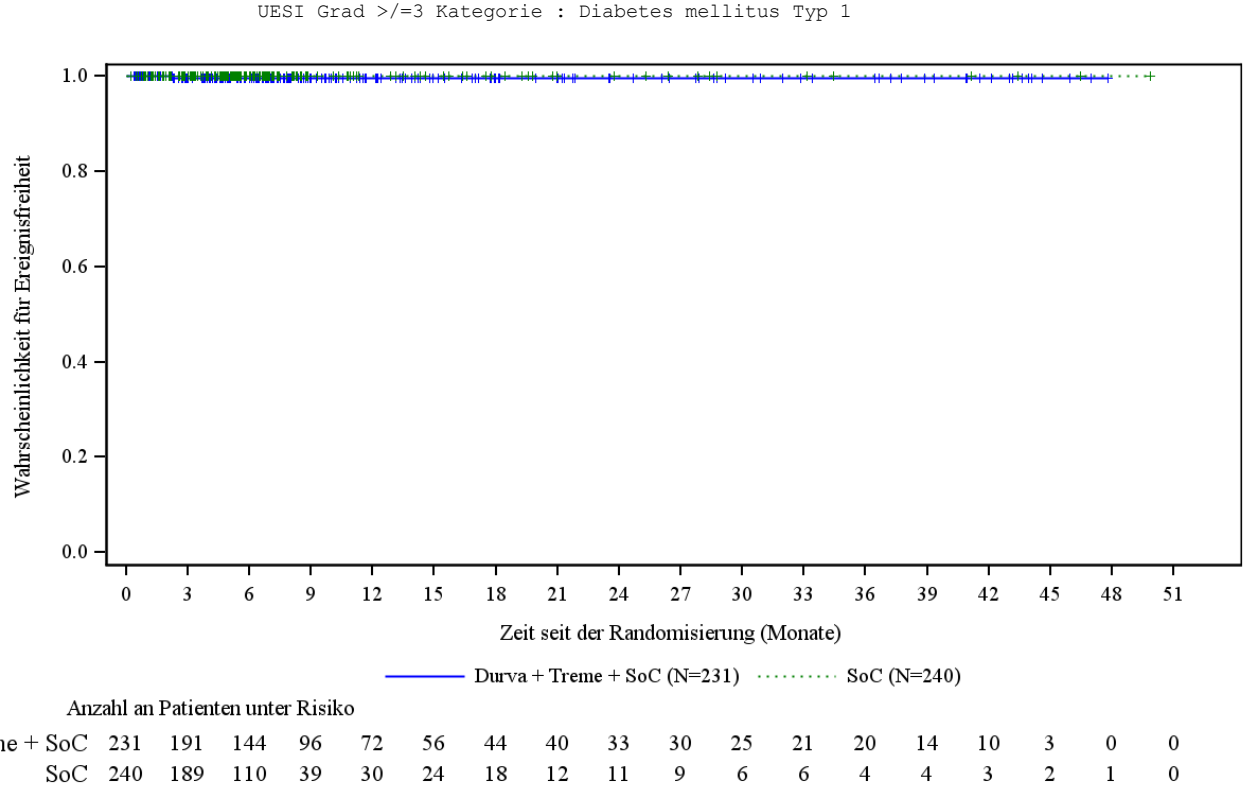

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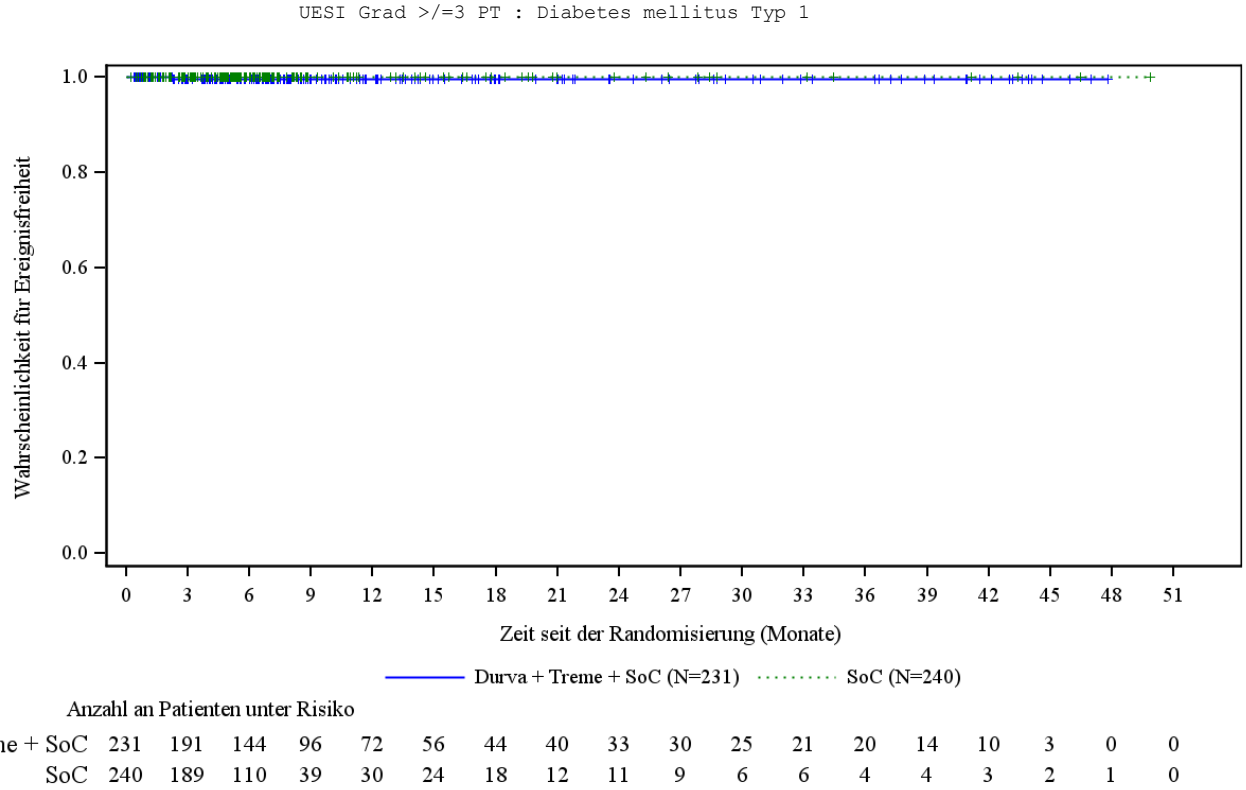

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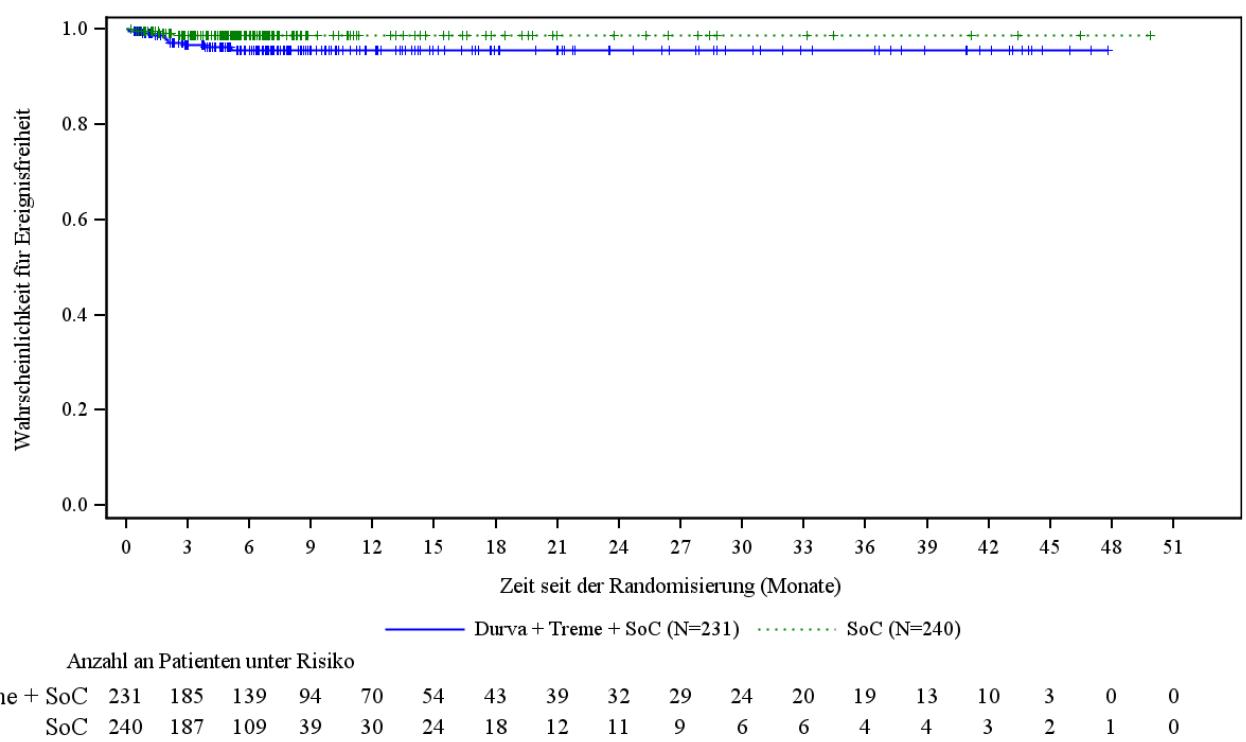

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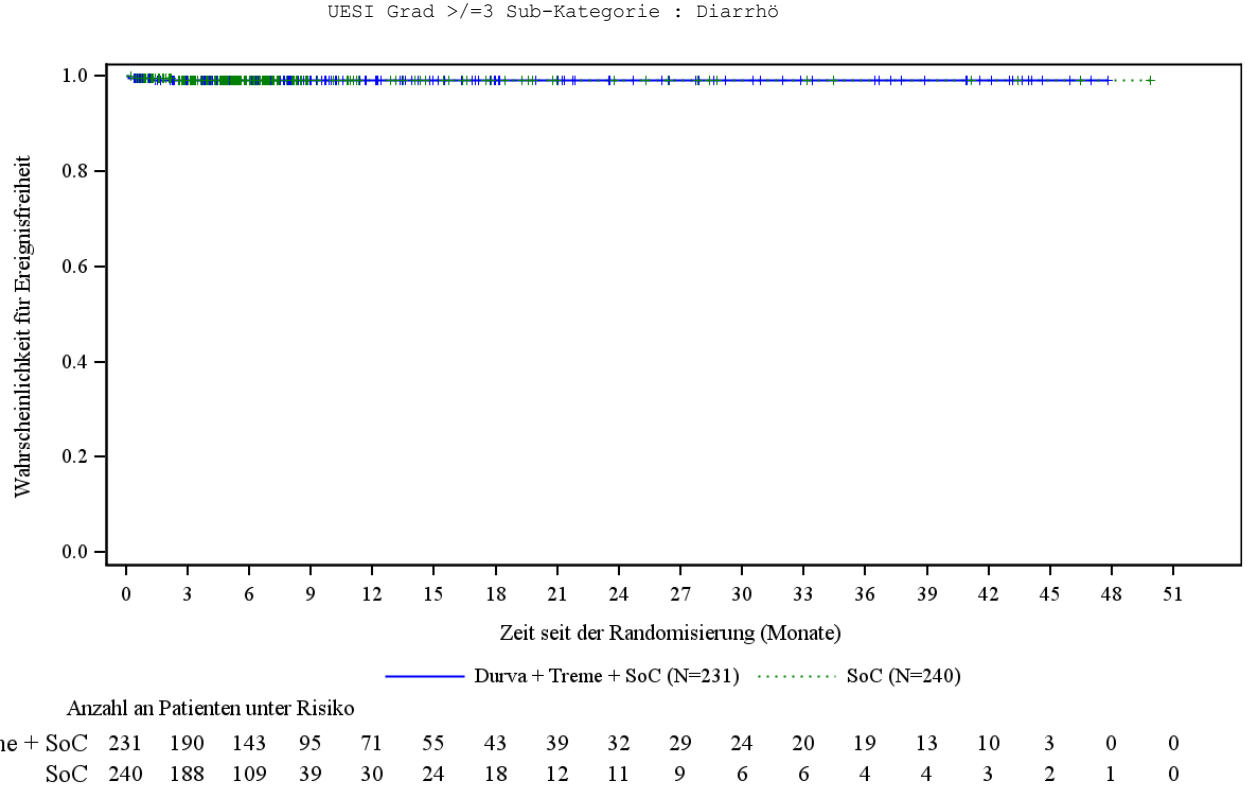

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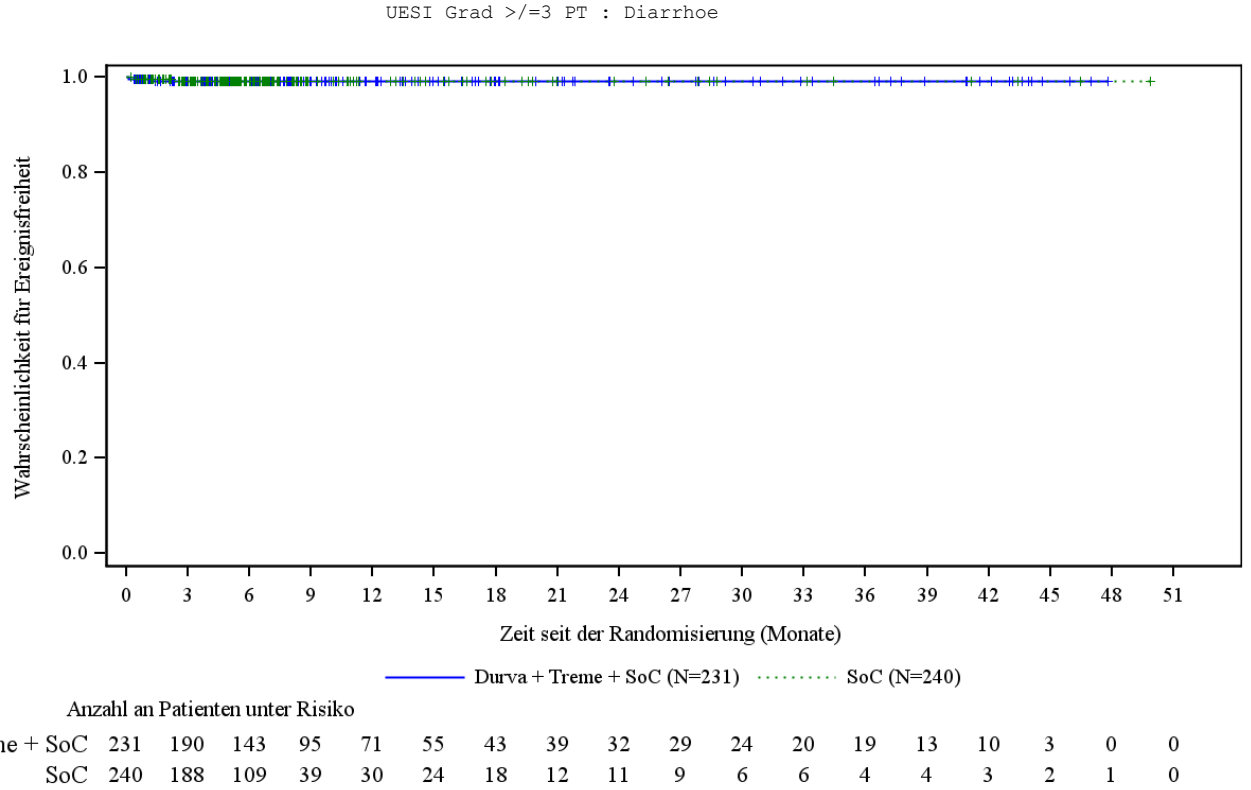

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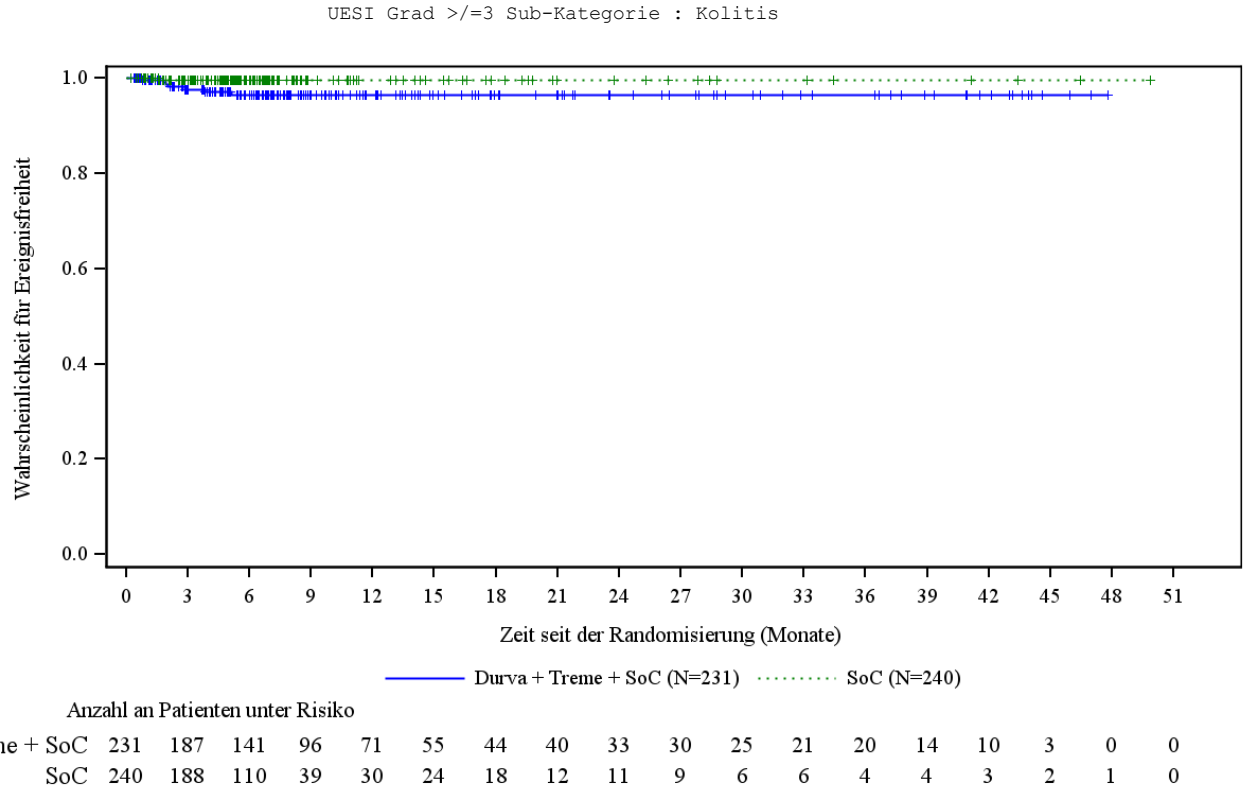

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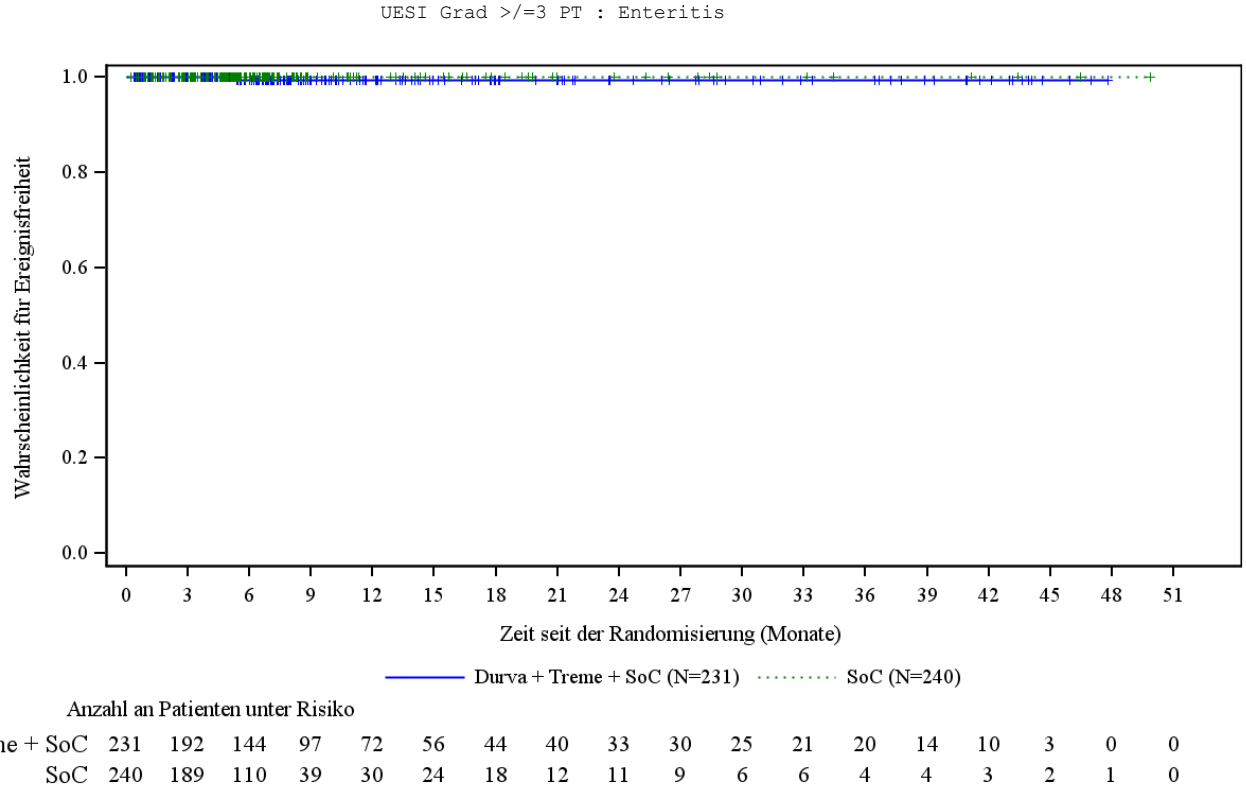

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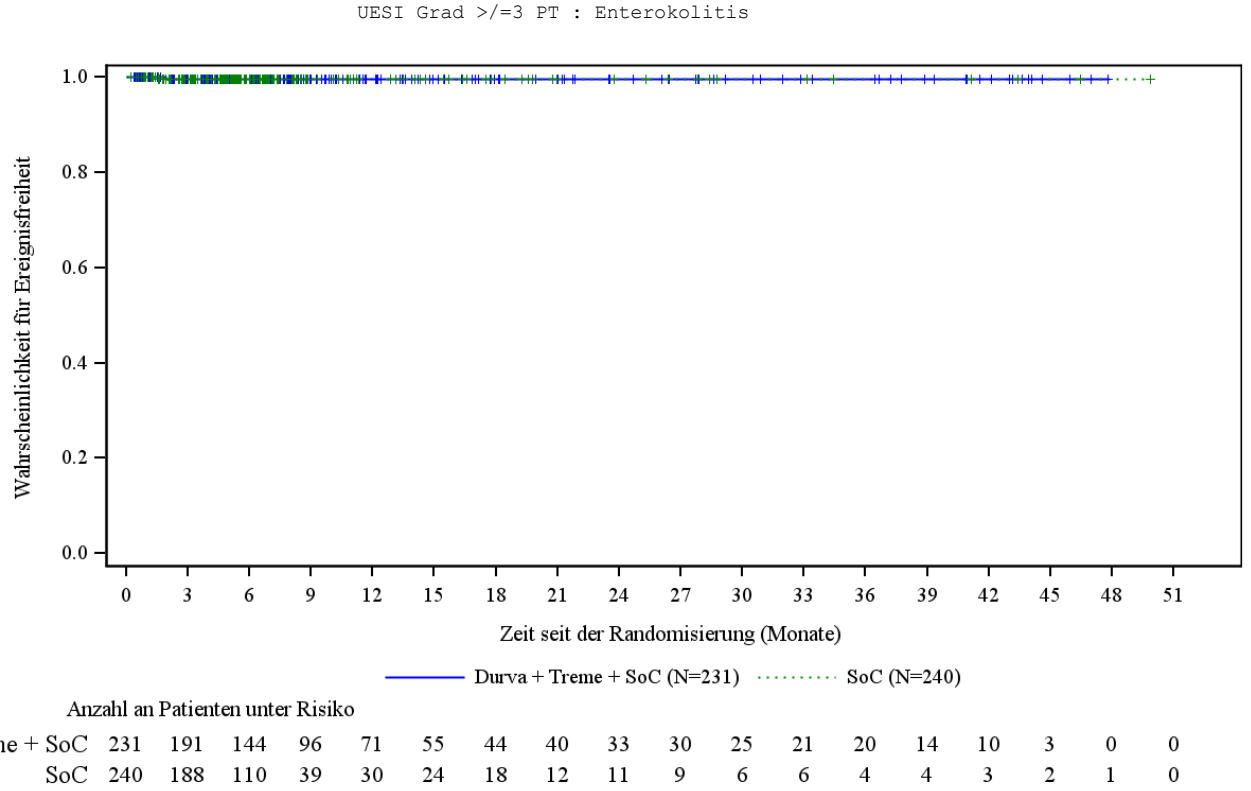

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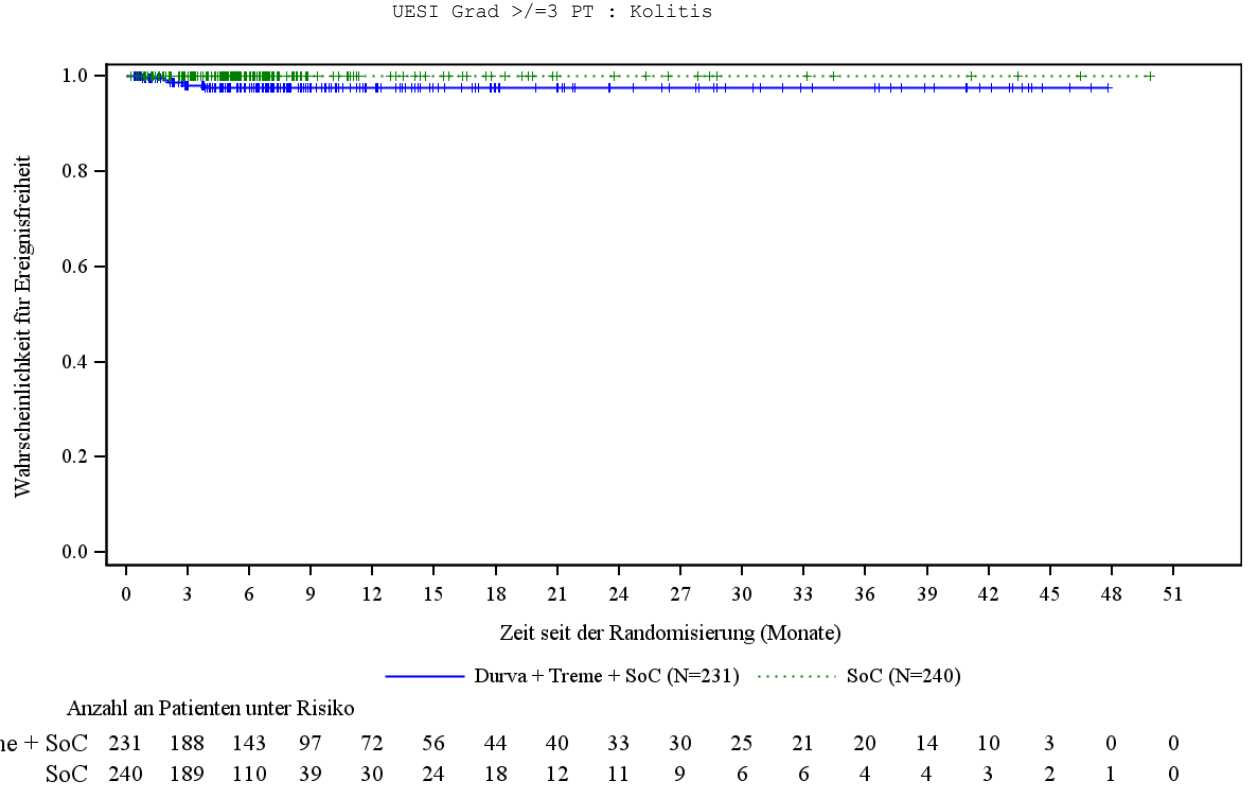

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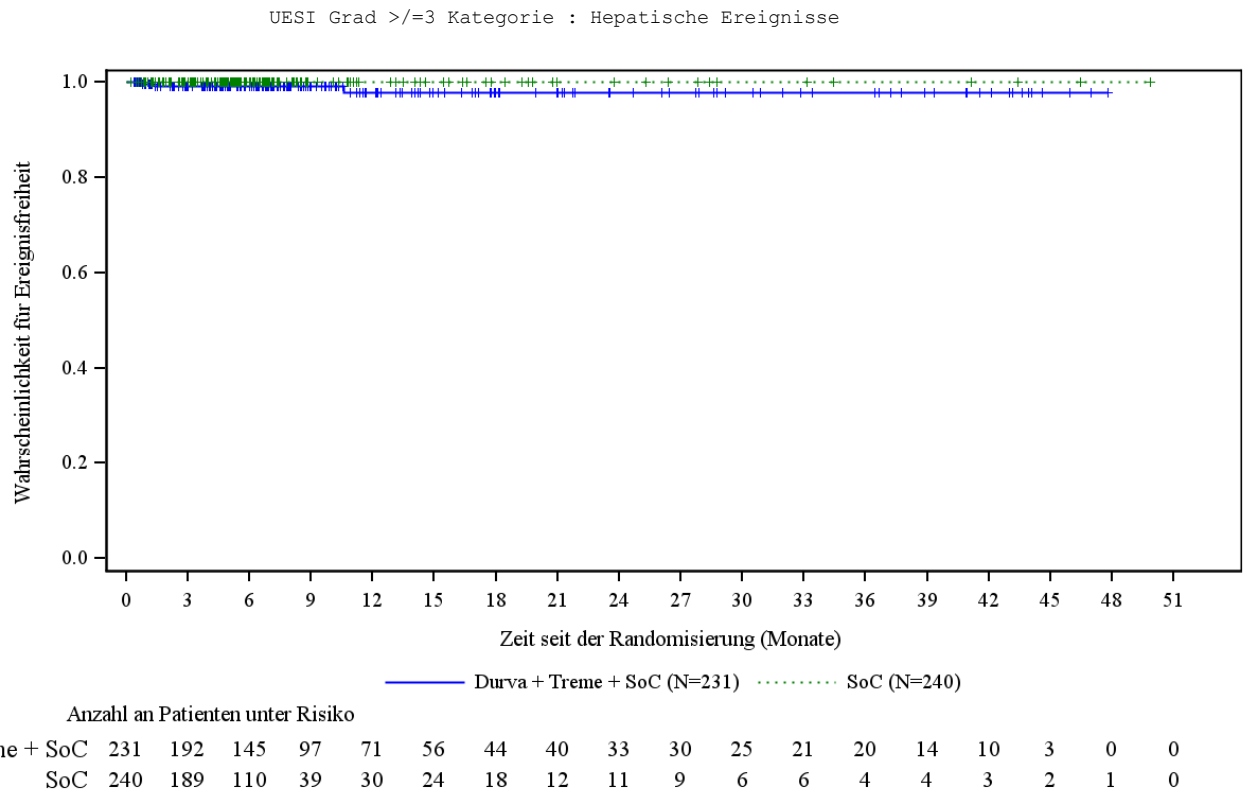

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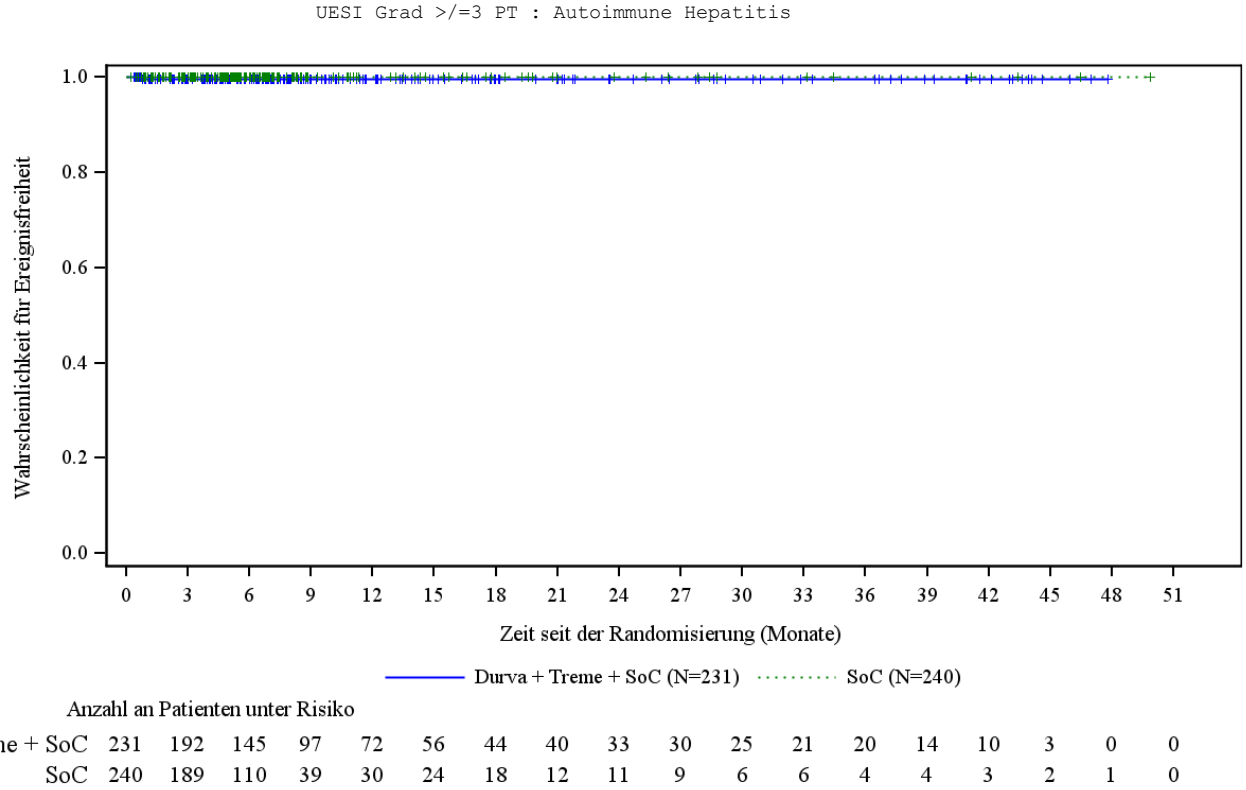

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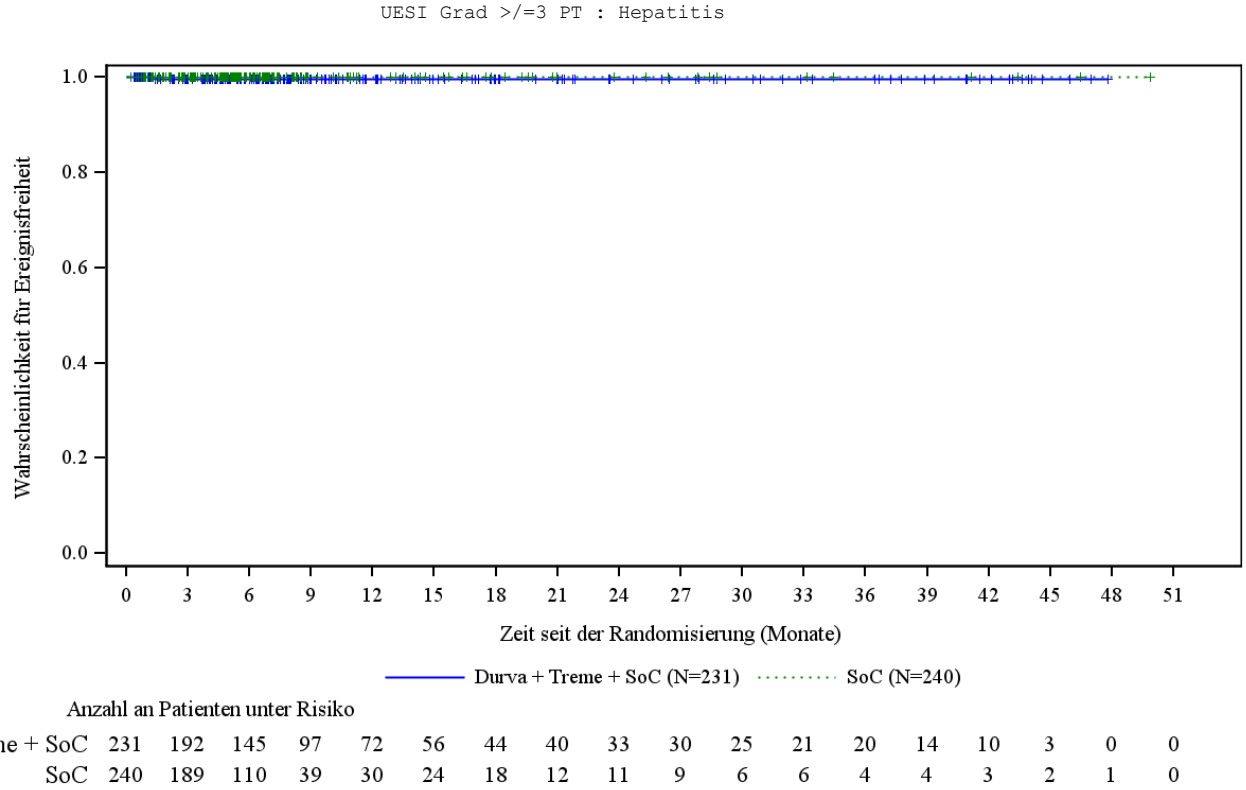

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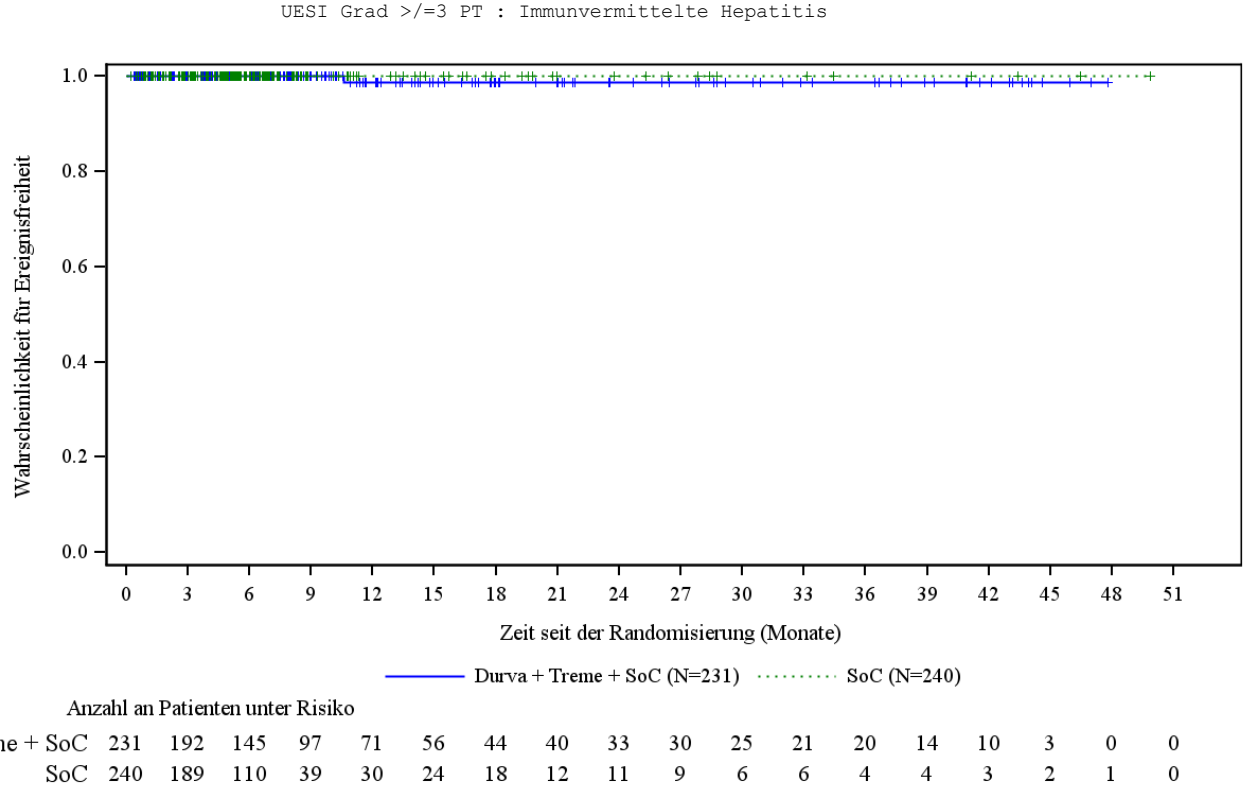

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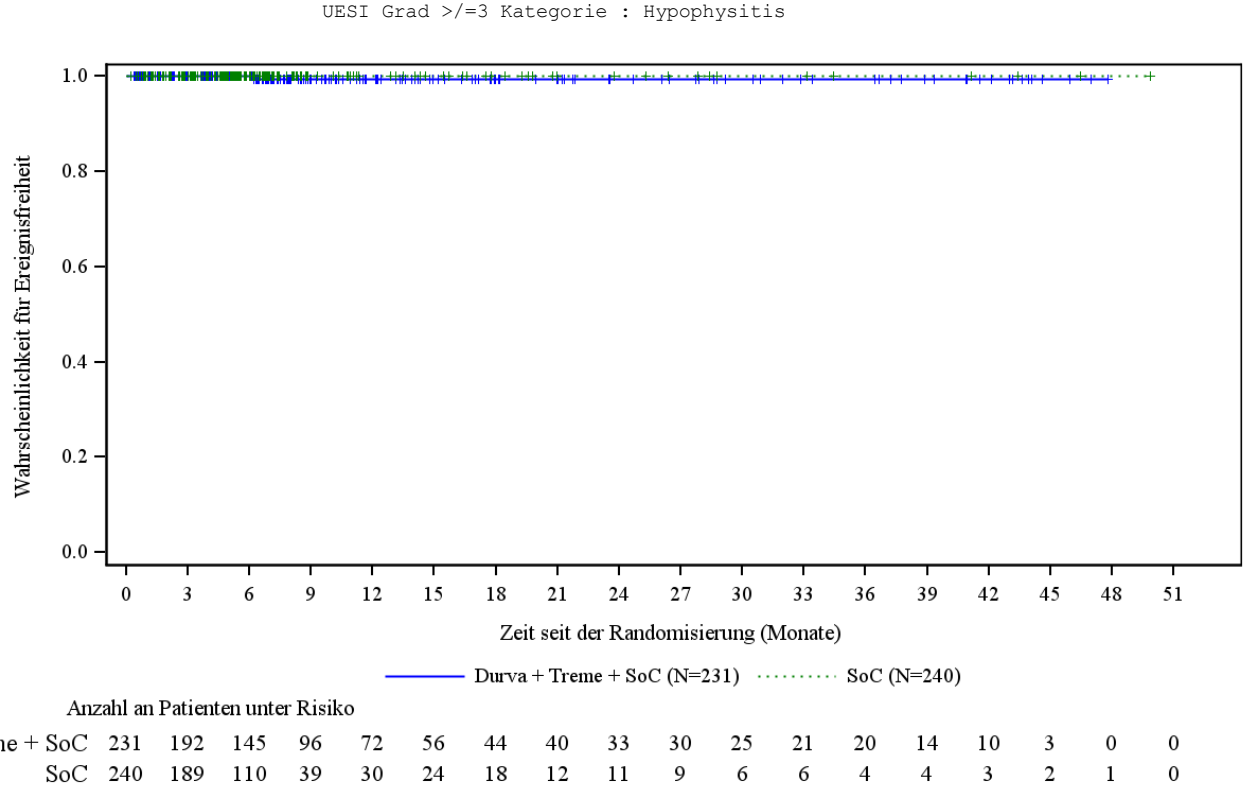

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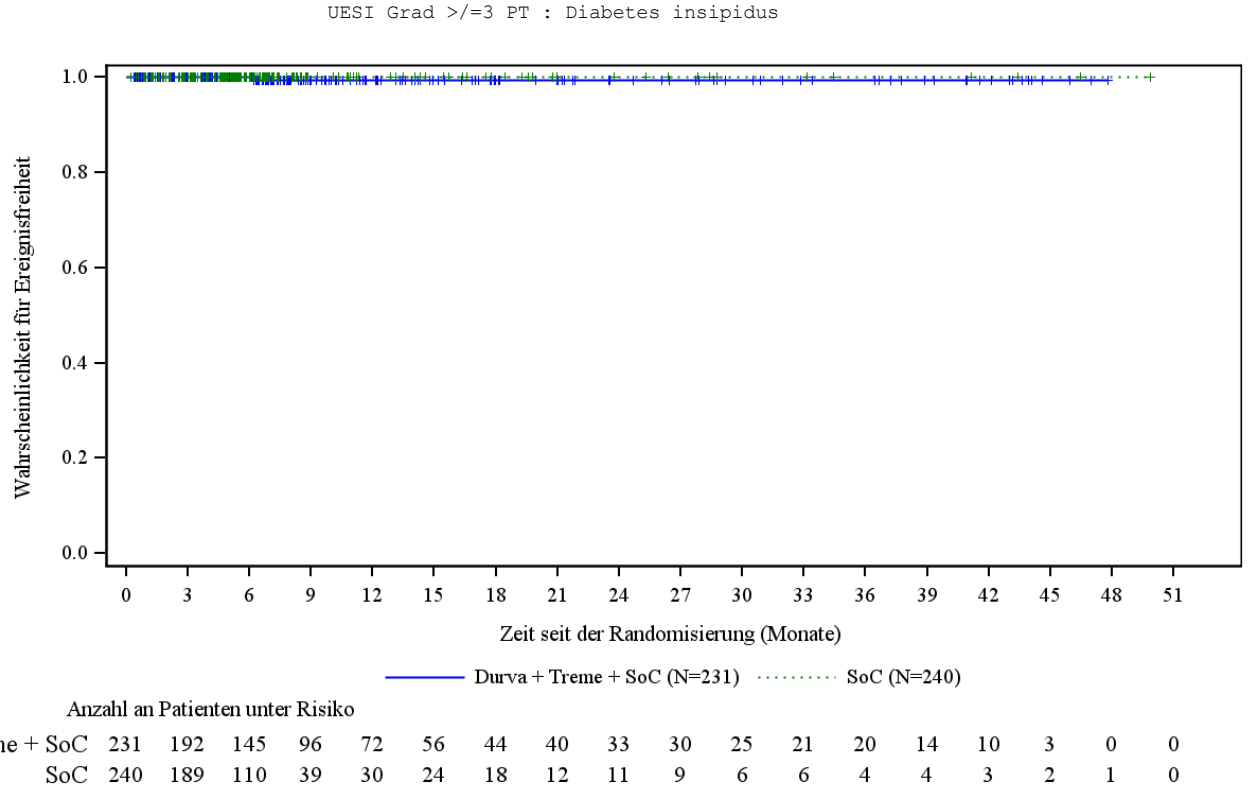

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UESI Grad >/=3 Kategorie : Infusions- und Überempfindlichkeitsreaktion

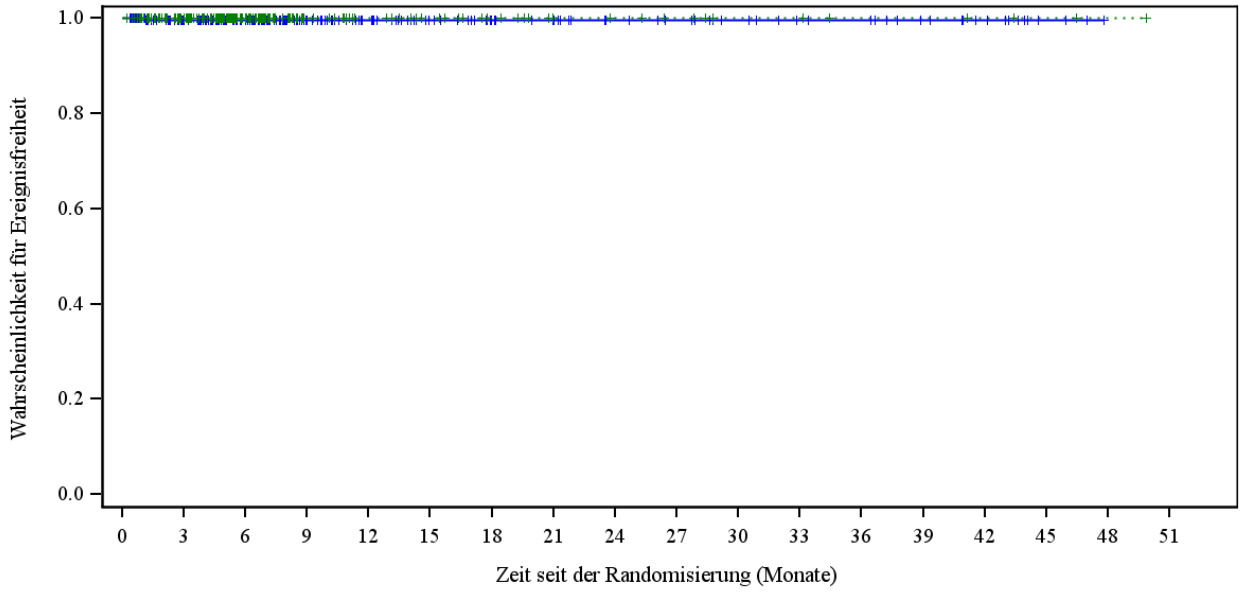

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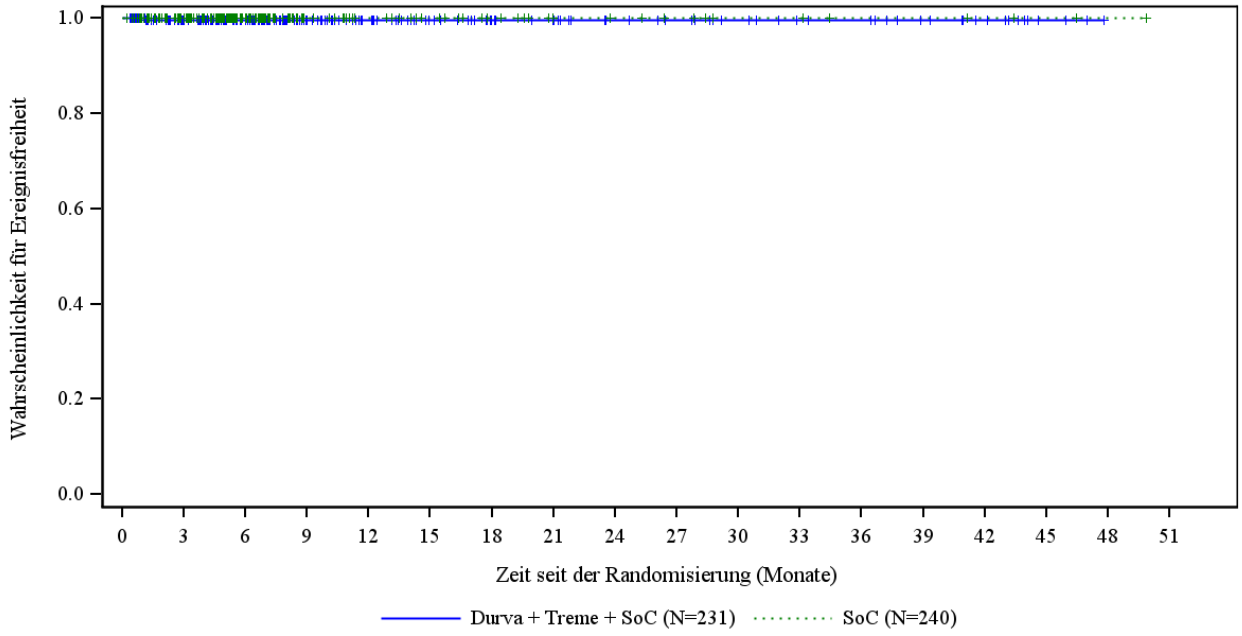
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Grad >/=3 Sub-Kategorie : Überempfindlichkeitsreaktion / Anaphylaktische Reaktion



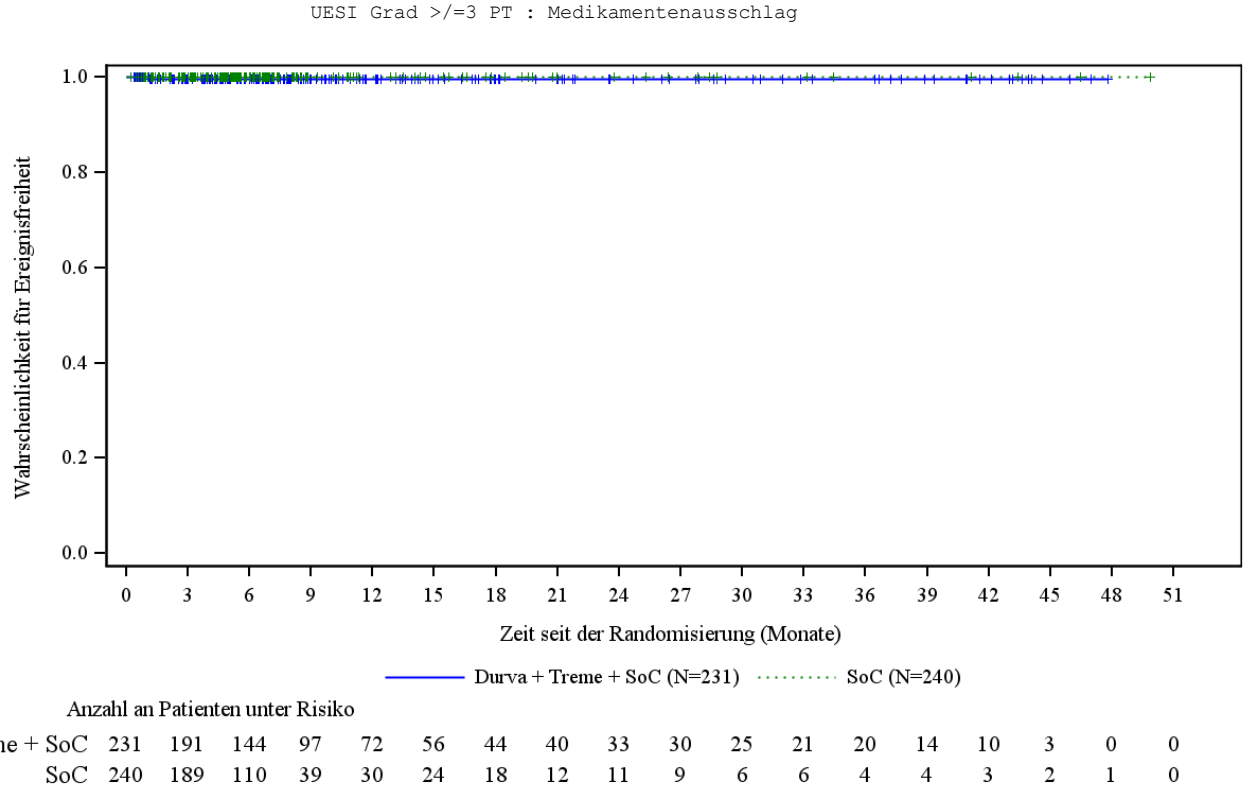
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	14	10	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae366g.sas Executed : 2022-11-22T132426

Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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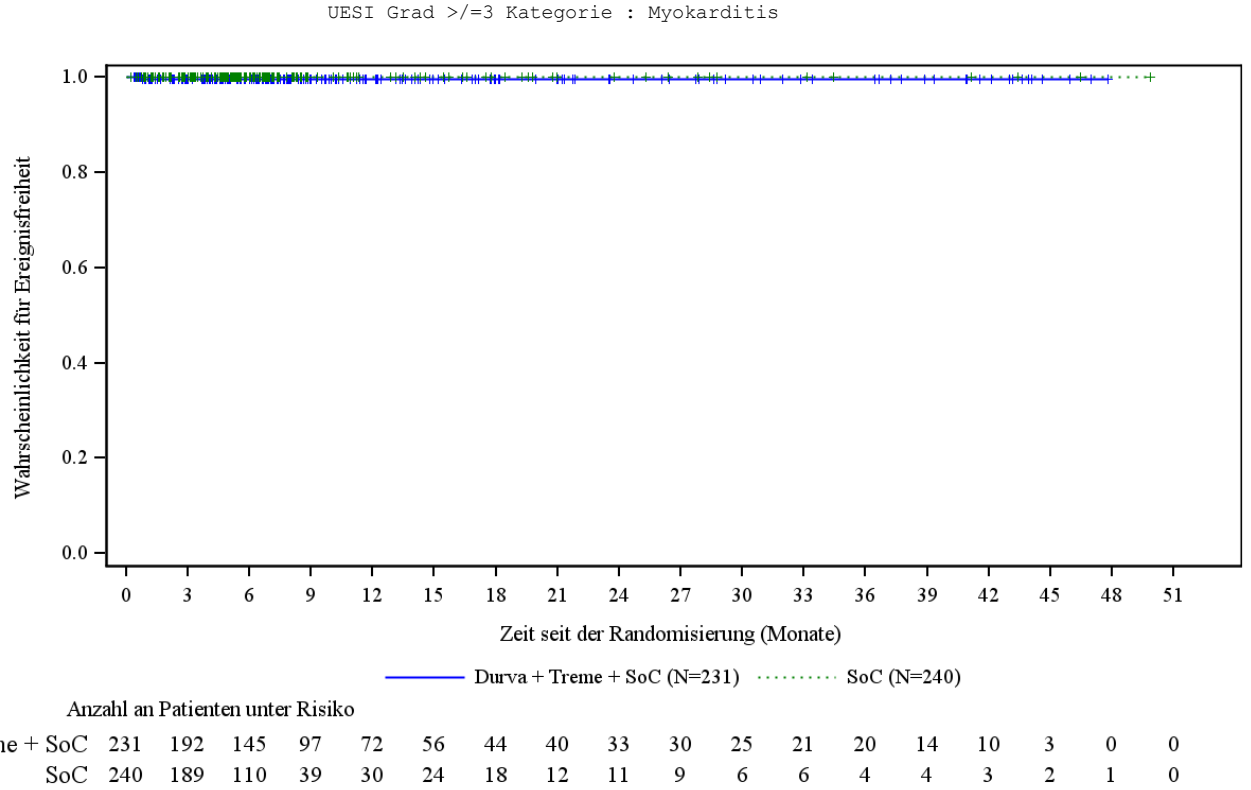
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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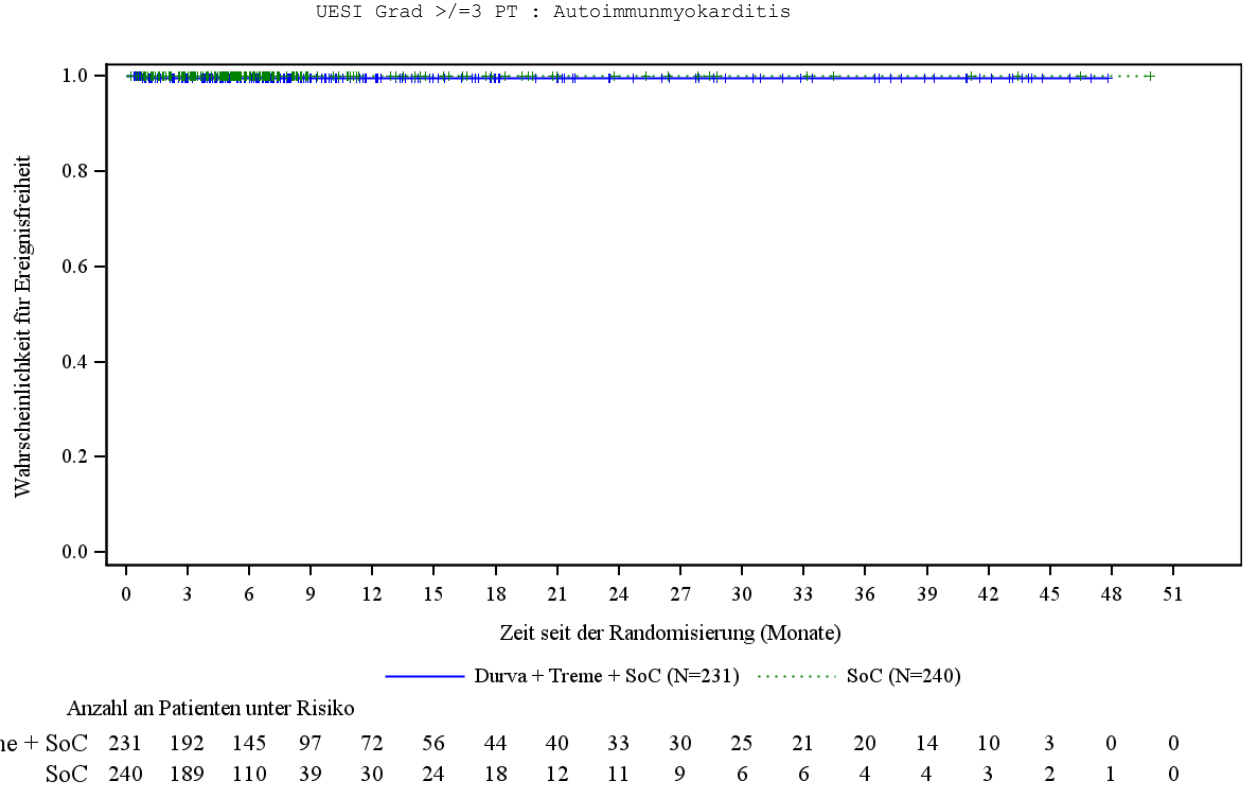
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae366g.sas Executed : 2022-11-22T132426

Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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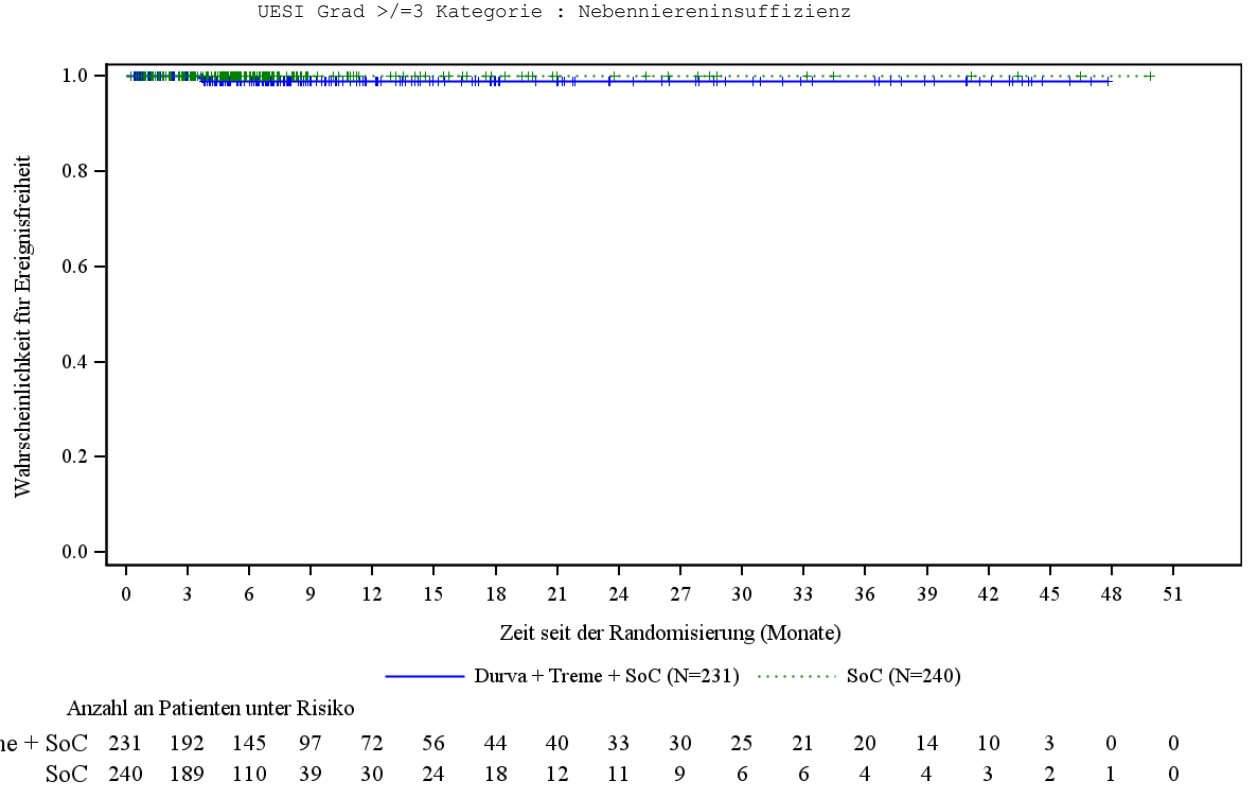
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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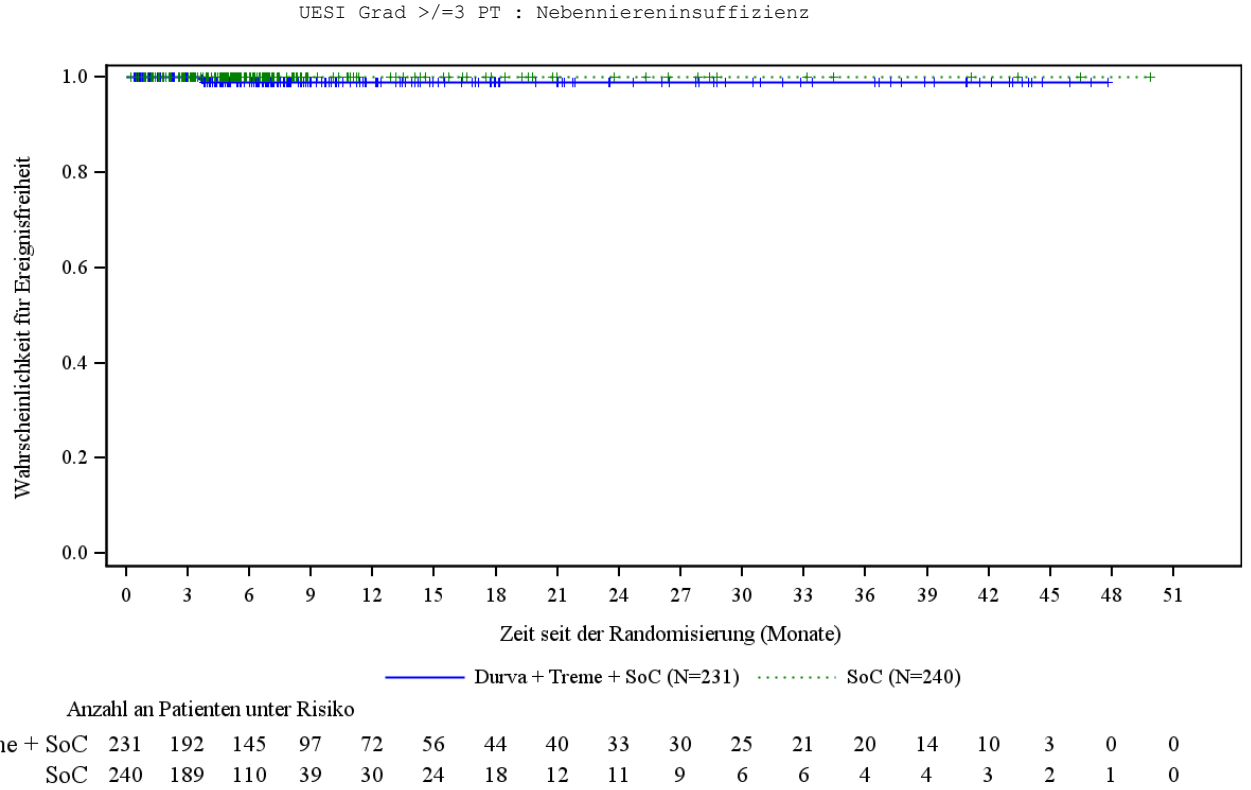
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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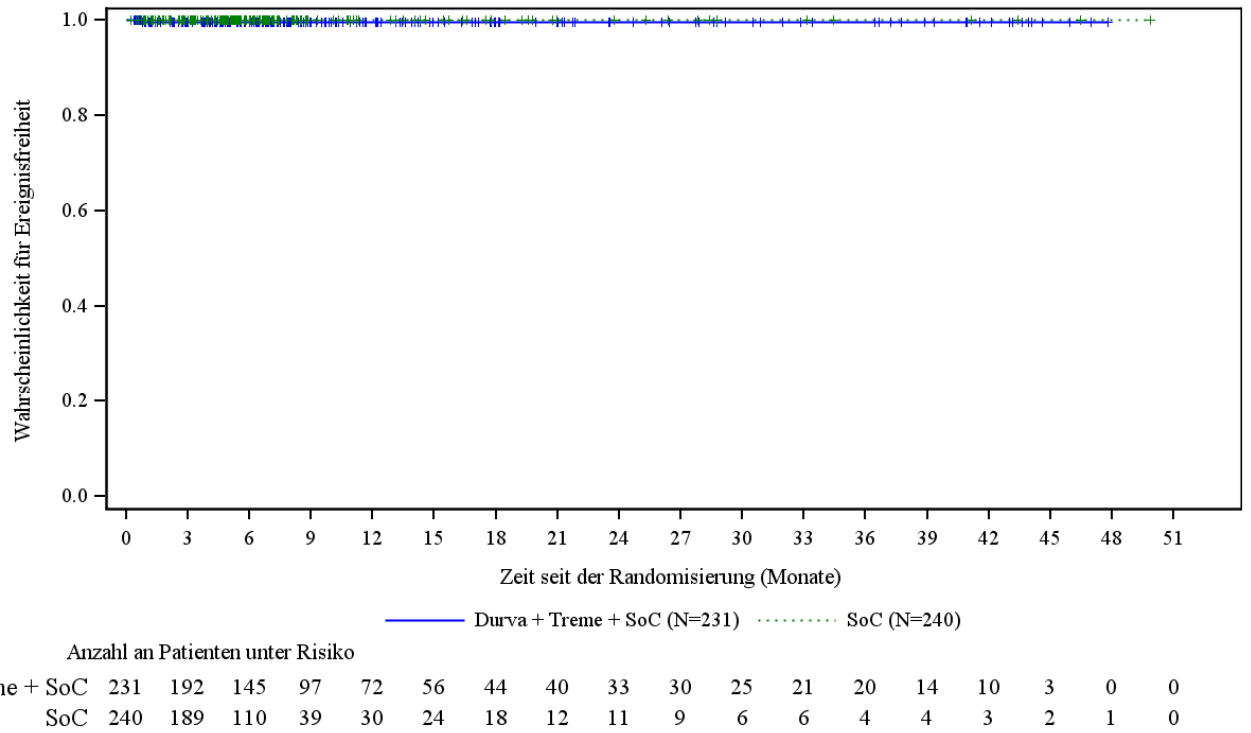
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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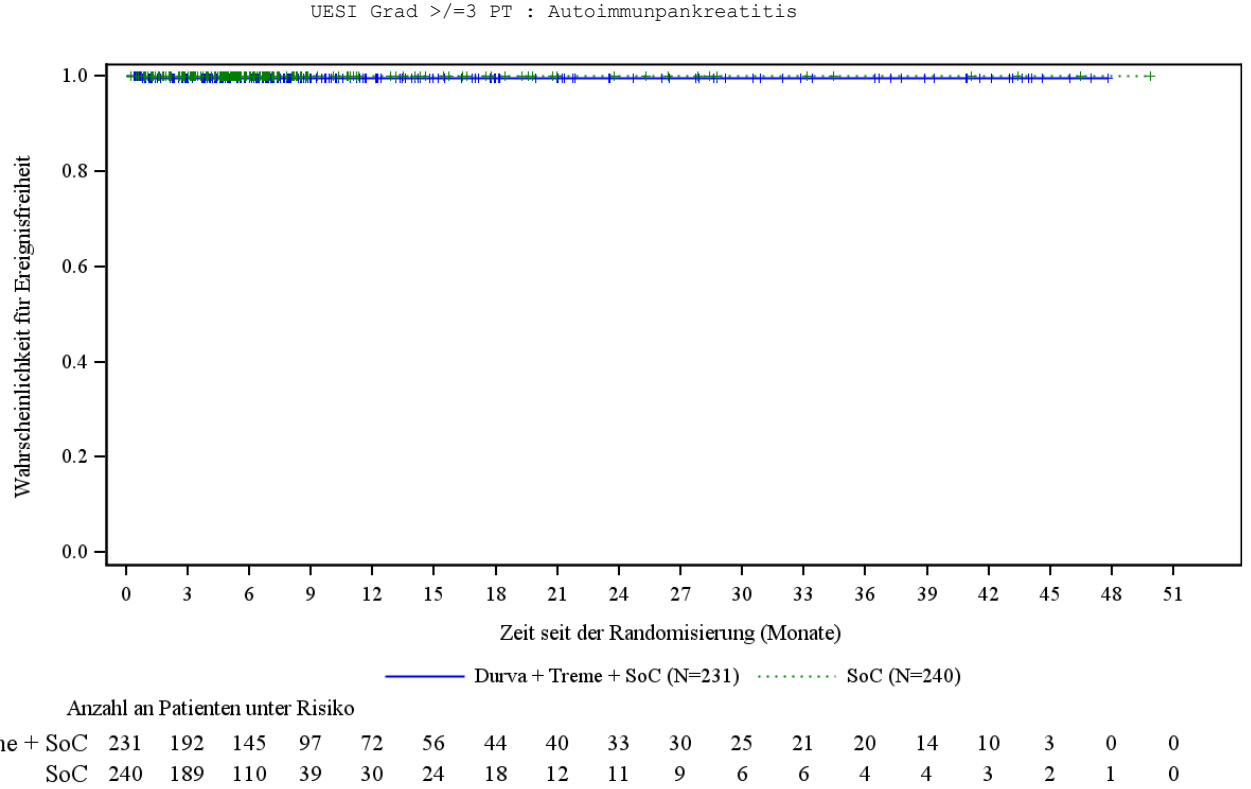
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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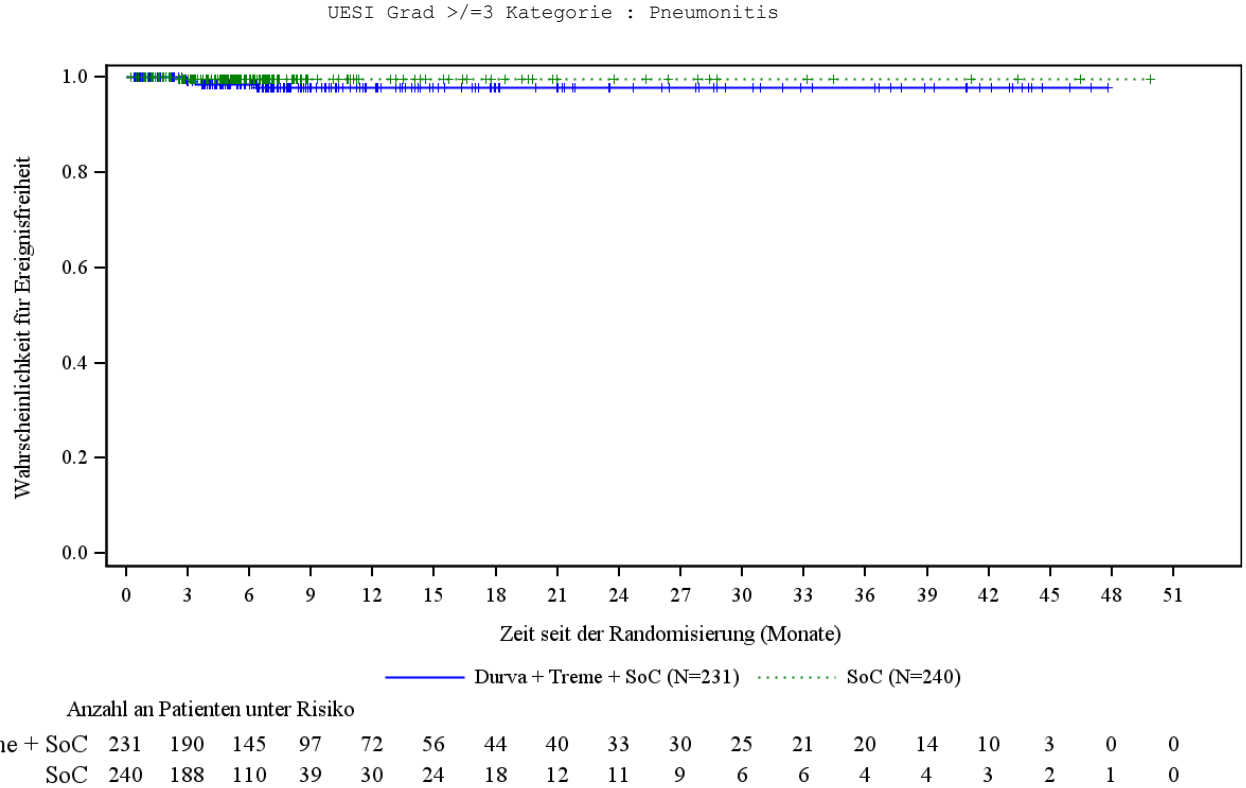
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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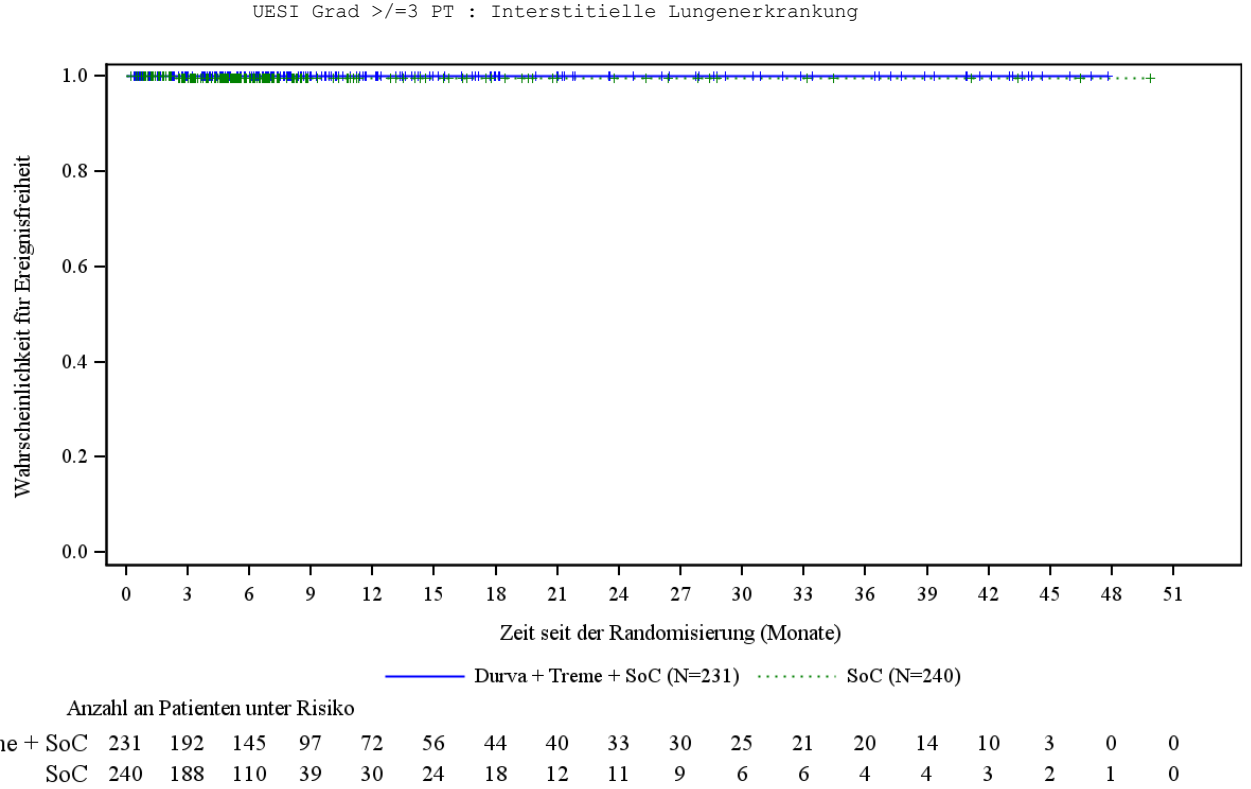
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



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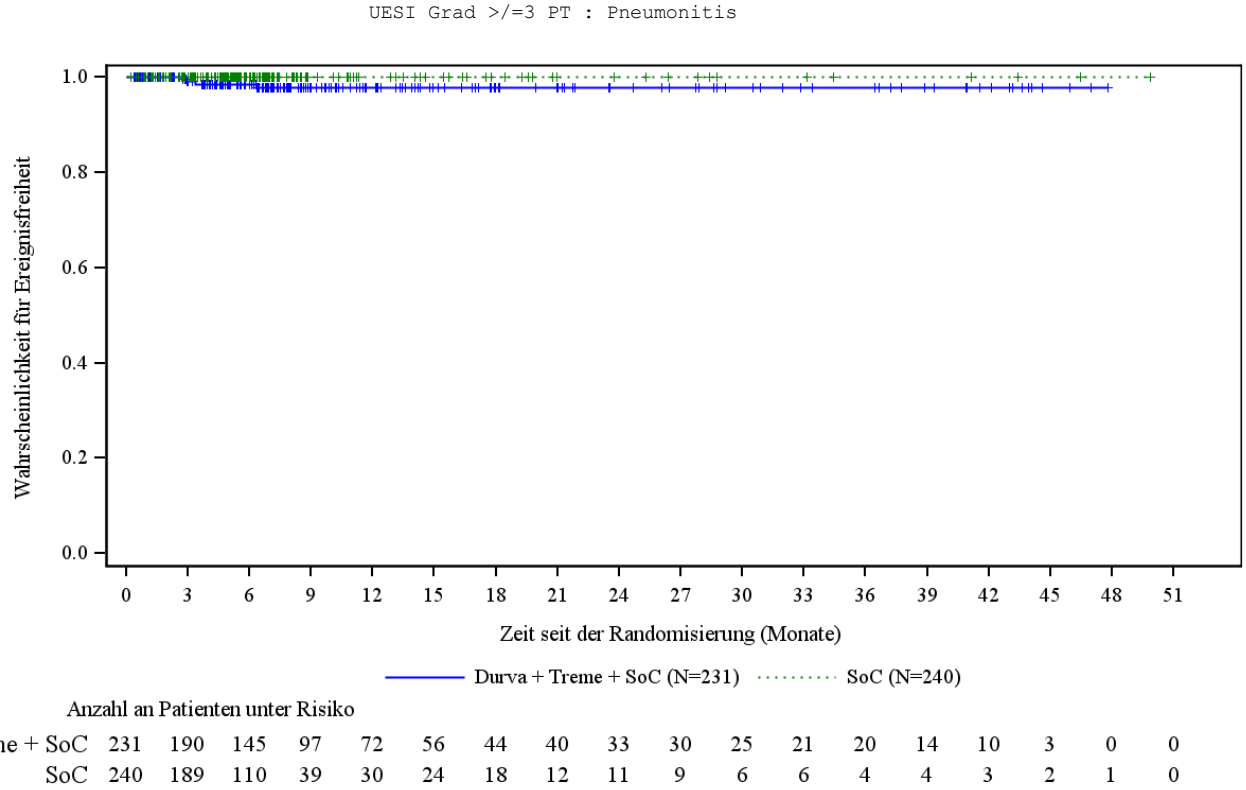
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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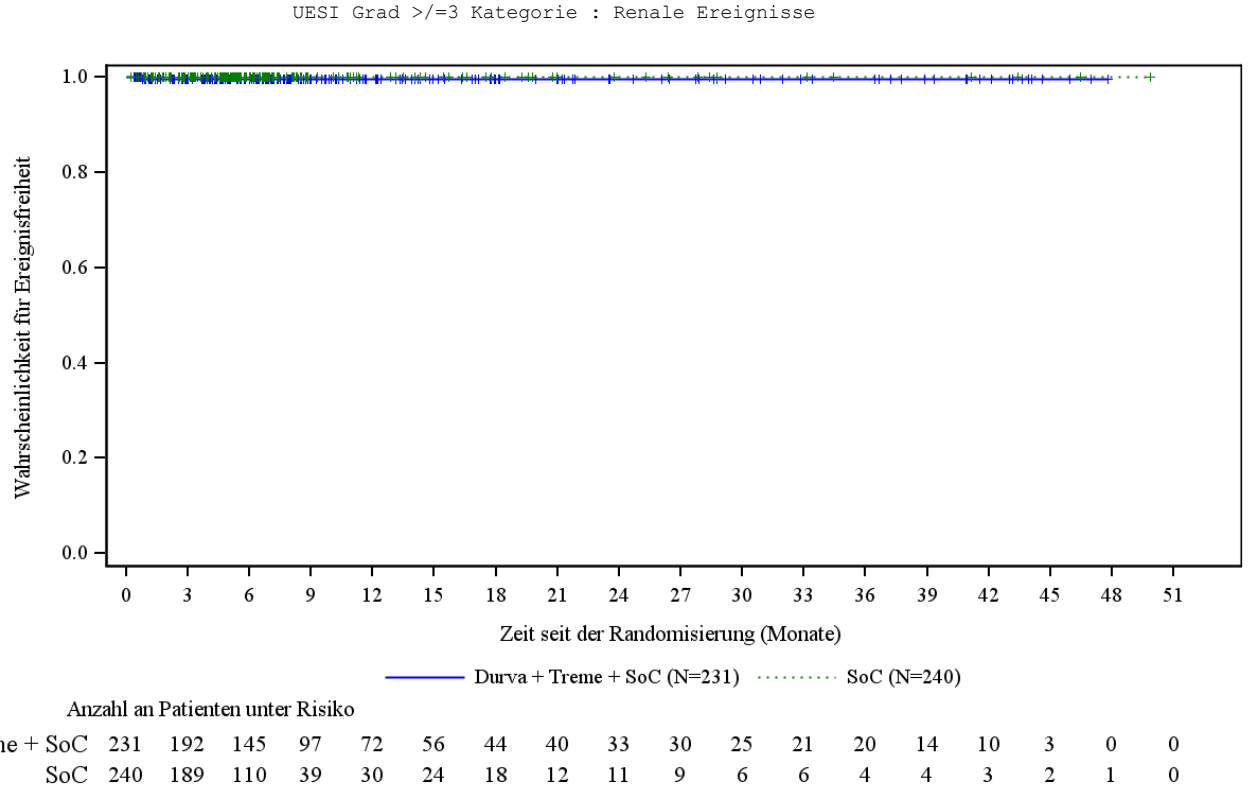
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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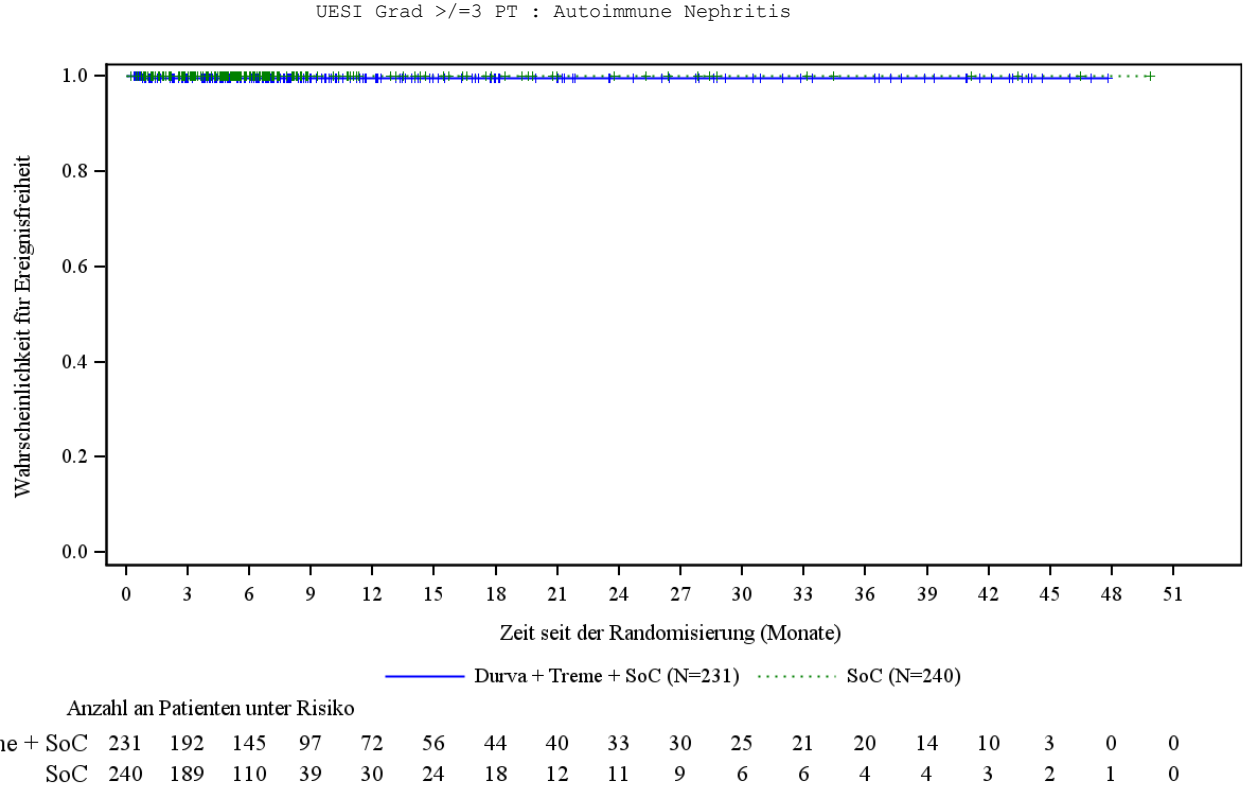
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae366g.sas Executed : 2022-11-22T132426

Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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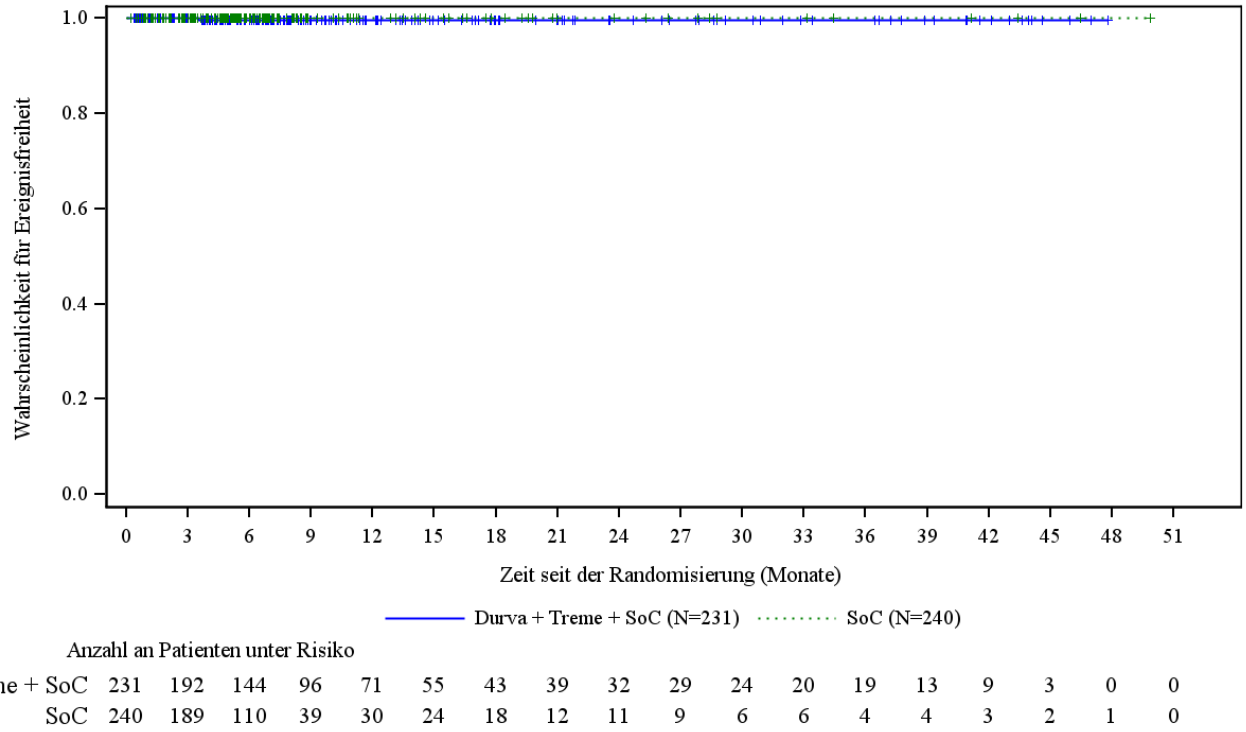
Figure 4.8.2.4 Kaplan-Meier of analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

UESI Grad >/=3 Kategorie : Sonstige seltene/Diverses



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	71	55	43	39	32	29	24	20	19	13	9	3	0	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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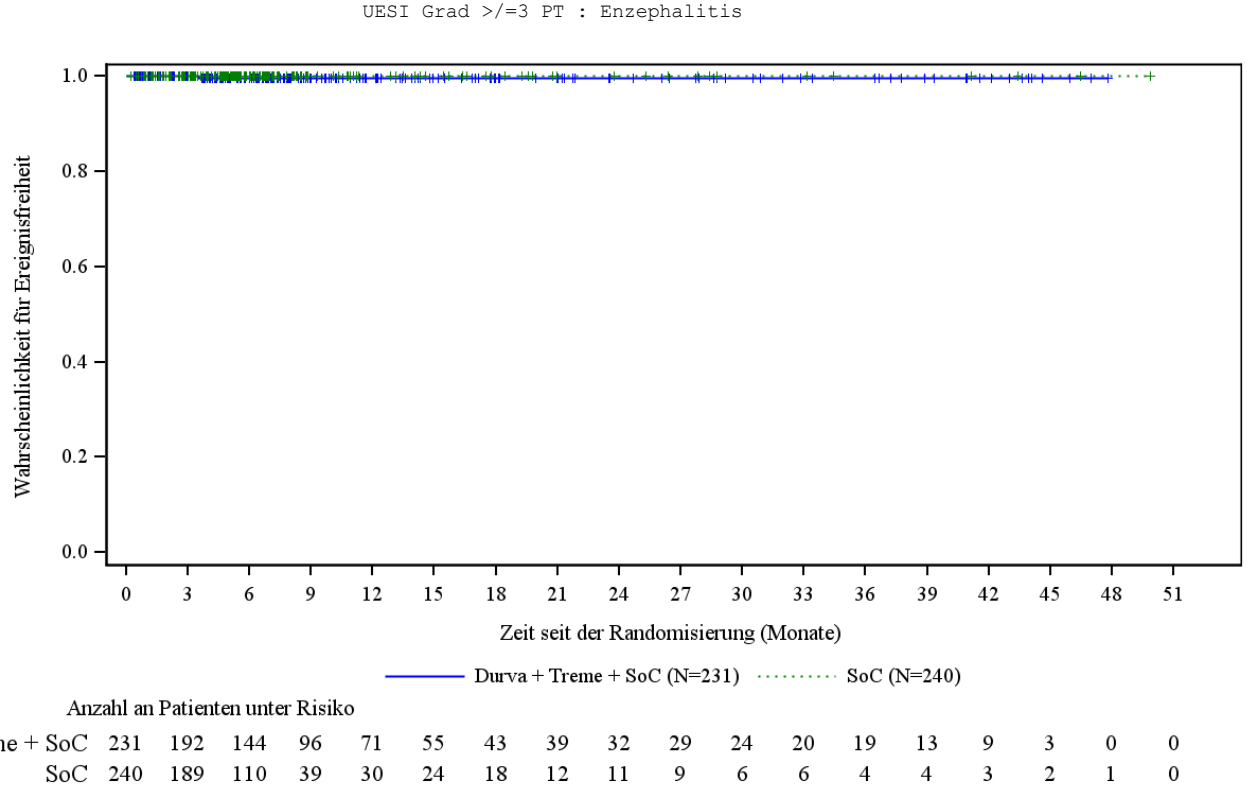
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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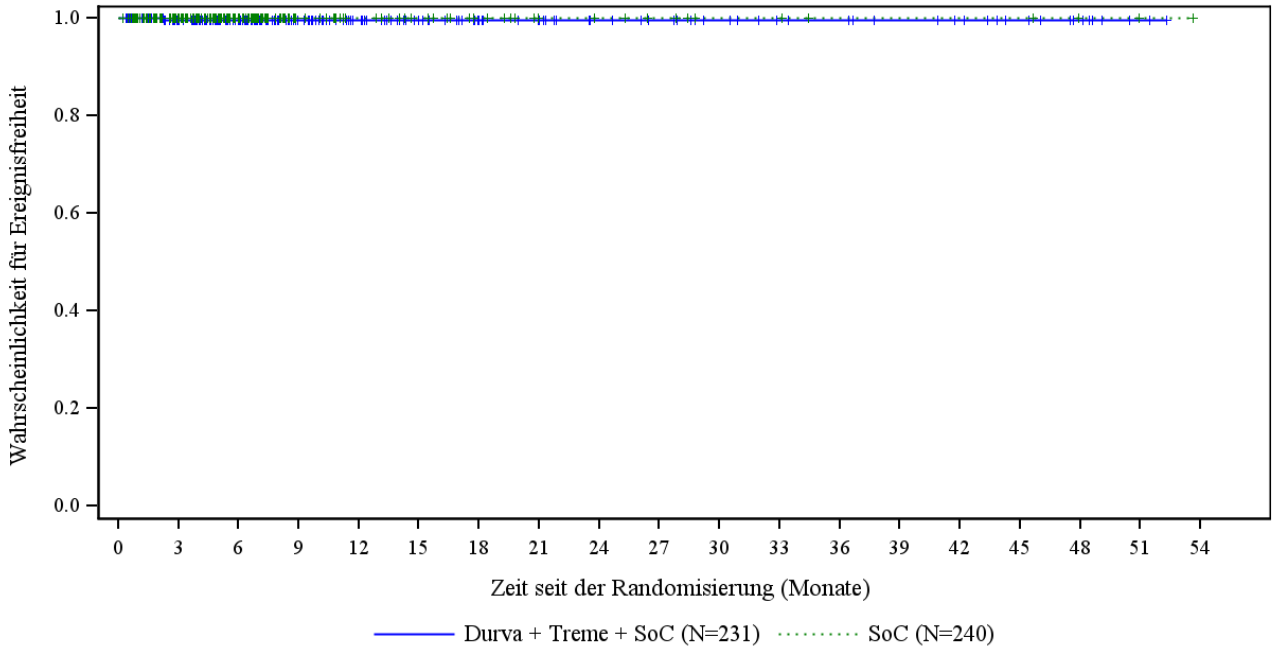
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae366g.sas Executed : 2022-11-22T132426

Anhang 4-G 1.2.2.3: Schwerwiegende unerwünschte Ereignisse von speziellem Interesse nach Kategorie und PT

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 34

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Kategorie : Diabetes mellitus Typ 1



Anzahl an Patienten unter Risiko

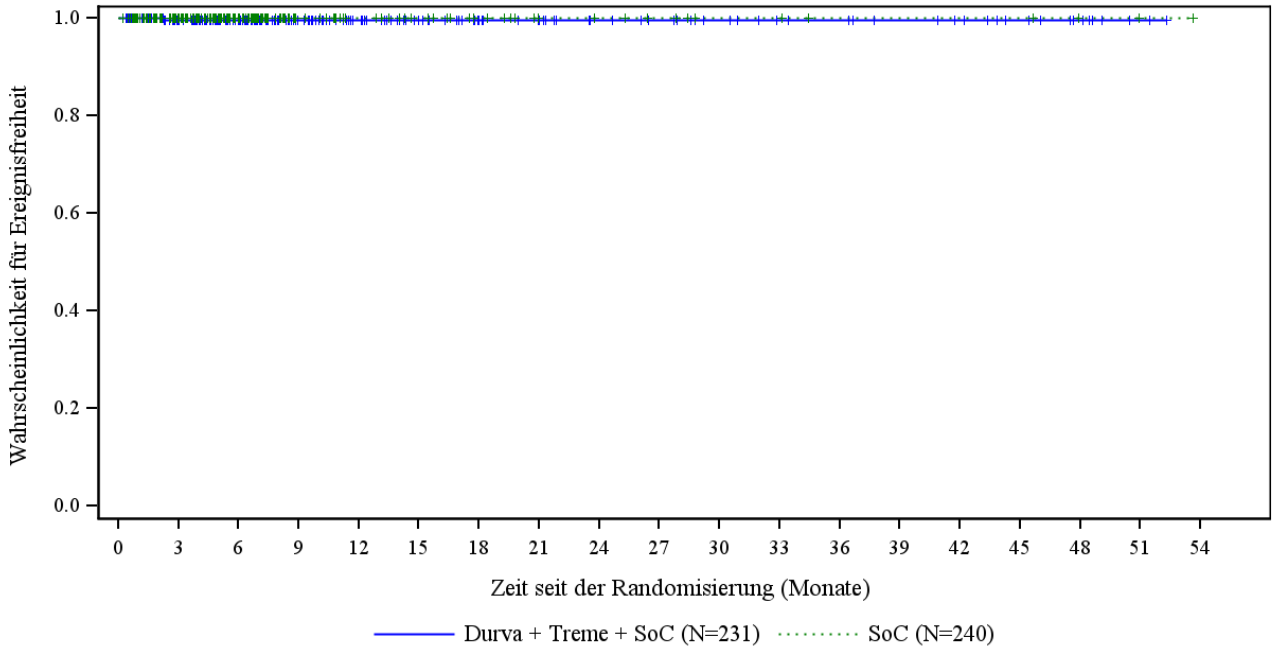
Durva + Treme + SoC	231	191	144	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Diabetes mellitus Typ 1



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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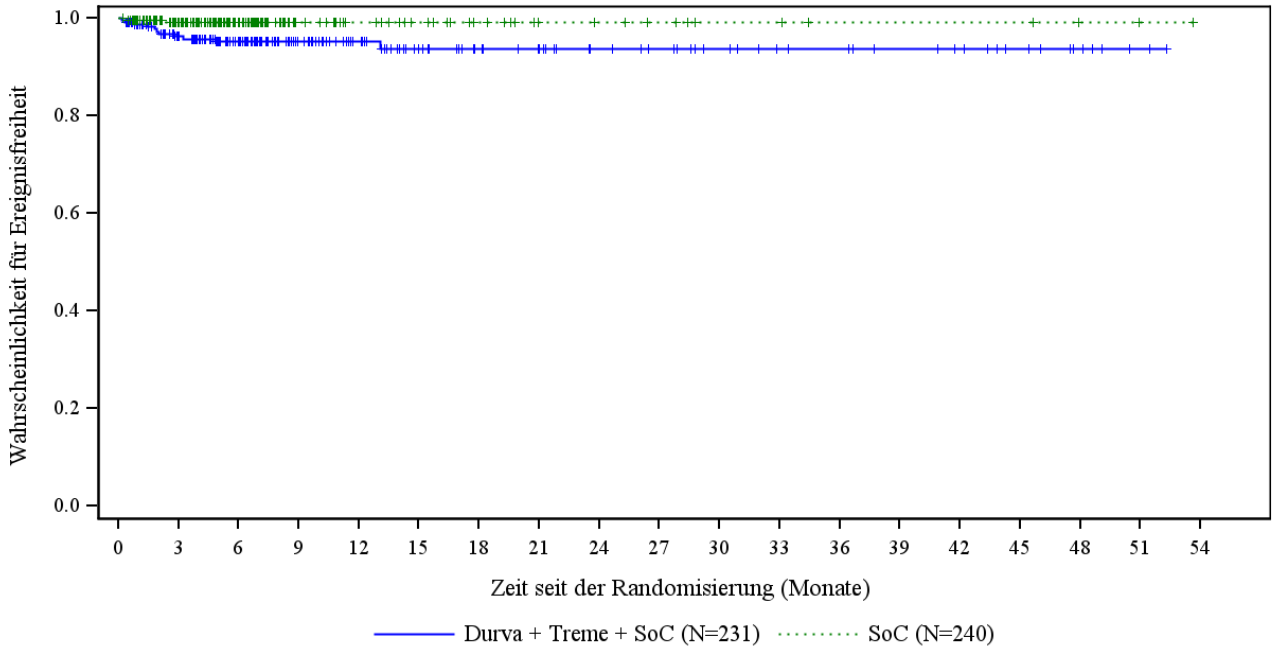
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Kategorie : Diarrhö / Kolitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	184	139	93	69	52	43	39	32	29	24	20	19	16	14	10	6	2	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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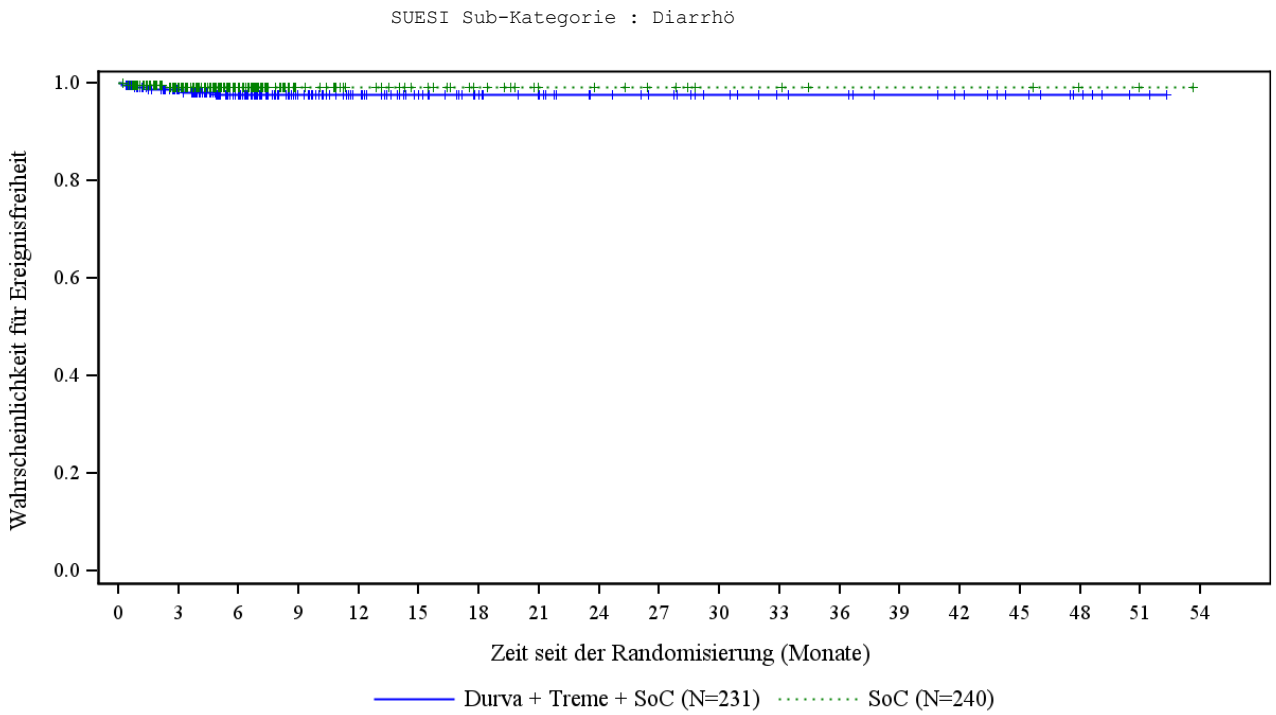
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	141	94	70	54	43	39	32	29	24	20	19	16	14	10	6	2	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
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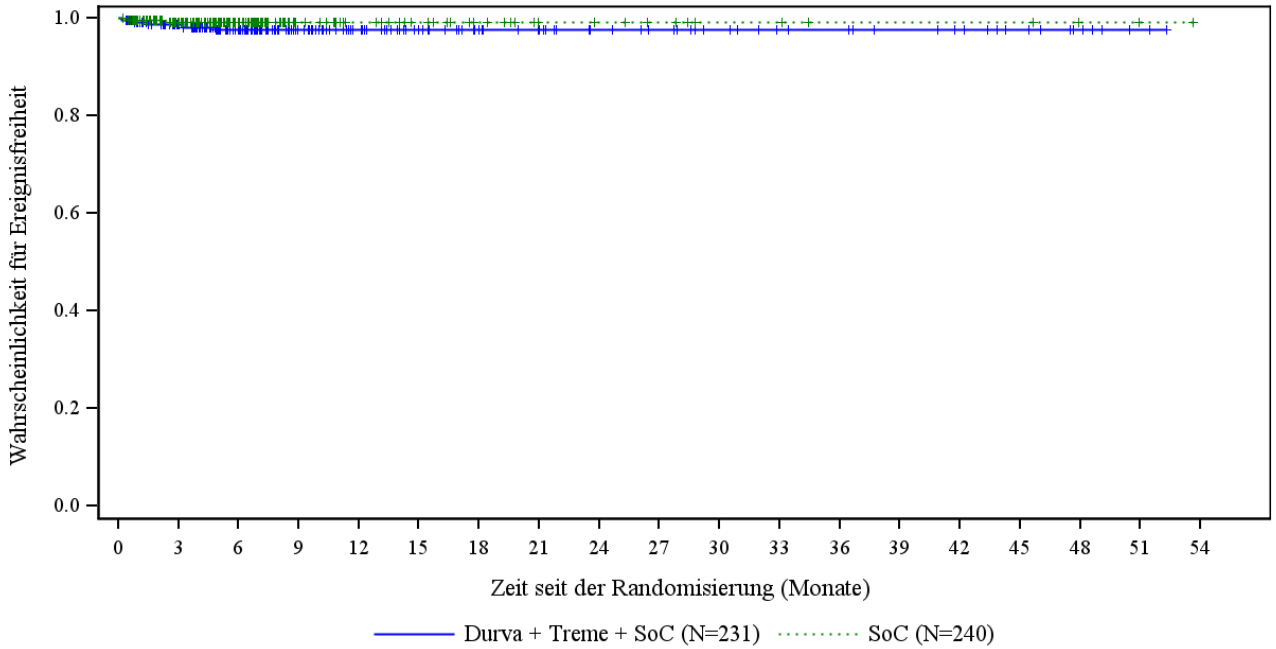
Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Diarrhoe



Anzahl an Patienten unter Risiko

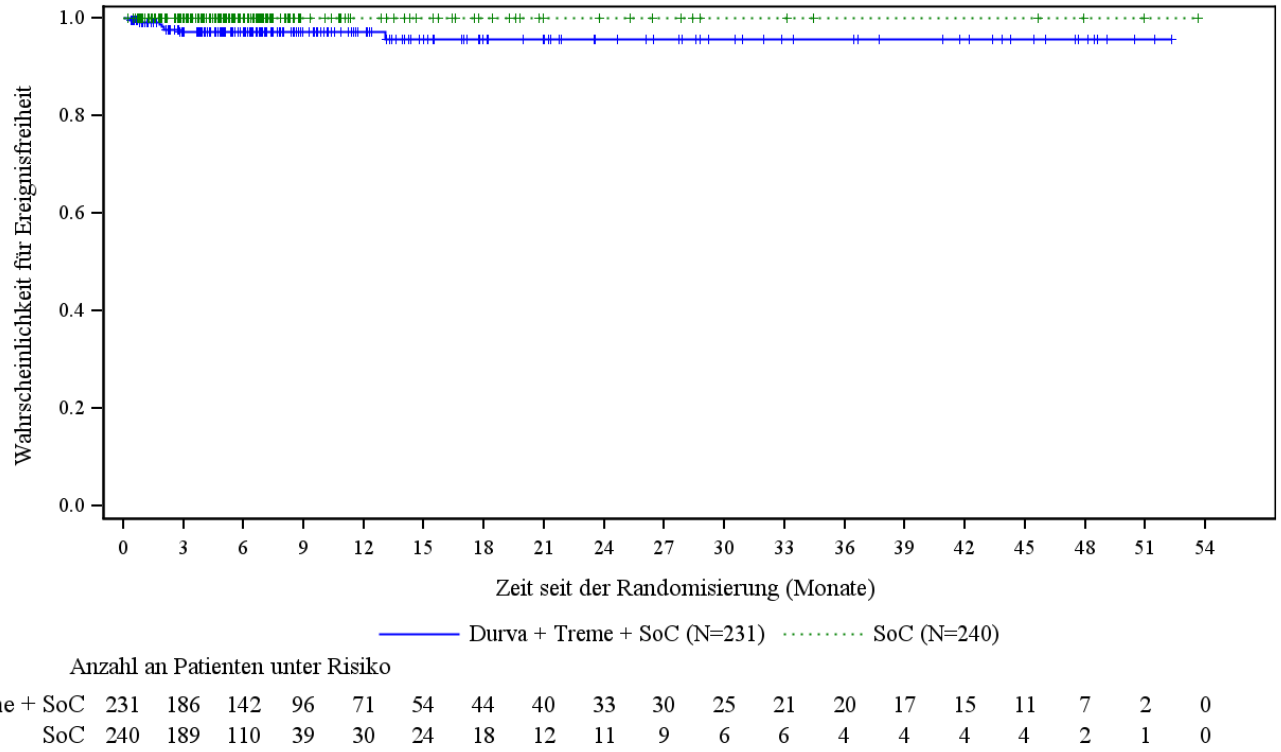
Durva + Treme + SoC	231	189	141	94	70	54	43	39	32	29	24	20	19	16	14	10	6	2	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Sub-Kategorie : Kolitis



Anzahl an Patienten unter Risiko

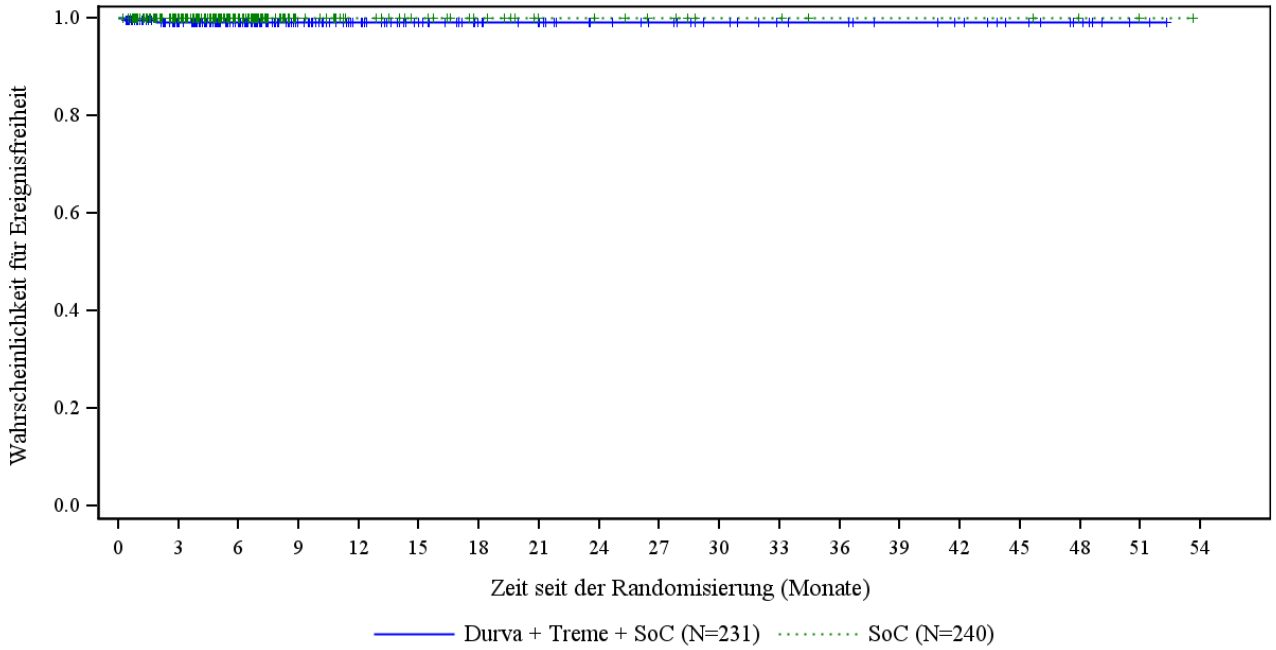
Durva + Treme + SoC	231	186	142	96	71	54	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Enterokolitis



Anzahl an Patienten unter Risiko

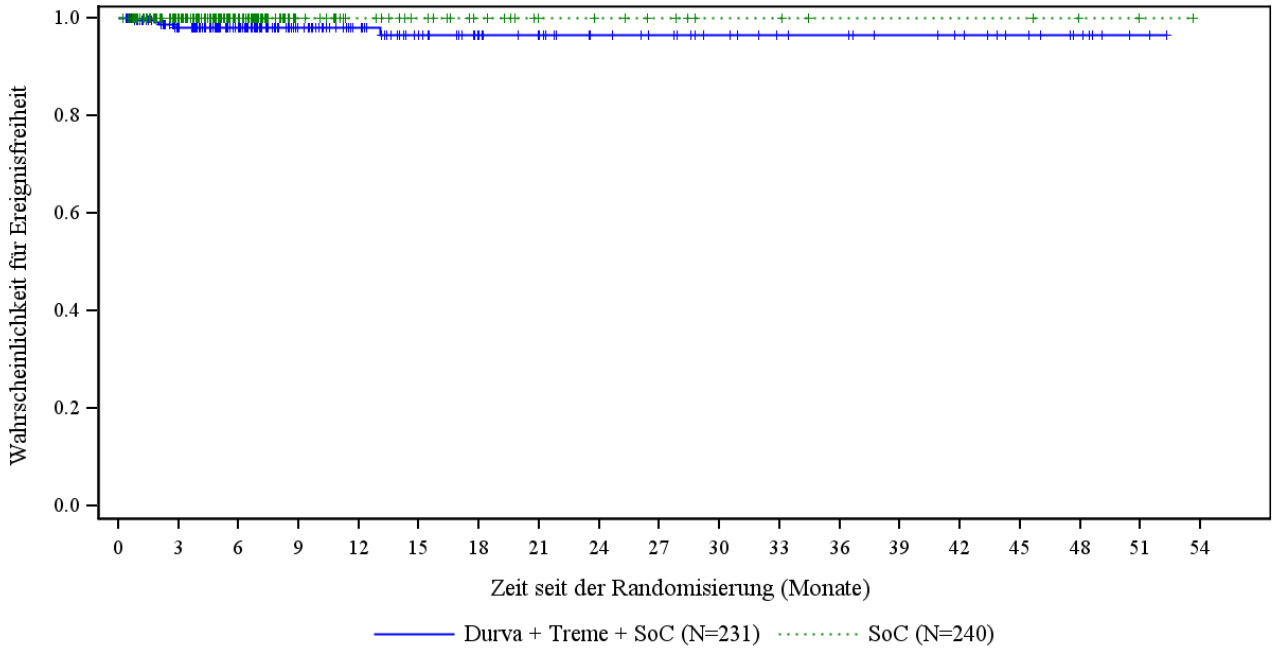
Durva + Treme + SoC	231	190	143	96	71	55	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Kolitis



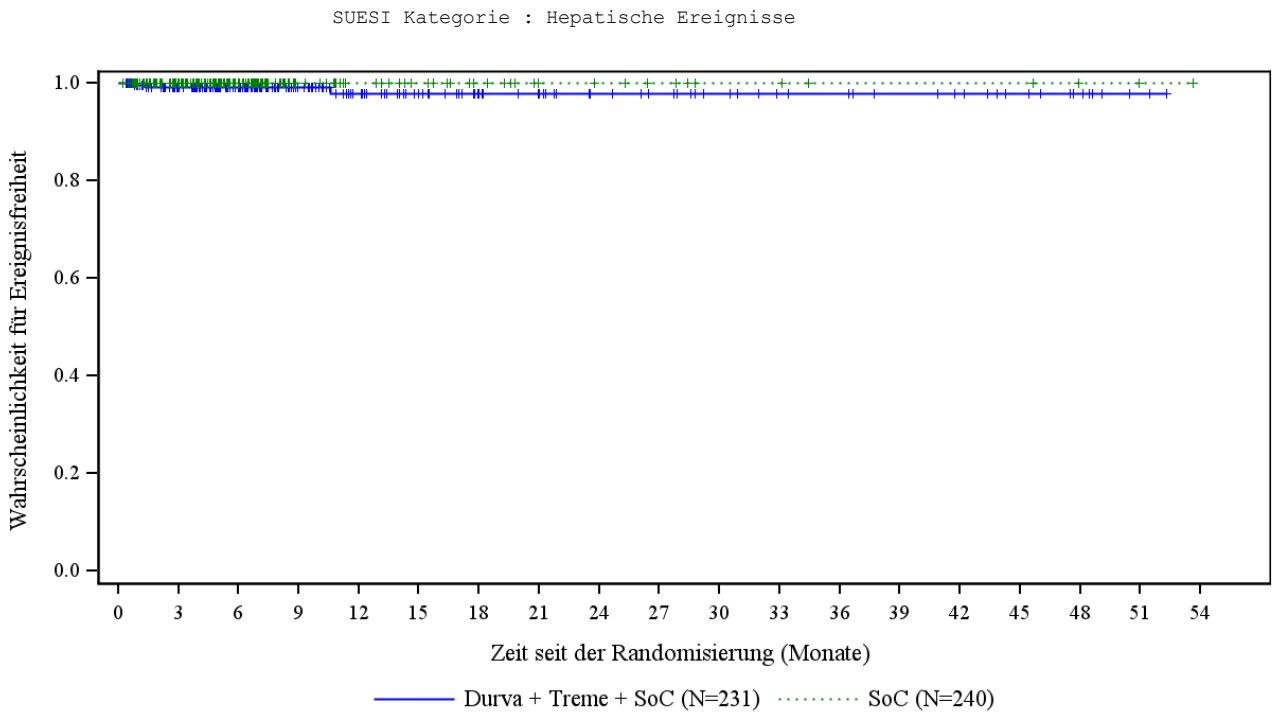
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	188	144	97	72	55	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

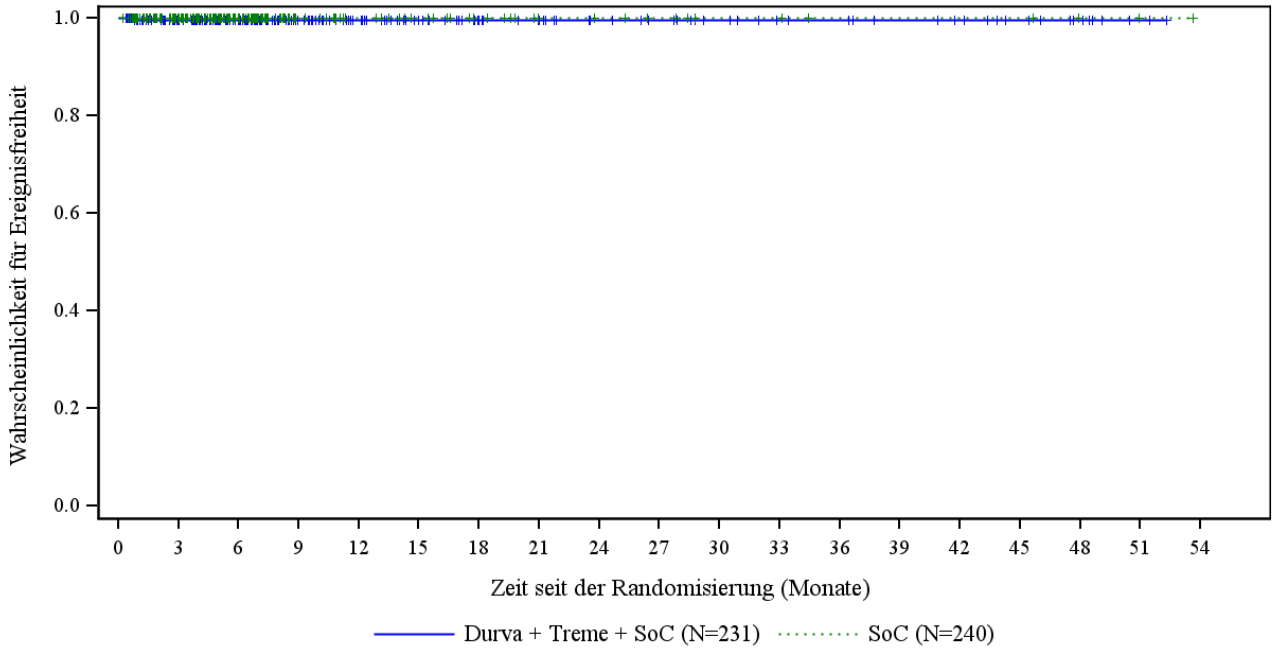
Durva + Treme + SoC	231	192	145	97	71	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Autoimmune Hepatitis



Anzahl an Patienten unter Risiko

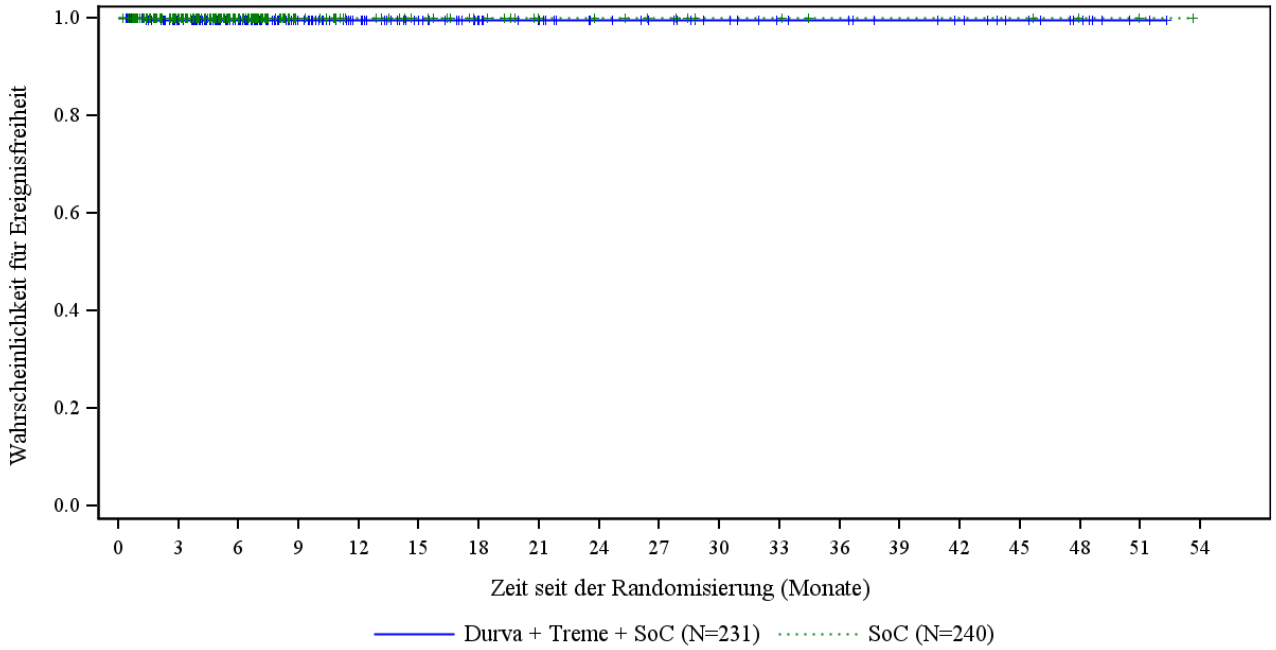
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Hepatitis



Anzahl an Patienten unter Risiko

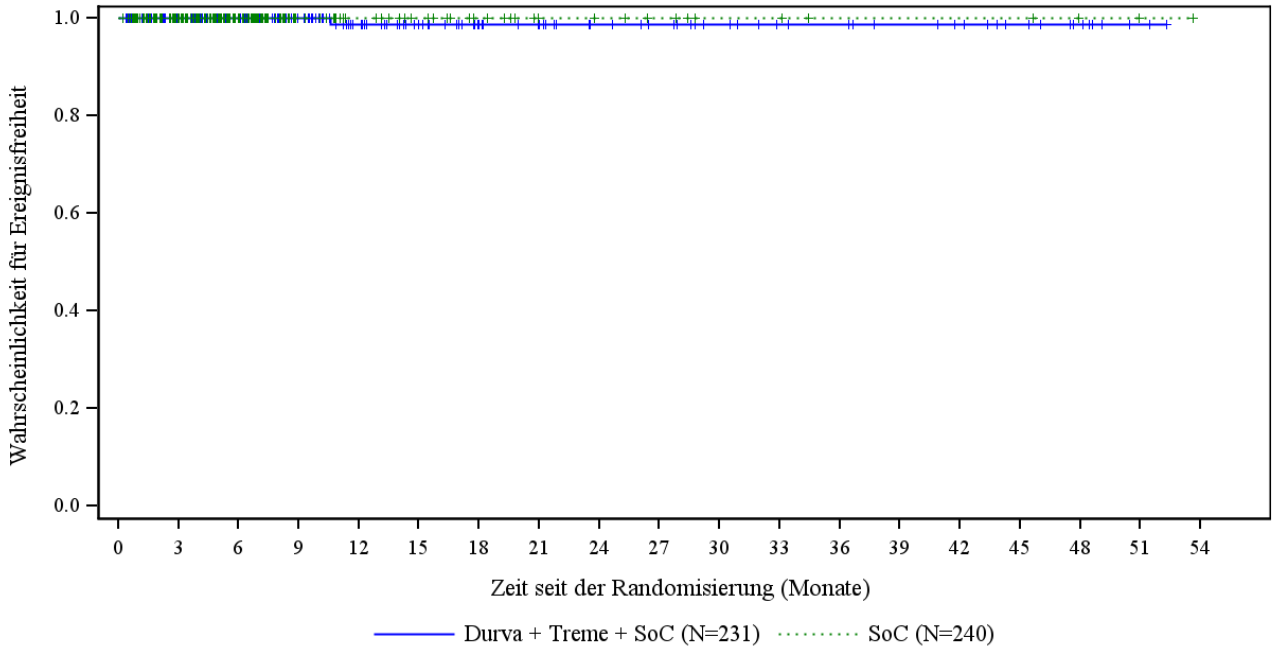
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Immunvermittelte Hepatitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	71	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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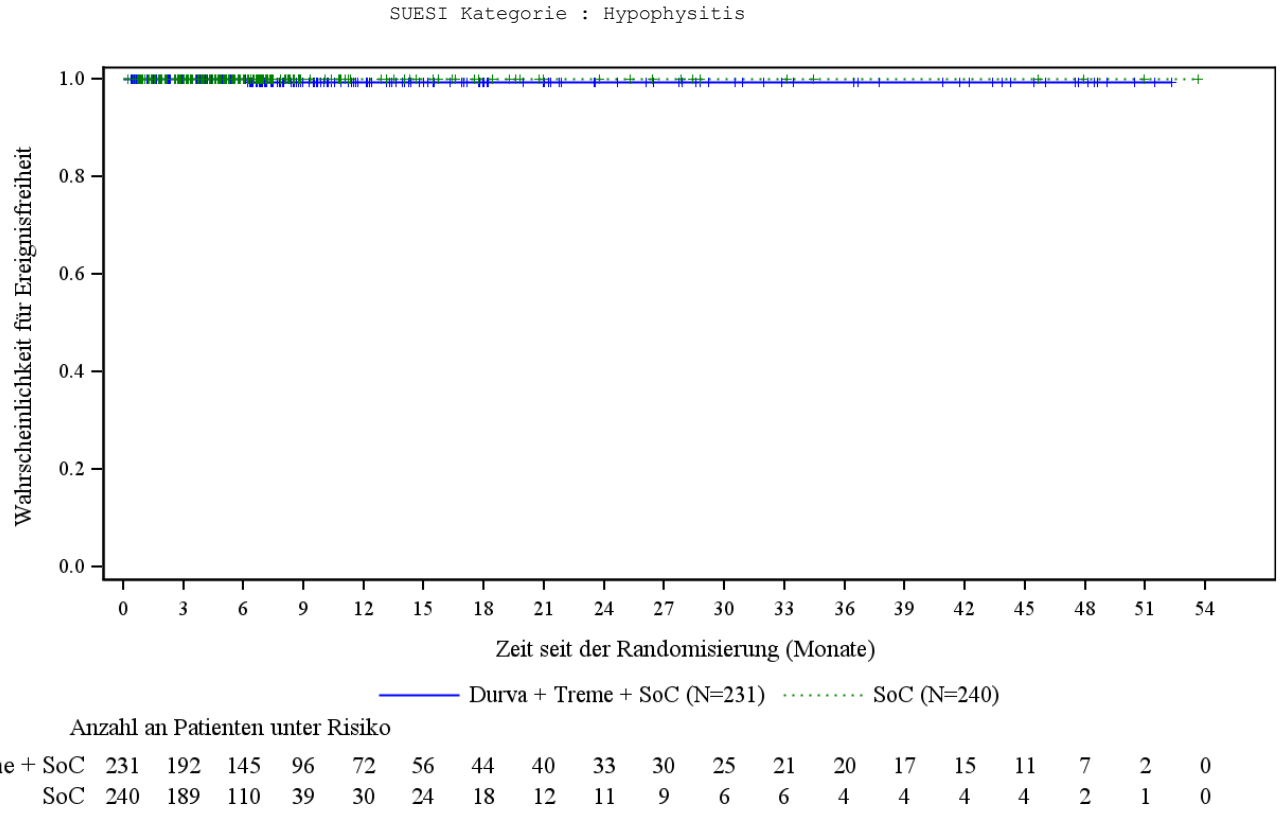
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
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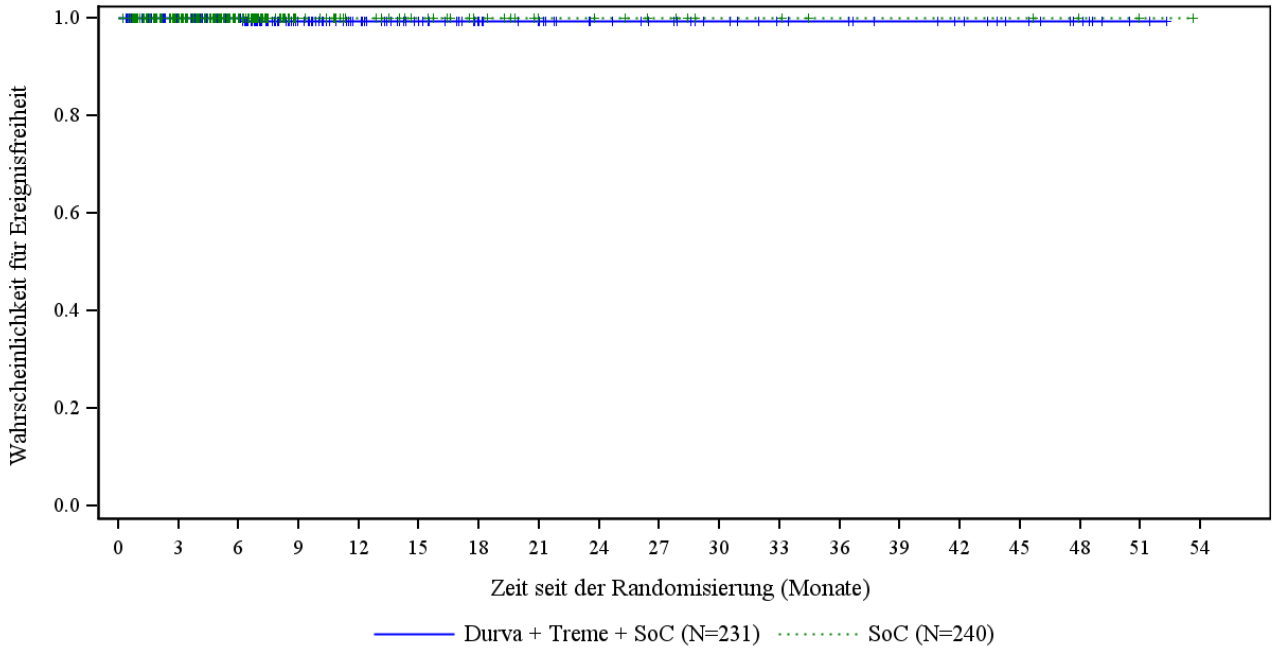
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Diabetes insipidus



Anzahl an Patienten unter Risiko

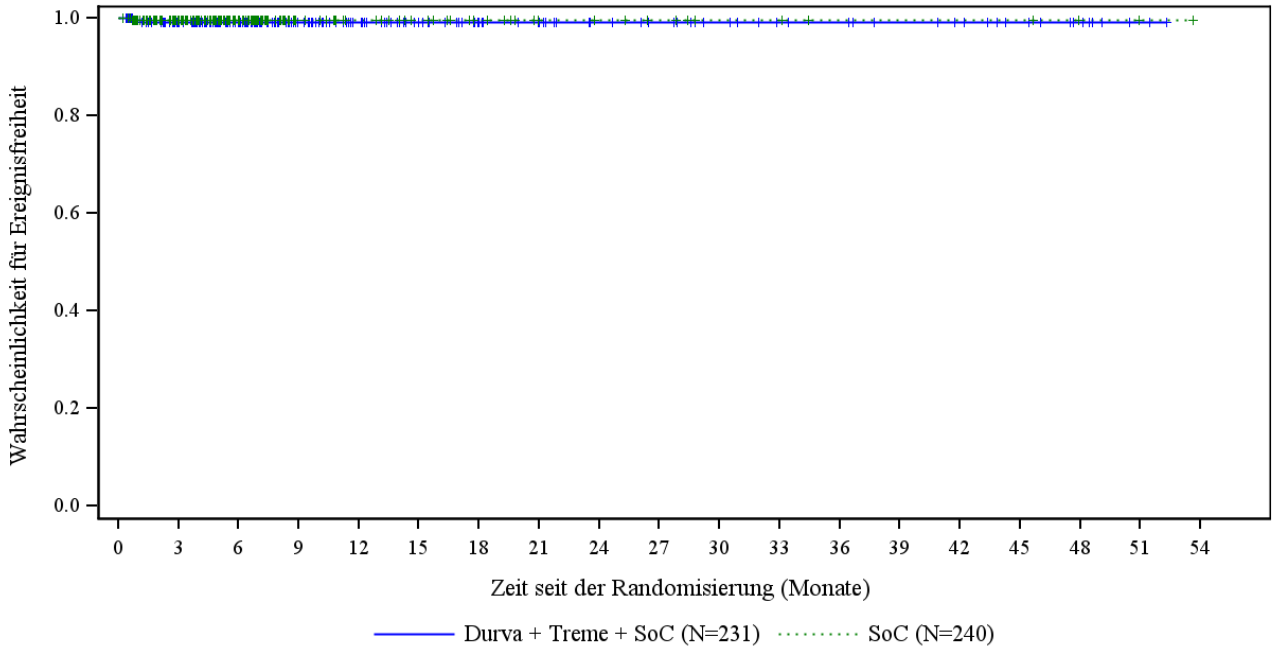
Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Kategorie : Infusions- und Überempfindlichkeitsreaktion



Anzahl an Patienten unter Risiko

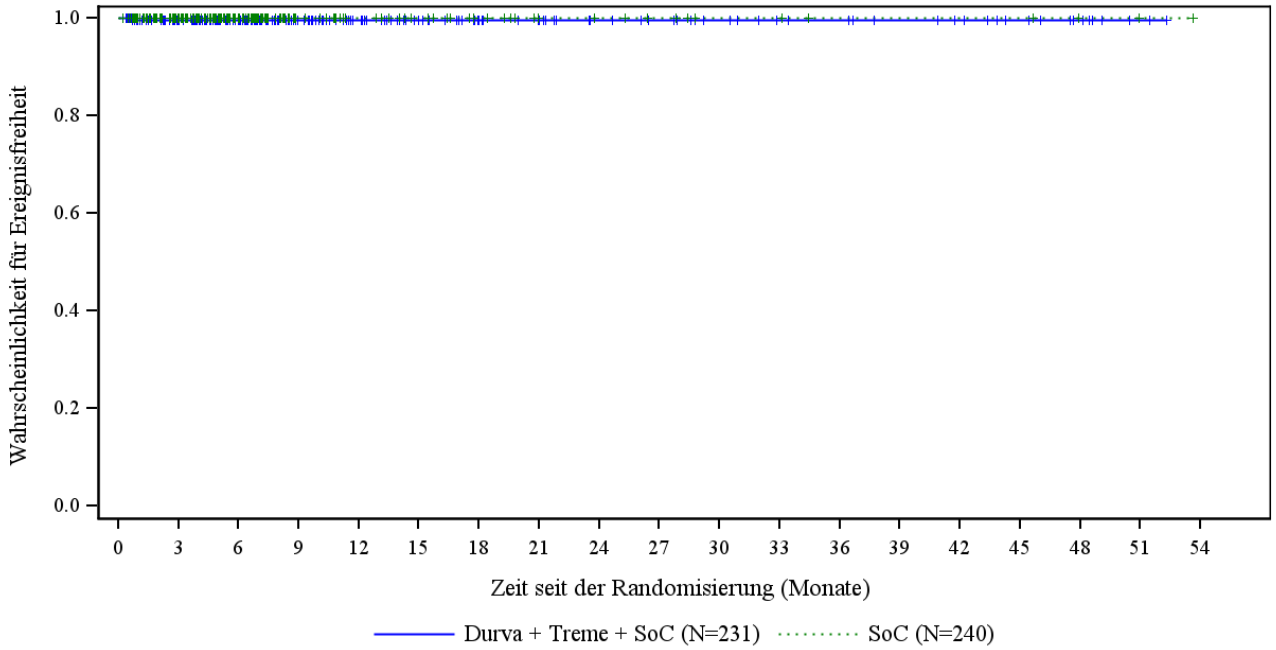
Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	188	109	38	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Sub-Kategorie : Reaktion im Zusammenhang mit einer Infusion



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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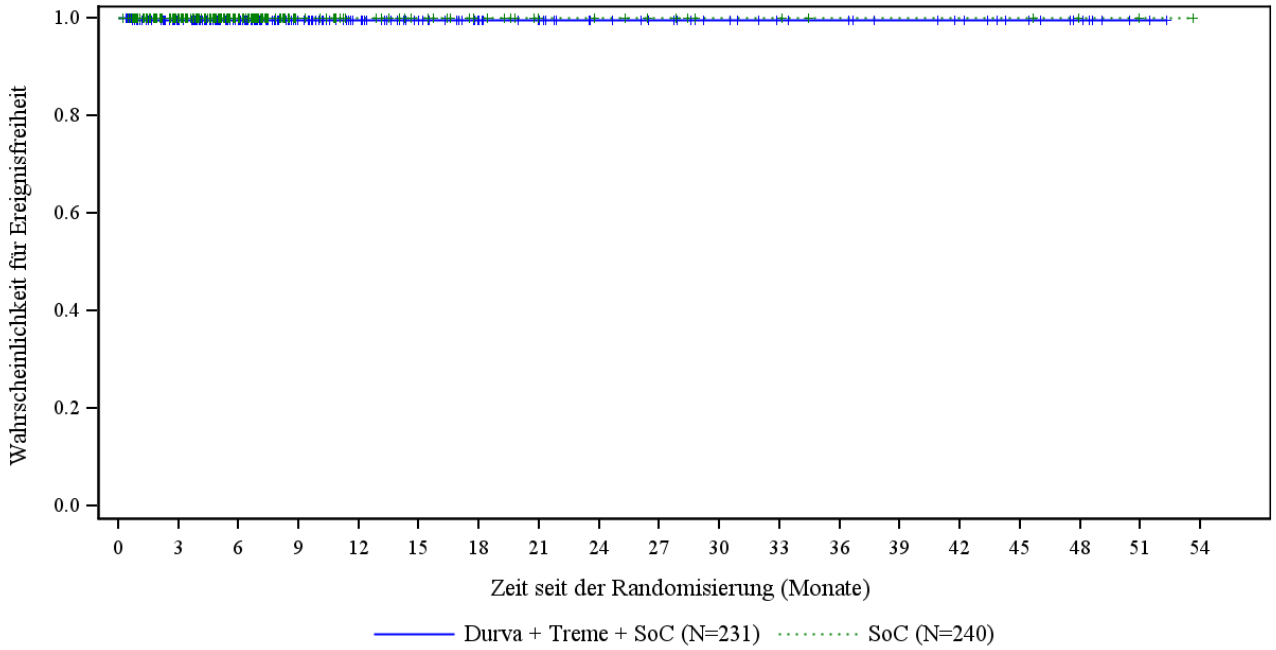
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Reaktion im Zusammenhang mit einer Infusion



Anzahl an Patienten unter Risiko

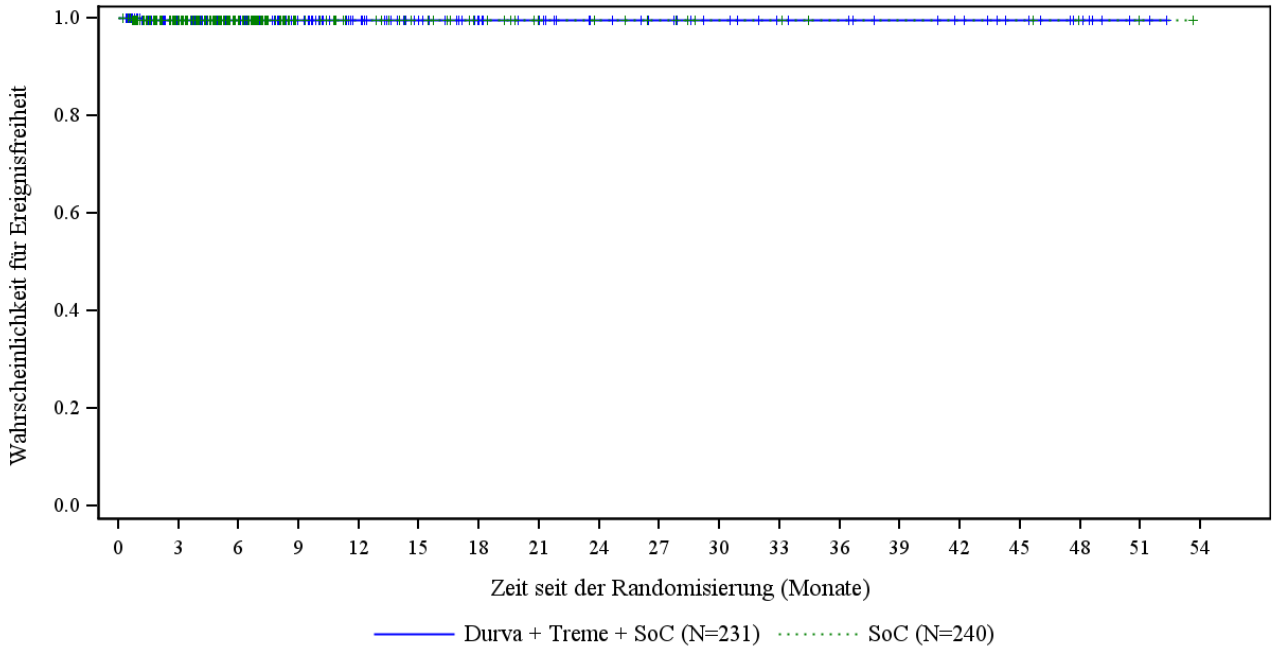
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Sub-Kategorie : Überempfindlichkeitsreaktion / Anaphylaktische Reaktion



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	188	109	38	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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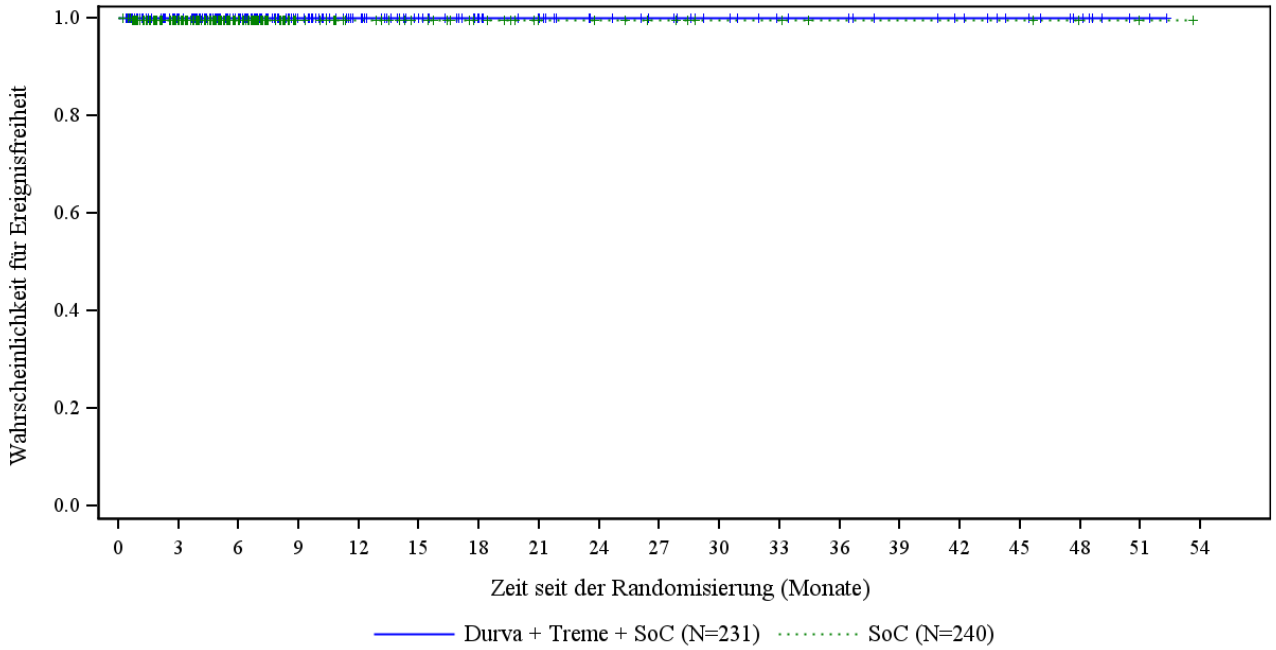
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Arzneimittelueberempfindlichkeit



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	188	109	38	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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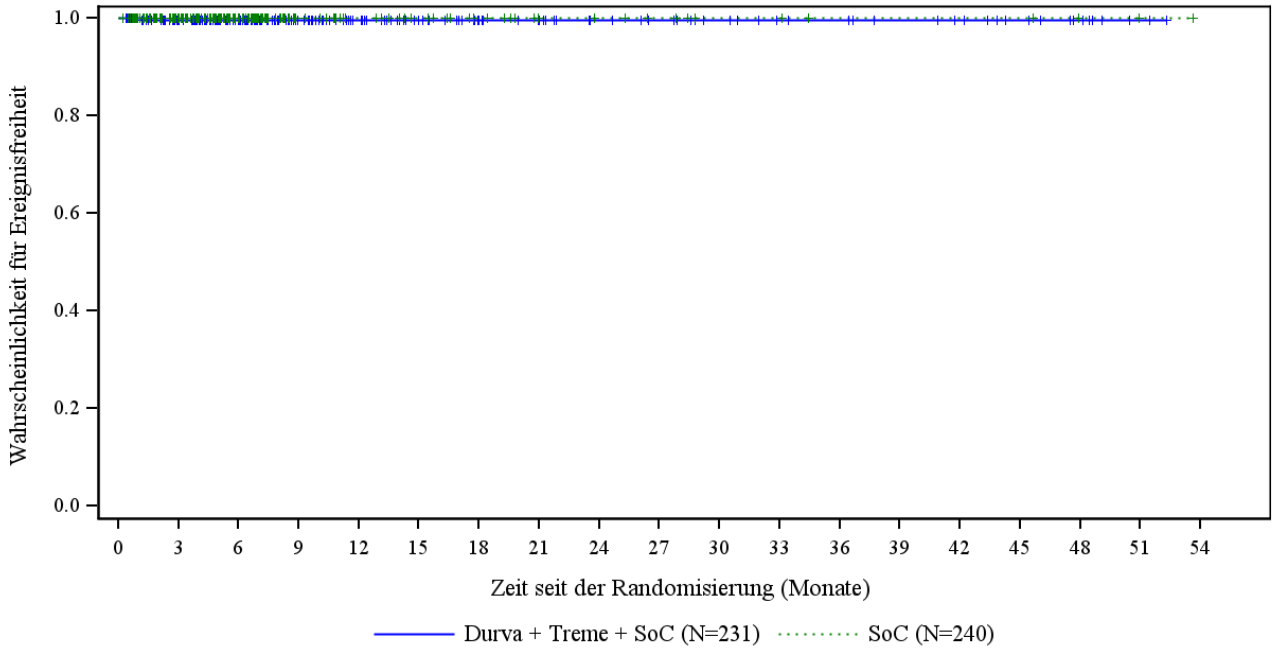
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Medikamentenausschlag



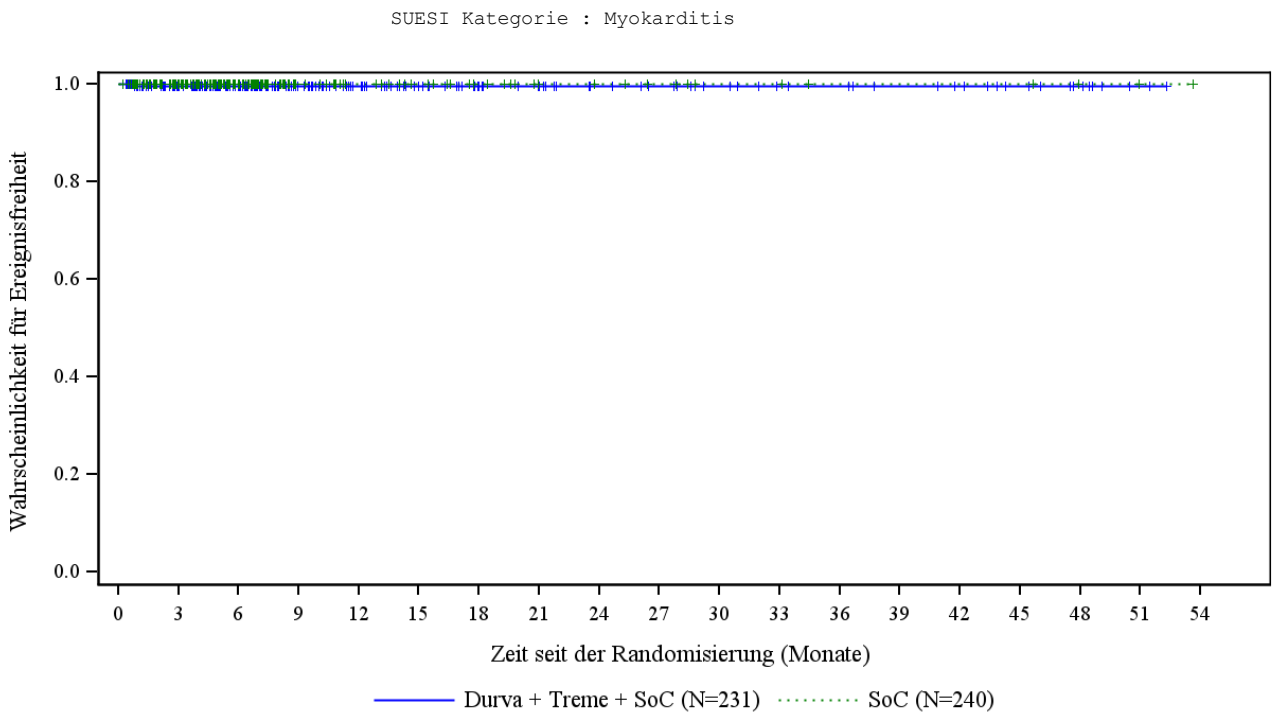
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	144	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

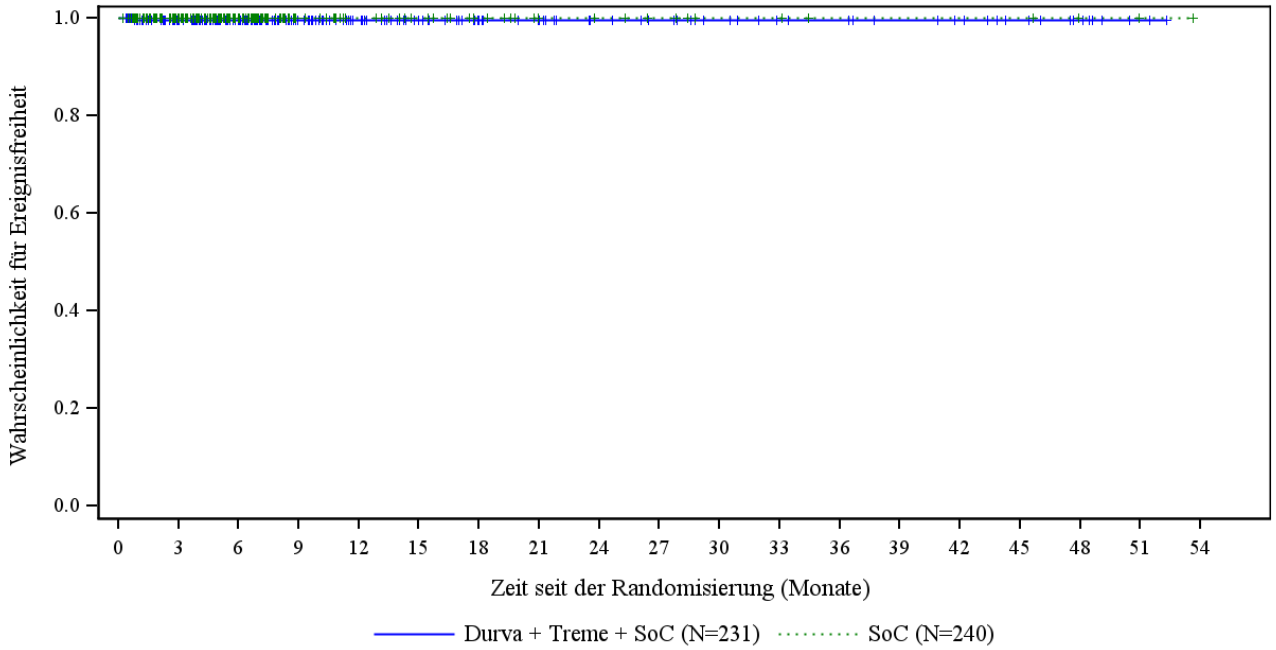
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Autoimmunmyokarditis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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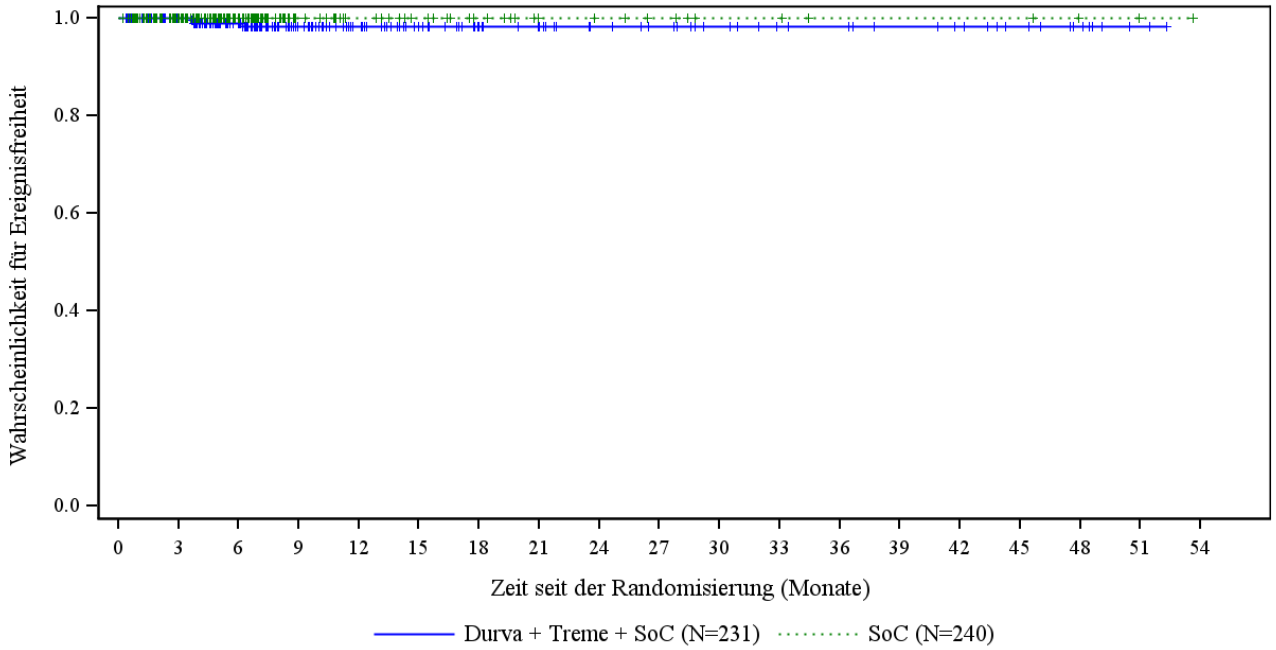
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI Kategorie : Nebenniereninsuffizienz



Anzahl an Patienten unter Risiko

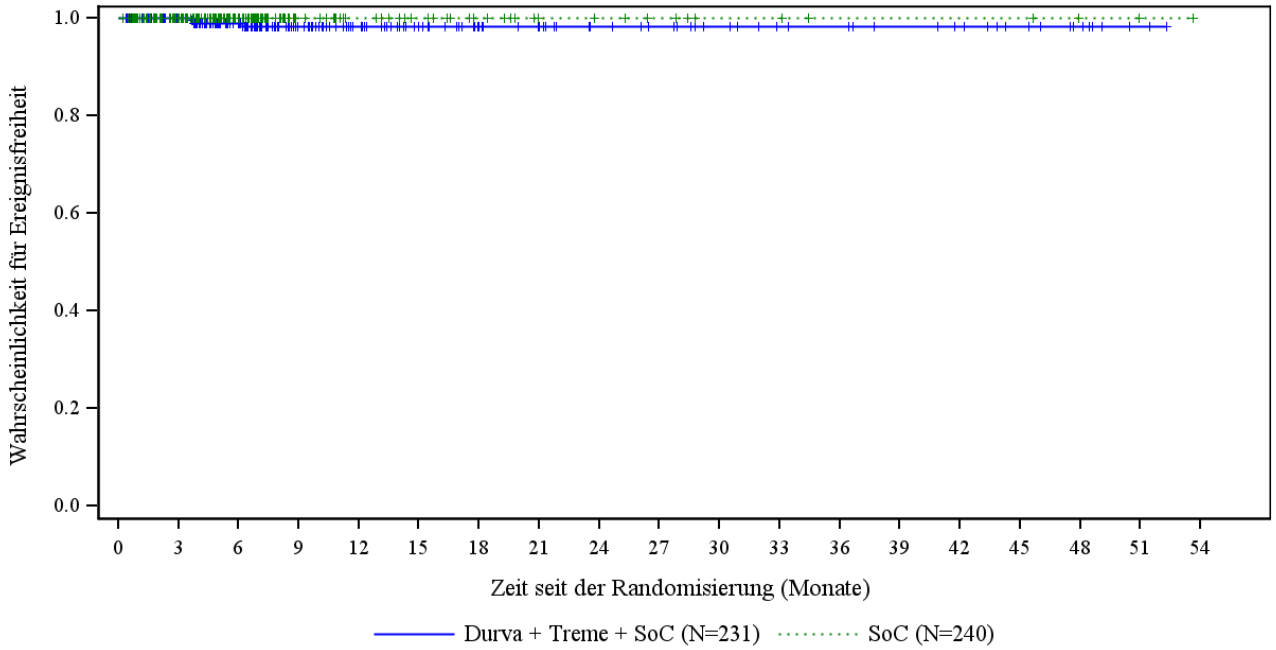
Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Nebenniereninsuffizienz



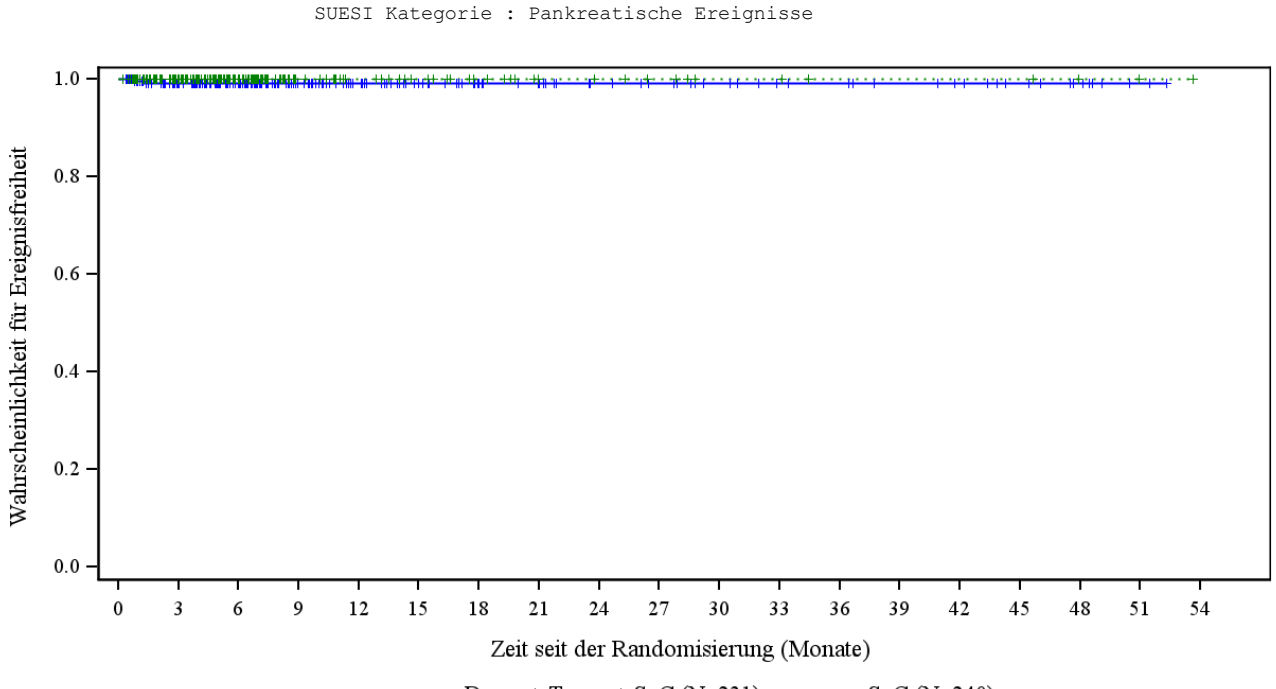
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	145	96	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

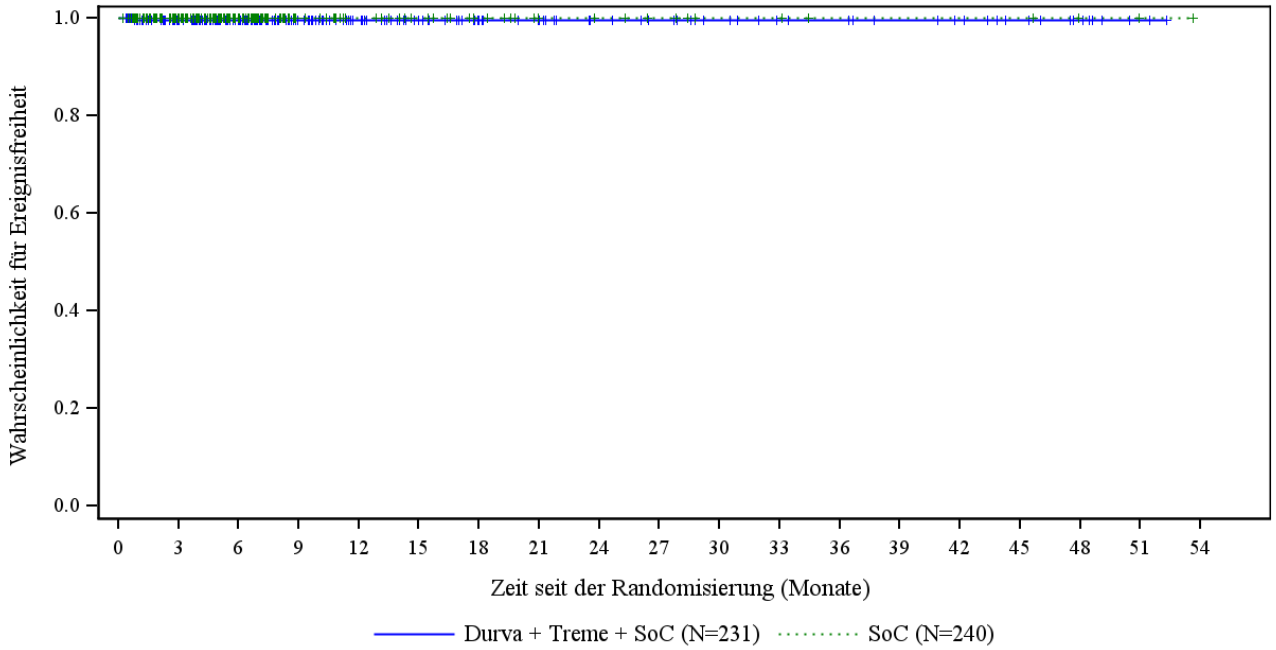
Durva + Treme + SoC	231	191	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Autoimmunpankreatitis



Anzahl an Patienten unter Risiko

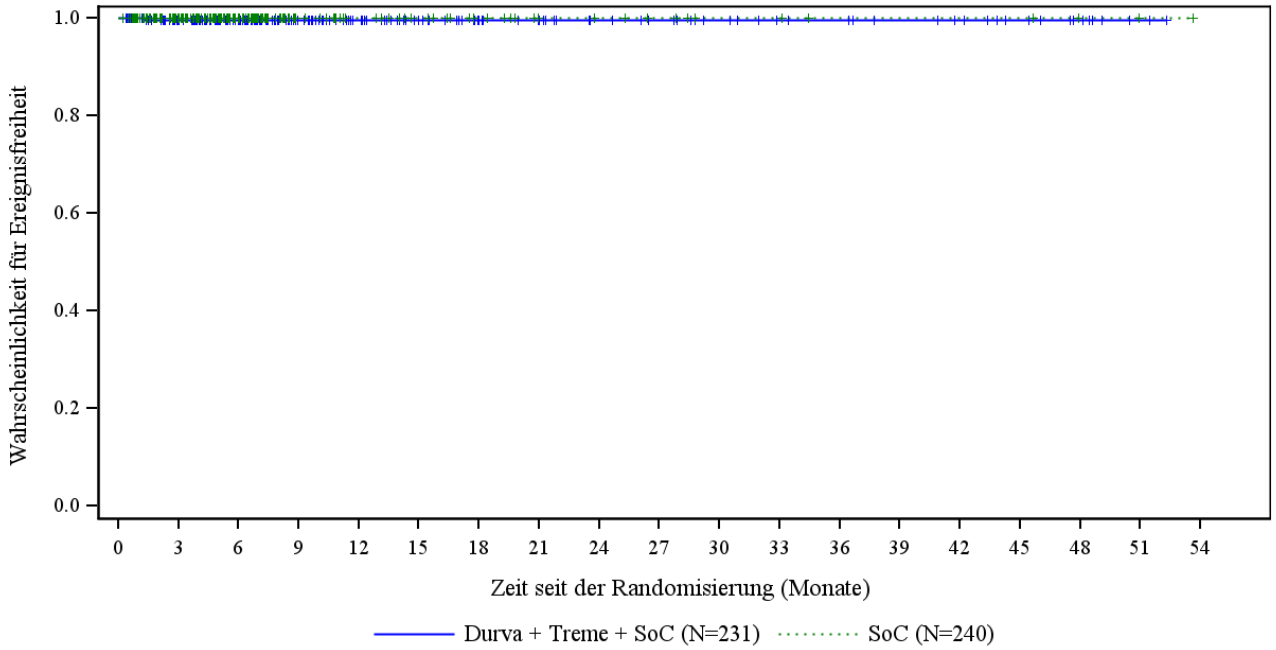
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Pankreatitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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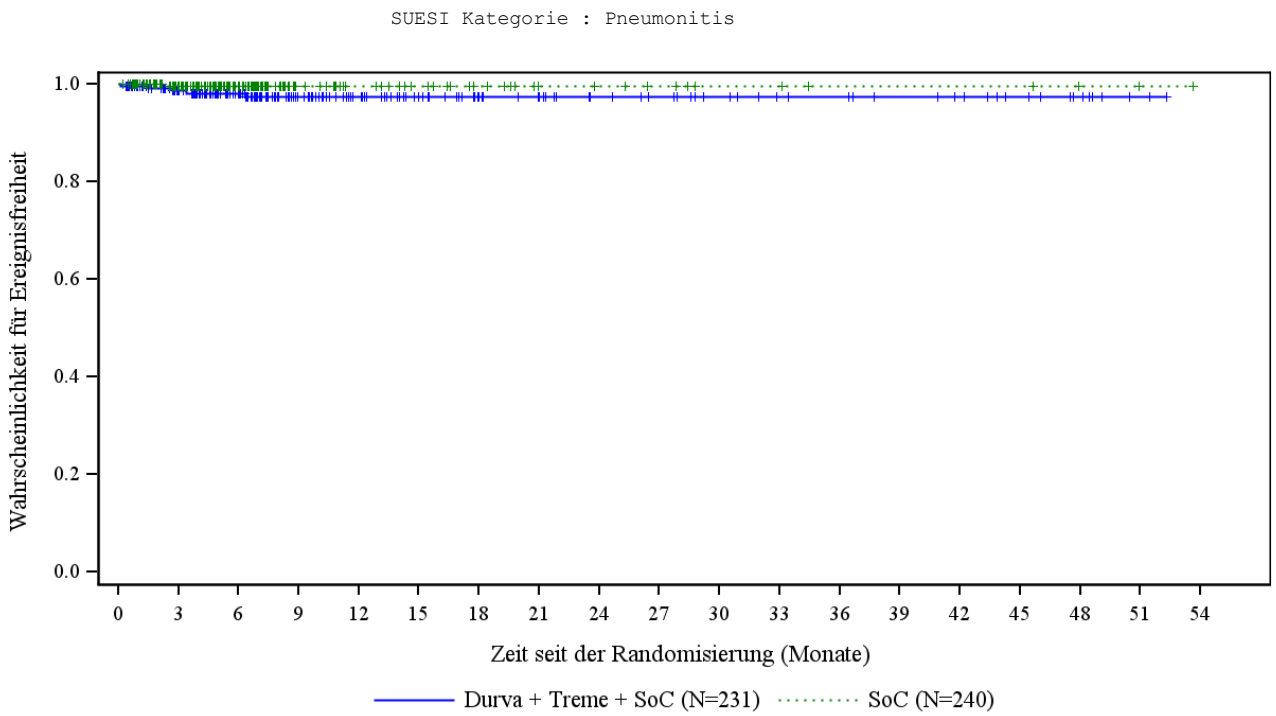
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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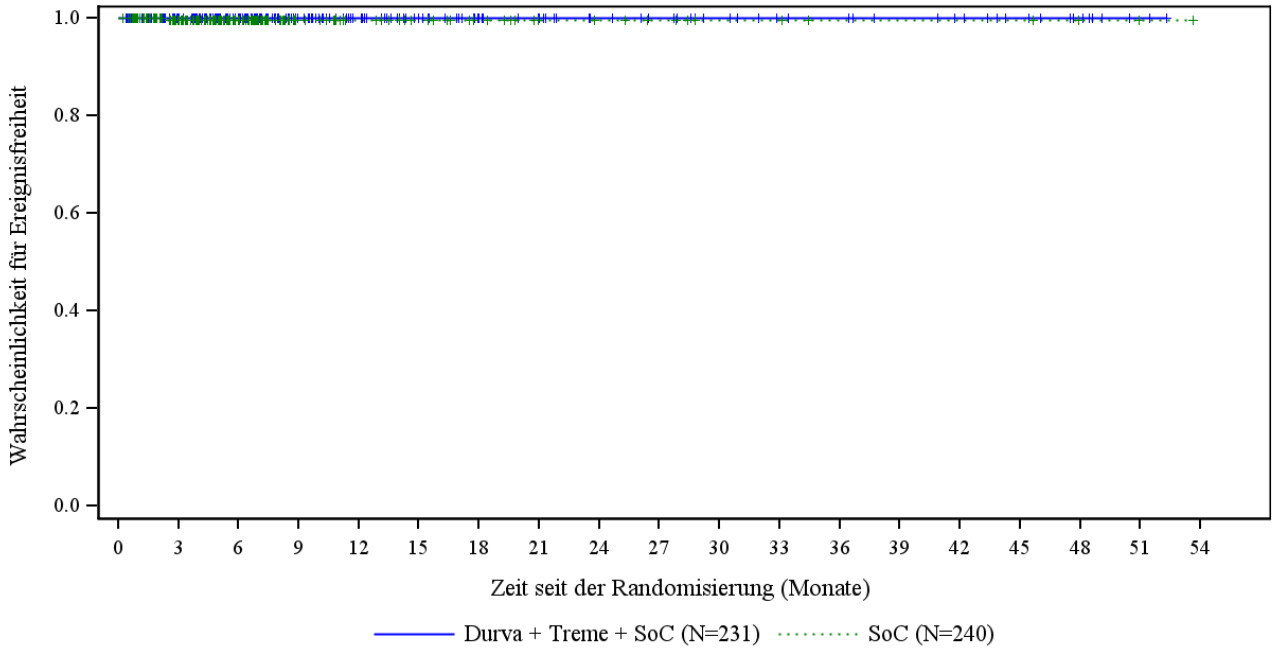
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Interstitielle Lungenerkrankung



Anzahl an Patienten unter Risiko

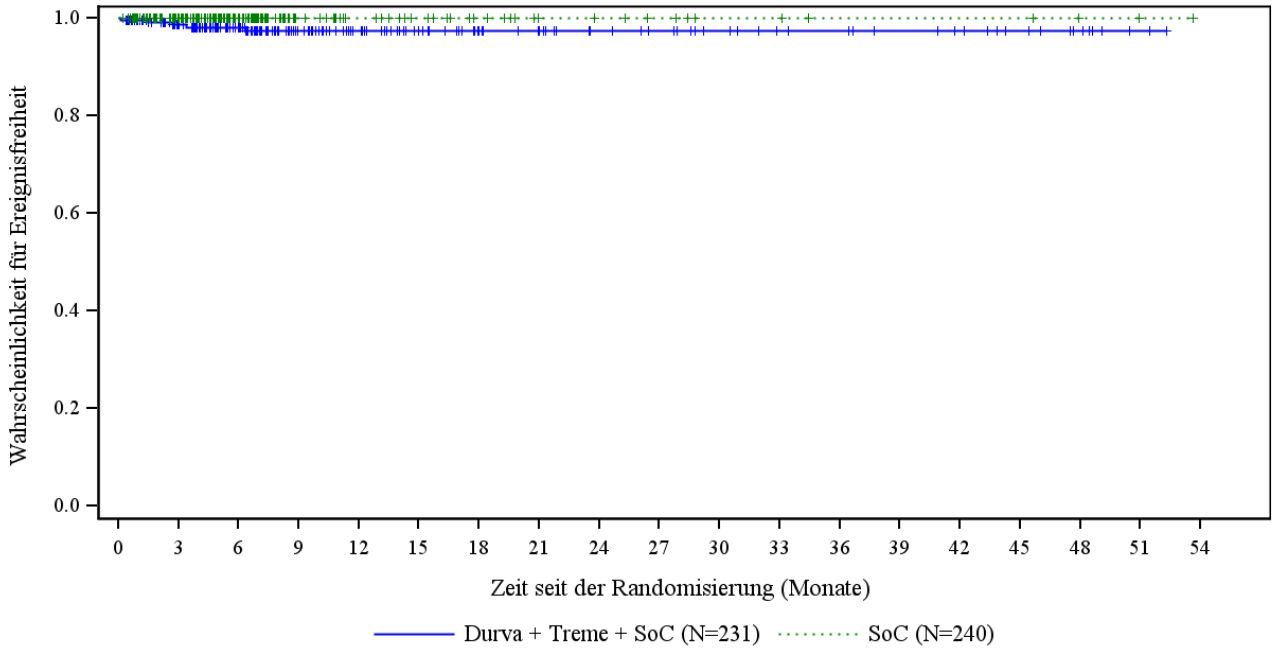
Durva + Treme + SoC	231	192	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	188	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Pneumonitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	189	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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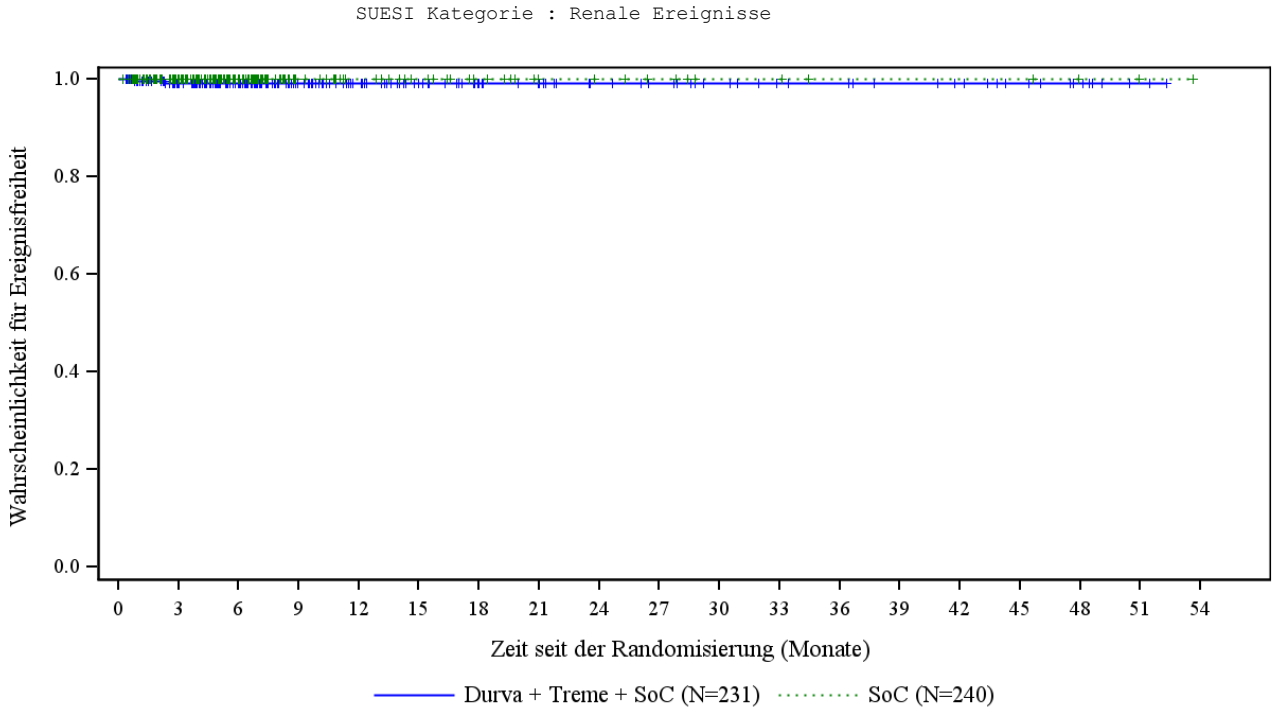
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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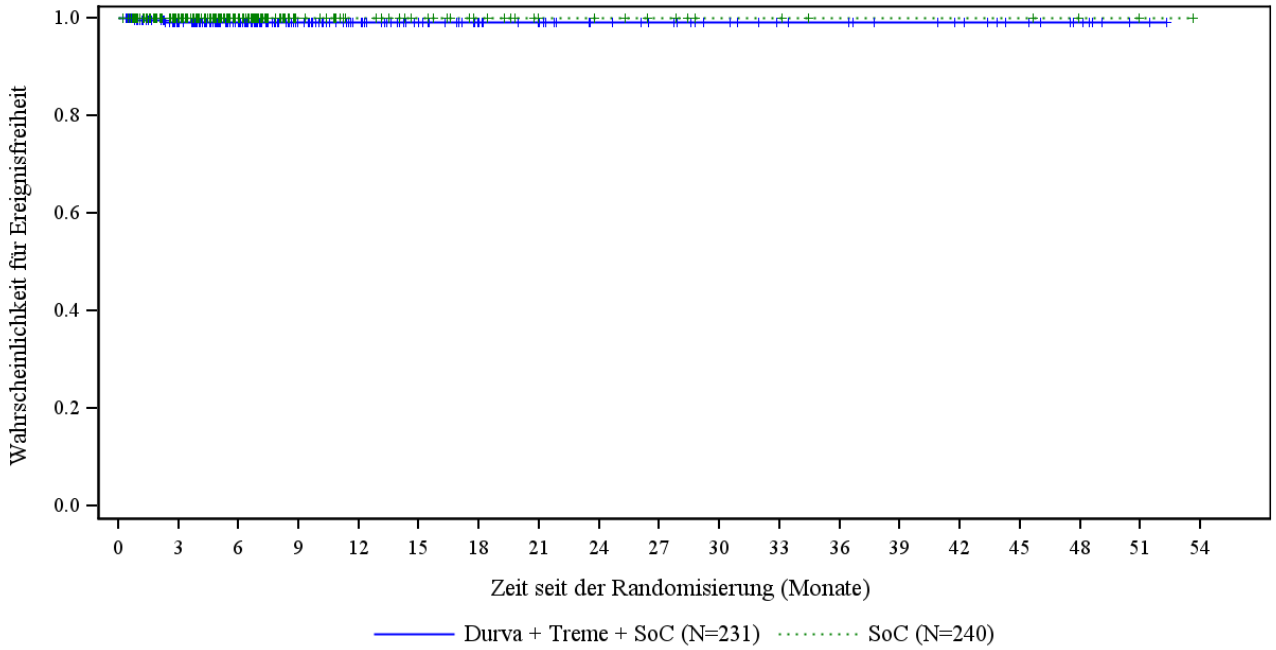
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Autoimmune Nephritis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	191	145	97	72	56	44	40	33	30	25	21	20	17	15	11	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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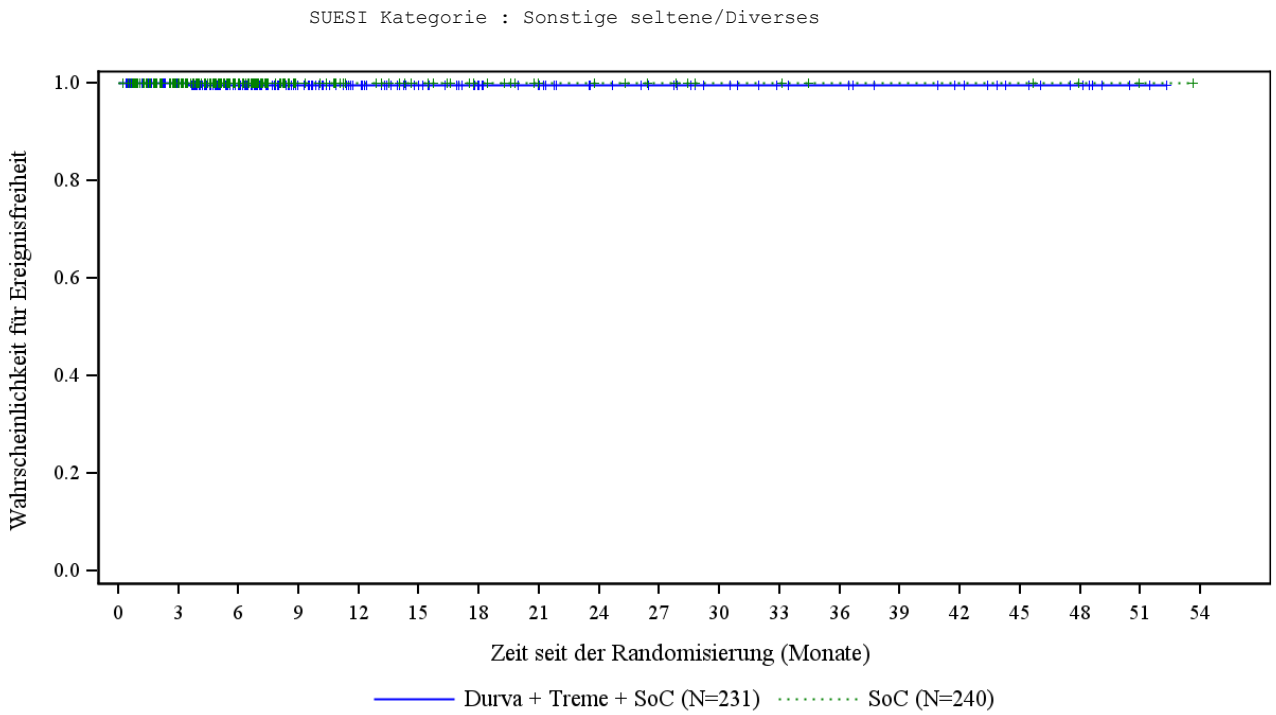
Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022



Anzahl an Patienten unter Risiko

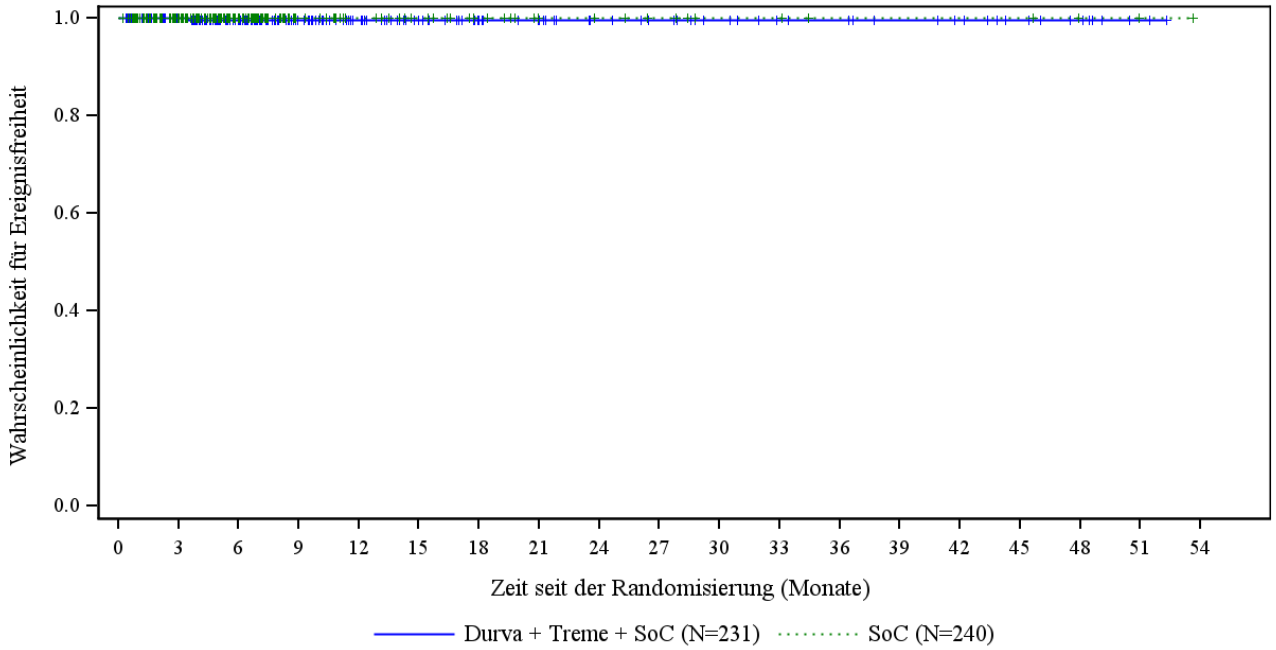
Durva + Treme + SoC	231	192	144	96	71	55	43	39	32	29	24	20	19	16	14	10	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae376g.sas Executed : 2022-11-22T133010

Figure 4.9.2.4 Kaplan-Meier of analyses of time to first occurrence of any serious adverse events of special interest by category/sub-category (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

SUESI PT : Enzephalitis



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	231	192	144	96	71	55	43	39	32	29	24	20	19	16	14	10	7	2	0
SoC	240	189	110	39	30	24	18	12	11	9	6	6	4	4	4	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (Cat, Sub-Cat, PT) categories.
Kaplan-Meier plots are only produced on Cat, Sub-Cat and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.+ indicates a censored observation.

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Anhang 4-G 1.3: Subgruppenanalysen

Anhang 4-G 1.3.1: Gesamtüberleben

Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	163 (83,6)	12,7 [9,5; 15,0]	179	167 (93,3)	10,6 [9,0; 12,6]	0,77	[0,62; 0,96]	0,0204
Weiblich	42	31 (73,8)	18,4 [10,4; 24,7]	61	50 (82,0)	16,0 [12,5; 24,2]	0,77	[0,49; 1,20]	0,2288
Interaktion p-Wert									0,9863
Alter									
<65 Jahre	130	102 (78,5)	14,0 [9,8; 17,8]	125	112 (89,6)	11,8 [10,5; 15,1]	0,78	[0,59; 1,02]	0,0862
>/= 65 Jahre	107	92 (86,0)	12,7 [8,9; 16,1]	115	105 (91,3)	12,0 [9,9; 15,3]	0,82	[0,62; 1,08]	0,1291
Interaktion p-Wert									0,7952

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	59 (88,1)	9,8 [6,5; 13,8]	83	70 (84,3)	18,3 [10,7; 24,6]	1,45	[1,03; 2,06]	0,0360
Nicht-Asiatisch	170	135 (79,4)	15,0 [11,6; 18,1]	157	147 (93,6)	10,9 [8,3; 12,6]	0,57	[0,45; 0,72]	<0,0001
Interaktion p-Wert									<0,0001
Performance status zu baseline									
0	82	61 (74,4)	17,1 [12,7; 24,1]	78	70 (89,7)	15,2 [11,0; 19,8]	0,73	[0,52; 1,03]	0,0751
1	155	133 (85,8)	11,6 [9,4; 14,6]	162	147 (90,7)	10,7 [8,6; 12,8]	0,83	[0,66; 1,05]	0,1256
Interaktion p-Wert									0,5459

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	102 (82,9)	15,6 [11,7; 18,6]	120	106 (88,3)	13,7 [11,2; 17,8]	0,85	[0,65; 1,12]	0,2330
Stadium IVB	112	92 (82,1)	10,0 [7,8; 14,1]	120	111 (92,5)	10,3 [6,8; 12,6]	0,77	[0,58; 1,02]	0,0938
Interaktion p-Wert									0,6094
Raucherstatus									
Aktiv	65	51 (78,5)	15,0 [9,5; 18,7]	49	46 (93,9)	10,5 [5,1; 13,4]	0,48	[0,32; 0,71]	0,0005
Ehemals	137	111 (81,0)	11,7 [8,9; 15,5]	133	119 (89,5)	12,2 [10,1; 15,6]	0,86	[0,66; 1,11]	0,3001
Nie	35	32 (91,4)	16,3 [10,0; 24,0]	58	52 (89,7)	14,2 [11,0; 20,1]	0,97	[0,62; 1,50]	0,9195
Interaktion p-Wert									0,0268

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef203g.sas Executed : 2022-10-31T155659

Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	114 (82,0)	14,0 [10,3; 17,1]	125	117 (93,6)	10,5 [7,0; 12,3]	0,61	[0,47; 0,79]	0,0002
Rest of the World	98	80 (81,6)	12,6 [9,0; 16,6]	115	100 (87,0)	16,2 [11,1; 20,1]	1,01	[0,75; 1,35]	0,9709
Interaktion p-Wert									0,0117

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	9 (75,0)	18,1 [9,7; NE]	12	12 (100)	12,1 [1,8; 22,8]	0,45	[0,18; 1,06]	0,0936
Pemetrexed-Doublette	142	114 (80,3)	16,3 [12,2; 21,0]	146	126 (86,3)	13,9 [11,0; 16,8]	0,80	[0,62; 1,04]	0,0707
Gemcitabin-Doublette	83	71 (85,5)	8,4 [7,1; 12,7]	82	79 (96,3)	10,1 [6,5; 11,4]	0,86	[0,62; 1,18]	0,3778
Interaktion p-Wert									0,3887

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	75 (85,2)	9,4 [7,2; 12,7]	90	87 (96,7)	10,3 [6,6; 11,4]	0,84	[0,62; 1,14]	0,3264
Nicht-Plattenepithelial	149	119 (79,9)	17,1 [12,6; 21,0]	150	130 (86,7)	13,9 [11,0; 17,8]	0,78	[0,61; 1,00]	0,0361
Interaktion p-Wert									0,7137
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	110 (88,0)	12,7 [9,9; 15,5]	130	119 (91,5)	11,0 [8,7; 12,7]	0,80	[0,61; 1,03]	0,0923
PD-L1 >/=1%	112	84 (75,0)	14,9 [9,4; 19,2]	110	98 (89,1)	15,2 [10,6; 18,3]	0,79	[0,59; 1,05]	0,1165
Interaktion p-Wert									0,9460

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	17 (73,9)	20,0 [3,8; 32,6]	34	30 (88,2)	14,5 [9,4; 24,2]	0,86	[0,47; 1,55]	0,5695
Nein	214	177 (82,7)	12,7 [9,9; 15,6]	206	187 (90,8)	11,4 [10,3; 13,7]	0,77	[0,63; 0,95]	0,0155
Interaktion p-Wert									0,7314

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef303g.sas Executed : 2022-11-21T152014

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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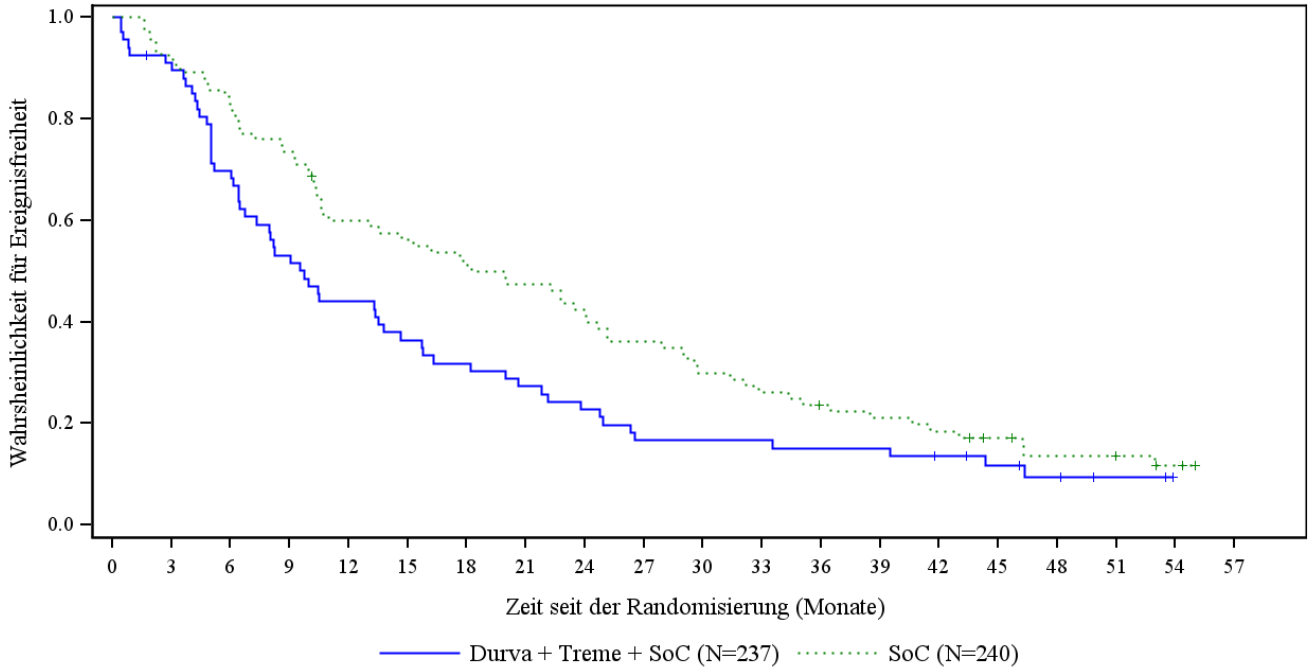
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Abstammung - Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	67	60	46	35	29	24	21	18	15	11	11	11	10	10	8	6	4	2	0	0
SoC	83	76	68	61	48	45	41	38	33	29	24	21	18	16	14	11	8	7	4	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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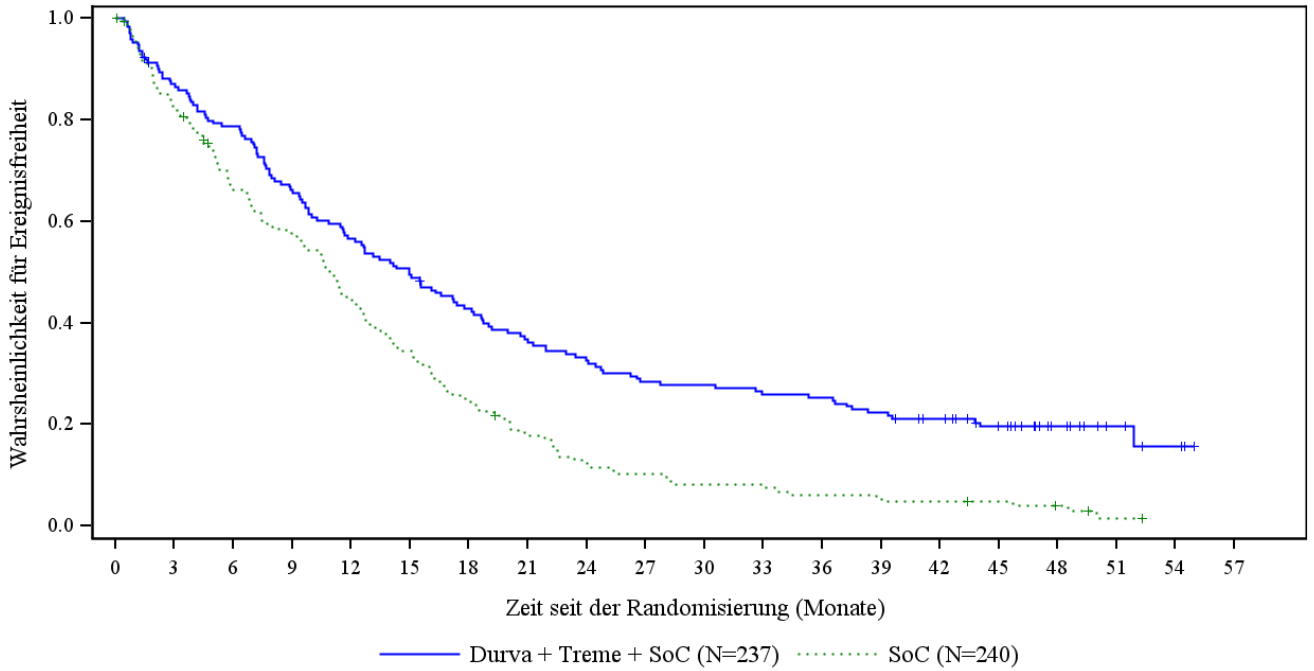
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Abstammung - Nicht-Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	170	146	132	111	95	83	71	61	54	47	46	43	42	37	32	24	14	6	3	0
SoC	157	127	100	86	68	52	38	26	18	15	12	12	9	8	7	6	4	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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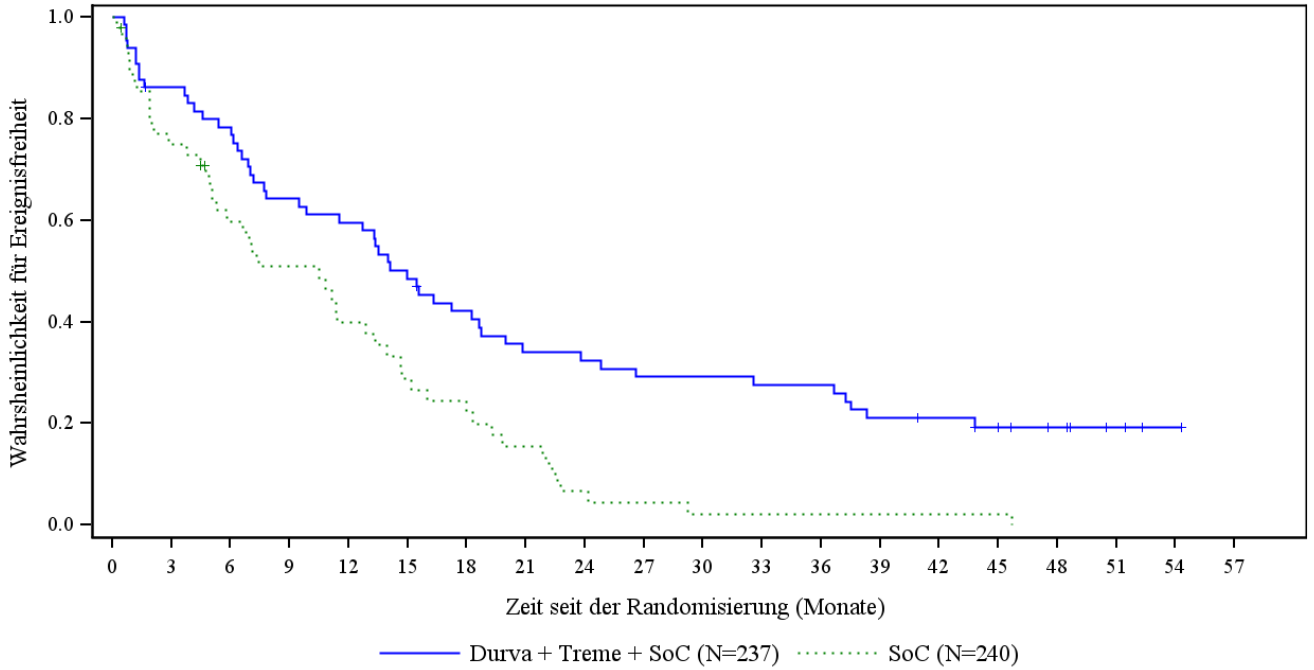
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Raucherstatus - Aktiv



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	65	55	50	41	38	31	26	21	20	18	18	17	17	13	12	9	6	3	1	0
SoC	49	36	27	23	18	13	11	7	3	2	1	1	1	1	1	1	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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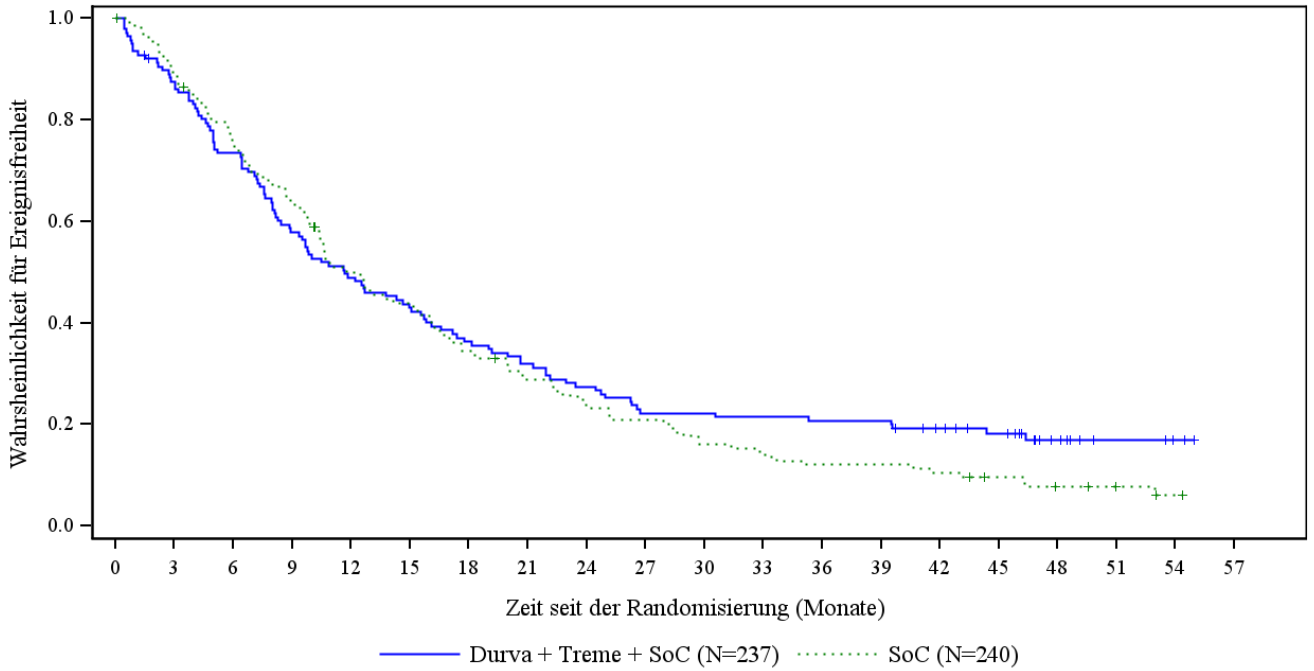
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Raucherstatus - Ehemals



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	137	118	99	78	66	58	49	43	37	30	30	29	28	28	23	18	9	4	2	0
SoC	133	117	98	83	64	56	44	36	29	26	20	18	15	15	13	10	7	5	2	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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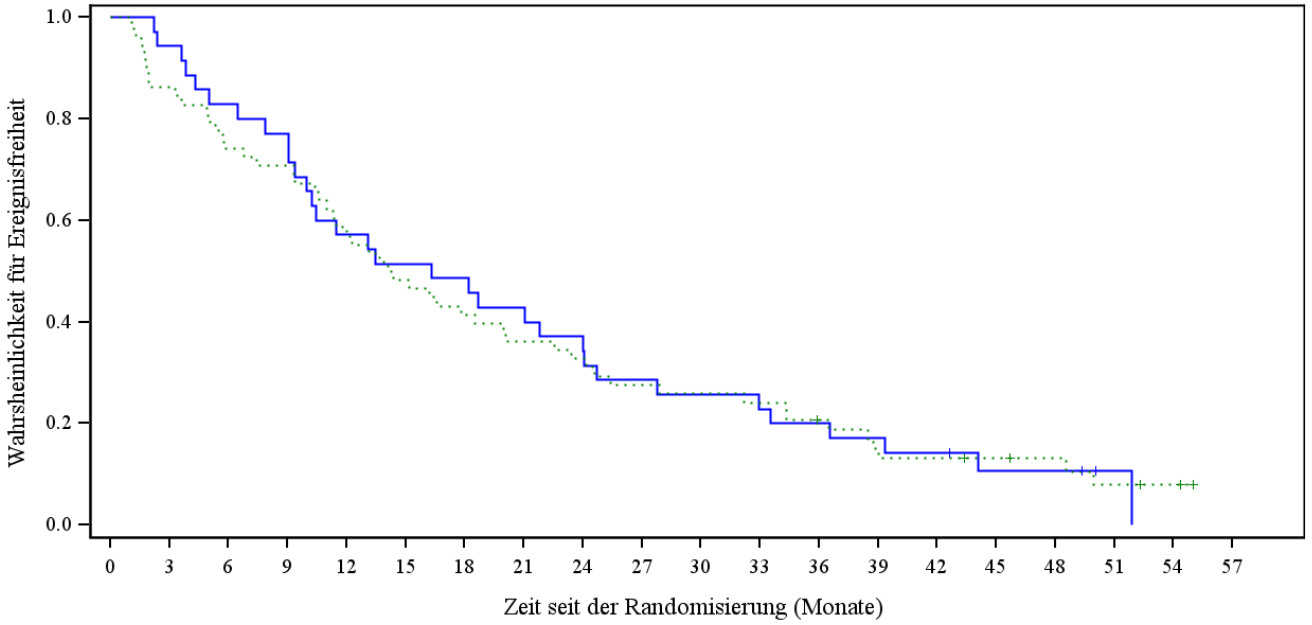
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Raucherstatus - Nie



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	35	33	29	27	20	18	17	15	12	10	9	8	7	6	5	3	3	1	0	0
SoC	58	50	43	41	34	28	24	21	19	16	15	14	11	8	7	6	5	3	2	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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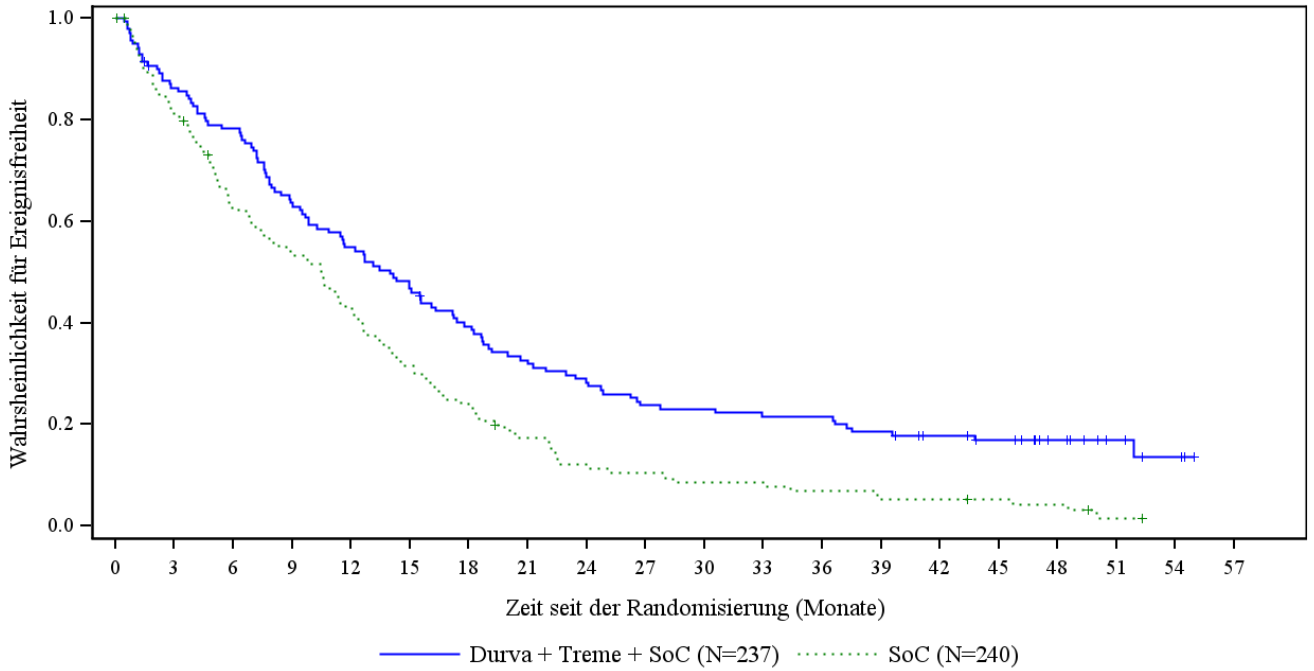
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Region - Europa und Nordamerika



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	139	118	107	87	75	64	53	44	38	32	31	29	29	25	21	18	12	6	3	0
SoC	125	100	75	64	52	38	29	20	13	12	10	10	8	7	6	5	4	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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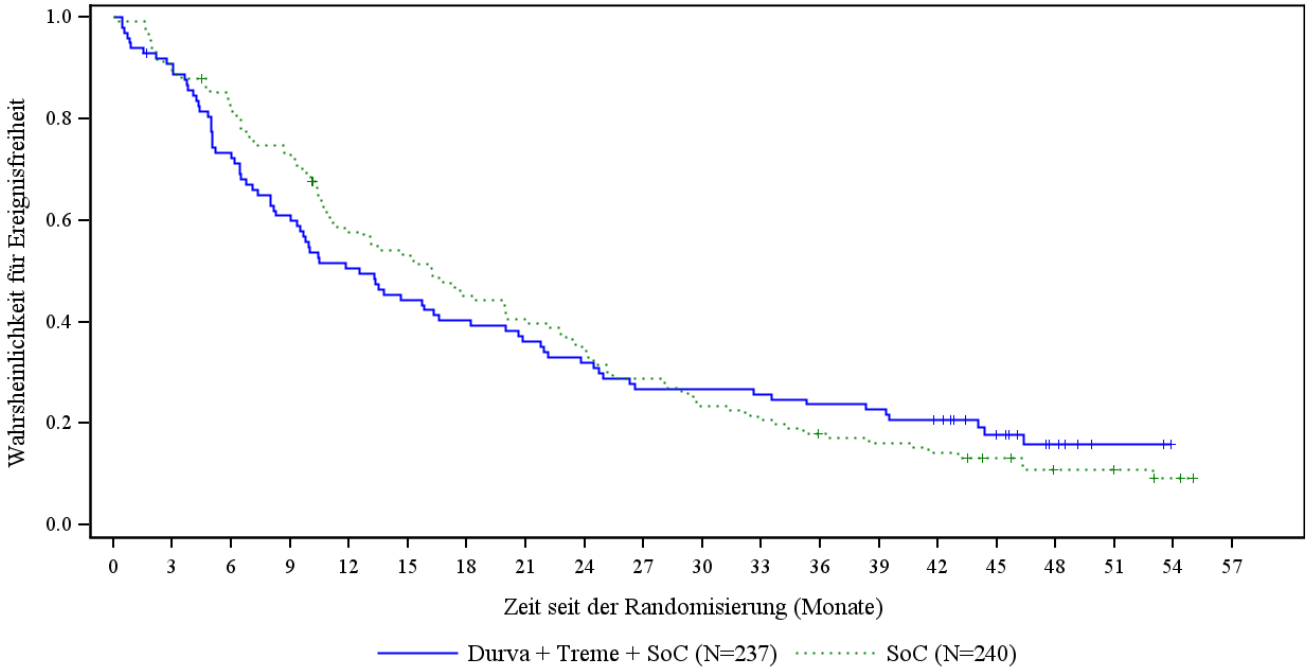
Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Region - Rest of the World



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	98	88	71	59	49	43	39	35	31	26	26	25	23	22	19	12	6	2	0	0
SoC	115	103	93	83	64	59	50	44	38	32	26	23	19	17	15	12	8	7	4	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1<50%)

Subgroup: Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Anhang 4-G 1.3.2: Symptomatik und Gesundheitszustand

Anhang 4-G 1.3.2.1: EORTC QLQ-C30 - Symptomskalen

Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	120 (61,5)	2,3 [1,4; 3,0]	179	110 (61,5)	2,1 [1,4; 2,2]	0,93	[0,72; 1,21]	0,6256
Weiblich	42	30 (71,4)	2,1 [1,4; 3,9]	61	40 (65,6)	2,1 [1,4; 8,3]	1,10	[0,68; 1,77]	0,7626
Interaktion p-Wert									0,5440
Alter									
<65 Jahre	130	80 (61,5)	2,2 [1,4; 3,3]	125	70 (56,0)	2,1 [1,4; 2,9]	1,07	[0,78; 1,48]	0,6667
>/= 65 Jahre	107	70 (65,4)	2,2 [1,4; 3,3]	115	80 (69,6)	1,6 [1,4; 2,2]	0,90	[0,65; 1,24]	0,5656
Interaktion p-Wert									0,4474

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	47 (70,1)	1,5 [1,2; 2,8]	83	62 (74,7)	2,1 [1,4; 2,4]	1,11	[0,76; 1,62]	0,5184
Nicht-Asiatisch	170	103 (60,6)	2,3 [1,5; 3,3]	157	88 (56,1)	1,8 [1,4; 2,6]	0,94	[0,70; 1,25]	0,6859
Interaktion p-Wert									0,4728
Performance status zu baseline									
0	82	54 (65,9)	1,4 [1,1; 2,4]	78	45 (57,7)	2,1 [1,4; 5,6]	1,26	[0,85; 1,88]	0,2587
1	155	96 (61,9)	2,8 [2,1; 3,6]	162	105 (64,8)	2,1 [1,4; 2,2]	0,86	[0,65; 1,14]	0,2677
Interaktion p-Wert									0,1237

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	81 (65,9)	2,2 [1,4; 3,0]	120	78 (65,0)	1,8 [1,4; 2,2]	0,95	[0,70; 1,30]	0,7967
Stadium IVB	112	68 (60,7)	2,1 [1,4; 3,3]	120	72 (60,0)	2,1 [1,4; 2,6]	1,00	[0,72; 1,40]	0,8934
Interaktion p-Wert									0,8195
Raucherstatus									
Aktiv	65	36 (55,4)	2,3 [1,2; 5,6]	49	27 (55,1)	1,9 [1,4; 2,9]	0,76	[0,46; 1,27]	0,3625
Ehemals	137	87 (63,5)	2,2 [1,4; 3,3]	133	86 (64,7)	2,1 [1,4; 3,4]	0,98	[0,72; 1,32]	0,9073
Nie	35	27 (77,1)	2,1 [1,4; 2,8]	58	37 (63,8)	2,1 [1,4; 5,0]	1,26	[0,76; 2,06]	0,4061
Interaktion p-Wert									0,3806

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	80 (57,6)	2,4 [1,5; 3,8]	125	70 (56,0)	1,9 [1,4; 2,9]	0,93	[0,68; 1,29]	0,7314
Rest of the World	98	70 (71,4)	1,9 [1,4; 2,8]	115	80 (69,6)	2,1 [1,4; 2,2]	1,06	[0,76; 1,46]	0,7504
Interaktion p-Wert									0,5863

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	7 (58,3)	3,6 [0,8; NE]	12	6 (50,0)	2,1 [0,8; NE]	0,79	[0,26; 2,45]	0,6719
Pemetrexed-Doublette	142	97 (68,3)	2,2 [1,5; 3,3]	146	98 (67,1)	2,1 [1,4; 2,4]	0,98	[0,74; 1,29]	0,8680
Gemcitabin-Doublette	83	46 (55,4)	1,9 [1,0; 2,9]	82	46 (56,1)	2,1 [1,4; 3,7]	1,02	[0,68; 1,54]	0,7918
Interaktion p-Wert									0,9082

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	49 (55,7)	2,1 [1,0; 3,3]	90	51 (56,7)	2,1 [1,4; 3,4]	1,00	[0,68; 1,49]	0,8412
Nicht-Plattenepithelial	149	101 (67,8)	2,3 [1,5; 3,3]	150	99 (66,0)	2,1 [1,4; 2,4]	0,96	[0,73; 1,27]	0,7781
Interaktion p-Wert									0,8675
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	74 (59,2)	3,3 [2,1; 4,7]	130	79 (60,8)	2,1 [1,4; 2,2]	0,83	[0,60; 1,14]	0,2694
PD-L1 >/=1%	112	76 (67,9)	1,4 [0,9; 2,2]	110	71 (64,5)	2,1 [1,4; 3,4]	1,18	[0,85; 1,63]	0,2956
Interaktion p-Wert									0,1290

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	15 (65,2)	0,8 [0,8; 2,2]	34	25 (73,5)	1,4 [0,8; 2,9]	1,19	[0,61; 2,23]	0,6684
Nein	214	135 (63,1)	2,3 [1,5; 3,0]	206	125 (60,7)	2,1 [1,5; 2,3]	0,98	[0,77; 1,25]	0,8654
Interaktion p-Wert									0,5766

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Figure 5.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 fatigue (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs353g.sas Executed : 2022-11-21T215823

Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	94 (48,2)	4,7 [2,8; 9,4]	179	79 (44,1)	5,3 [2,3; NE]	1,03	[0,76; 1,39]	0,8091
Weiblich	42	26 (61,9)	2,9 [1,0; 8,3]	61	33 (54,1)	2,9 [1,4; 6,2]	1,05	[0,62; 1,75]	0,8427
Interaktion p-Wert									0,9553
Alter									
<65 Jahre	130	63 (48,5)	5,6 [2,8; 15,5]	125	61 (48,8)	2,4 [1,5; 32,6]	0,83	[0,58; 1,19]	0,3813
>/= 65 Jahre	107	57 (53,3)	3,7 [1,7; 7,9]	115	51 (44,3)	5,8 [2,8; NE]	1,26	[0,86; 1,84]	0,2094
Interaktion p-Wert									0,1179

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	30 (44,8)	9,2 [2,1; NE]	83	42 (50,6)	5,3 [2,2; NE]	0,94	[0,58; 1,49]	0,8445
Nicht-Asiatisch	170	90 (52,9)	3,9 [1,7; 8,3]	157	70 (44,6)	2,8 [1,7; 6,7]	1,01	[0,74; 1,39]	0,9921
Interaktion p-Wert									0,8015
Performance status zu baseline									
0	82	47 (57,3)	3,7 [1,8; 8,3]	78	40 (51,3)	2,4 [1,4; NE]	0,95	[0,62; 1,46]	0,7960
1	155	73 (47,1)	4,7 [2,1; 12,3]	162	72 (44,4)	5,8 [2,8; NE]	1,04	[0,75; 1,45]	0,8018
Interaktion p-Wert									0,7314

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	63 (51,2)	5,6 [2,4; 15,9]	120	55 (45,8)	4,7 [2,8; NE]	1,06	[0,74; 1,53]	0,8921
Stadium IVB	112	56 (50,0)	3,7 [1,6; 8,8]	120	57 (47,5)	2,1 [1,4; NE]	0,98	[0,67; 1,41]	0,9859
Interaktion p-Wert									0,7525
Raucherstatus									
Aktiv	65	31 (47,7)	7,9 [2,5; 26,7]	49	16 (32,7)	5,3 [1,9; NE]	1,11	[0,61; 2,08]	0,7841
Ehemals	137	69 (50,4)	3,9 [1,8; 9,3]	133	67 (50,4)	3,8 [2,1; 6,7]	1,03	[0,74; 1,45]	0,8441
Nie	35	20 (57,1)	3,0 [1,4; 20,3]	58	29 (50,0)	2,2 [1,4; NE]	1,00	[0,55; 1,75]	0,9524
Interaktion p-Wert									0,9670

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs263g.sas Executed : 2022-10-17T211123

Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	68 (48,9)	4,2 [1,5; 9,8]	125	55 (44,0)	3,7 [2,0; NE]	1,00	[0,70; 1,43]	0,9396
Rest of the World	98	52 (53,1)	3,9 [2,1; 9,4]	115	57 (49,6)	3,8 [2,1; NE]	1,03	[0,71; 1,50]	0,8384
Interaktion p-Wert									0,8926

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	3 (25,0)	NE [2,8; NE]	12	5 (41,7)	NE [0,8; NE]	0,30	[0,06; 1,24]	0,0901
Pemetrexed-Doublette	142	81 (57,0)	3,7 [1,5; 8,8]	146	74 (50,7)	2,9 [2,1; 6,5]	1,11	[0,81; 1,53]	0,5176
Gemcitabin-Doublette	83	36 (43,4)	4,7 [1,6; NE]	82	33 (40,2)	5,3 [2,1; NE]	1,01	[0,63; 1,63]	0,8050
Interaktion p-Wert									0,2213

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	37 (42,0)	5,7 [2,1; NE]	90	37 (41,1)	5,3 [2,1; NE]	0,94	[0,59; 1,48]	0,9175
Nicht-Plattenepithelial	149	83 (55,7)	3,7 [1,7; 9,3]	150	75 (50,0)	2,9 [2,2; 6,5]	1,06	[0,77; 1,45]	0,7639
Interaktion p-Wert									0,6703
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	51 (40,8)	9,2 [4,2; NE]	130	59 (45,4)	3,7 [2,1; NE]	0,77	[0,53; 1,13]	0,2189
PD-L1 >/=1%	112	69 (61,6)	2,5 [1,5; 3,7]	110	53 (48,2)	3,8 [2,0; 32,6]	1,32	[0,92; 1,89]	0,1388
Interaktion p-Wert									0,0446

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	10 (43,5)	4,7 [0,8; NE]	34	19 (55,9)	1,4 [0,8; NE]	0,74	[0,33; 1,55]	0,4513
Nein	214	110 (51,4)	4,2 [2,8; 9,2]	206	93 (45,1)	4,9 [2,8; 32,6]	1,07	[0,81; 1,42]	0,6881
Interaktion p-Wert									0,3670

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs263g.sas Executed : 2022-10-17T211123

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

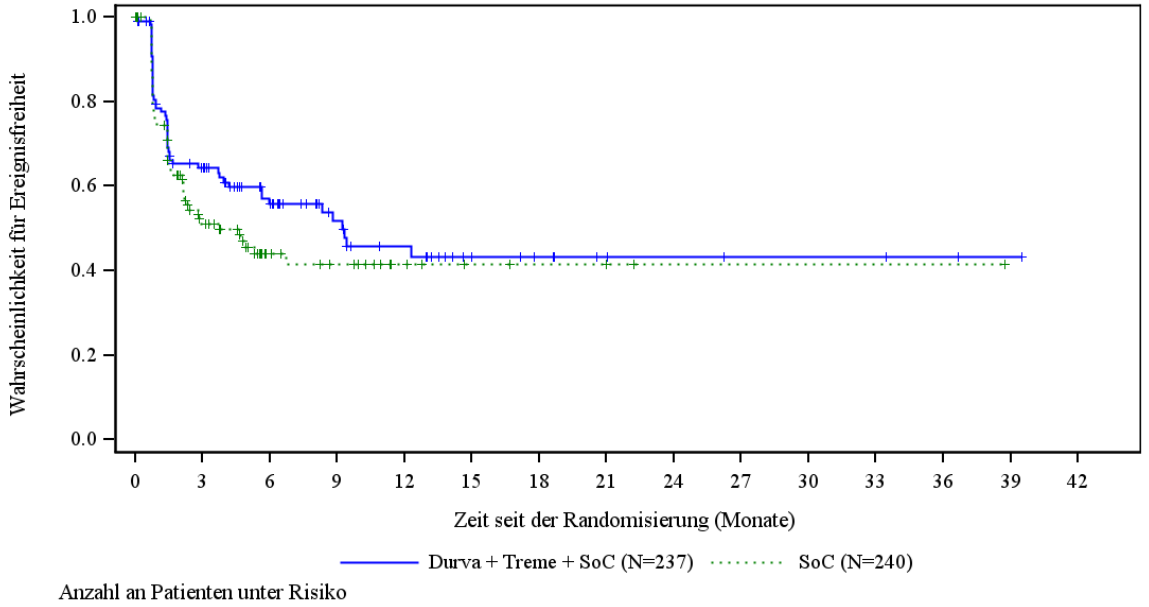
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%



Anzahl an Patienten unter Risiko

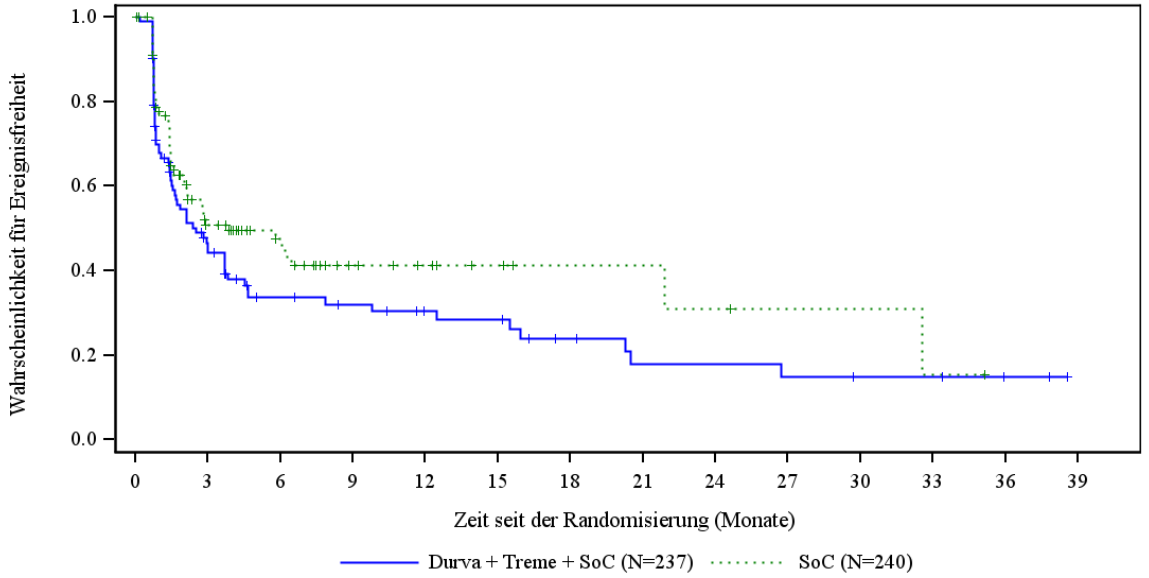
Durva + Treme + SoC	125	64	41	26	19	10	8	5	4	3	3	3	2	1	0
SoC	130	45	20	15	8	4	3	2	1	1	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	112	37	22	19	15	14	9	6	6	5	4	4	2	0
SoC	110	40	23	12	9	6	4	4	3	2	2	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Figure 5.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 nausea and vomiting (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs363g.sas Executed : 2022-11-21T220132

Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	90 (46,2)	6,5 [4,7; 10,1]	179	89 (49,7)	4,6 [3,4; 6,2]	0,77	[0,57; 1,03]	0,0849
Weiblich	42	24 (57,1)	3,9 [1,4; 9,5]	61	36 (59,0)	4,7 [2,1; 8,3]	0,97	[0,57; 1,62]	0,7911
Interaktion p-Wert									0,4486
Alter									
<65 Jahre	130	62 (47,7)	7,1 [4,6; 14,3]	125	59 (47,2)	5,6 [3,7; 7,7]	0,78	[0,55; 1,12]	0,1950
>/= 65 Jahre	107	52 (48,6)	5,1 [3,8; 7,6]	115	66 (57,4)	3,9 [2,8; 5,6]	0,84	[0,58; 1,21]	0,3633
Interaktion p-Wert									0,7838

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs273g.sas Executed : 2022-10-17T211533

Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	33 (49,3)	5,6 [3,7; 6,8]	83	53 (63,9)	3,9 [2,9; 5,6]	0,81	[0,52; 1,24]	0,3146
Nicht-Asiatisch	170	81 (47,6)	7,6 [4,3; 10,4]	157	72 (45,9)	5,4 [3,3; 8,3]	0,80	[0,58; 1,11]	0,1498
Interaktion p-Wert									0,9939
Performance status zu baseline									
0	82	46 (56,1)	4,8 [2,5; 9,0]	78	40 (51,3)	4,6 [3,5; 7,7]	1,05	[0,69; 1,62]	0,8882
1	155	68 (43,9)	7,1 [4,7; 14,3]	162	85 (52,5)	4,6 [2,8; 7,4]	0,68	[0,49; 0,94]	0,0235
Interaktion p-Wert									0,1089

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs273g.sas Executed : 2022-10-17T211533

Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	60 (48,8)	7,6 [4,7; 10,4]	120	57 (47,5)	5,4 [3,7; 8,5]	0,87	[0,61; 1,26]	0,4659
Stadium IVB	112	54 (48,2)	5,1 [3,3; 7,1]	120	68 (56,7)	3,9 [2,4; 6,5]	0,76	[0,53; 1,09]	0,1384
Interaktion p-Wert									0,5941
Raucherstatus									
Aktiv	65	28 (43,1)	6,1 [4,2; NE]	49	21 (42,9)	3,9 [2,3; 8,3]	0,65	[0,37; 1,16]	0,1738
Ehemals	137	64 (46,7)	5,8 [4,6; 10,1]	133	70 (52,6)	5,6 [3,7; 8,3]	0,84	[0,59; 1,17]	0,2981
Nie	35	22 (62,9)	3,3 [1,4; 14,3]	58	34 (58,6)	3,7 [2,0; 7,5]	0,98	[0,56; 1,66]	0,9146
Interaktion p-Wert									0,5894

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs273g.sas Executed : 2022-10-17T211533

Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	61 (43,9)	7,7 [4,6; 14,4]	125	56 (44,8)	5,4 [3,0; 8,3]	0,78	[0,54; 1,13]	0,1705
Rest of the World	98	53 (54,1)	5,6 [3,7; 7,1]	115	69 (60,0)	3,9 [2,9; 5,6]	0,84	[0,58; 1,20]	0,3355
Interaktion p-Wert									0,7870

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs273g.sas Executed : 2022-10-17T211533

Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	2 (16,7)	NE [3,7; NE]	12	5 (41,7)	3,7 [0,8; NE]	0,17	[0,02; 0,80]	0,0905
Pemetrexed-Doublette	142	76 (53,5)	5,8 [4,0; 9,2]	146	86 (58,9)	4,6 [3,3; 6,2]	0,81	[0,59; 1,10]	0,1889
Gemcitabin-Doublette	83	36 (43,4)	4,7 [3,7; 9,3]	82	34 (41,5)	5,6 [2,8; NE]	0,94	[0,59; 1,51]	0,7777
Interaktion p-Wert									0,1455

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	37 (42,0)	5,1 [3,7; 9,3]	90	38 (42,2)	4,6 [2,8; 8,5]	0,87	[0,55; 1,36]	0,4701
Nicht-Plattenepithelial	149	77 (51,7)	6,5 [4,6; 10,1]	150	87 (58,0)	4,6 [3,3; 6,5]	0,77	[0,56; 1,04]	0,0989
Interaktion p-Wert									0,6683
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	63 (50,4)	5,1 [3,8; 9,2]	130	74 (56,9)	3,9 [2,8; 5,6]	0,77	[0,55; 1,07]	0,1173
PD-L1 >/=1%	112	51 (45,5)	6,8 [4,7; 14,1]	110	51 (46,4)	5,6 [3,7; 13,6]	0,84	[0,57; 1,25]	0,5058
Interaktion p-Wert									0,7171

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	2,1 [0,8; NE]	34	23 (67,6)	3,5 [1,1; 7,7]	0,82	[0,39; 1,61]	0,4722
Nein	214	102 (47,7)	6,5 [4,7; 9,3]	206	102 (49,5)	4,7 [3,7; 6,5]	0,82	[0,62; 1,08]	0,1542
Interaktion p-Wert									0,9863

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs373g.sas Executed : 2022-11-21T220417

Figure 5.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 pain (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	93 (47,7)	6,8 [3,8; 11,2]	179	75 (41,9)	6,7 [3,7; 16,6]	1,01	[0,74; 1,37]	0,9050
Weiblich	42	14 (33,3)	32,5 [6,5; NE]	61	27 (44,3)	9,3 [2,9; NE]	0,61	[0,31; 1,15]	0,0987
Interaktion p-Wert									0,1694
Alter									
<65 Jahre	130	59 (45,4)	9,4 [4,7; 24,5]	125	51 (40,8)	6,5 [2,8; NE]	0,91	[0,63; 1,34]	0,6892
>/= 65 Jahre	107	48 (44,9)	6,5 [3,8; 15,0]	115	51 (44,3)	6,7 [3,7; 10,3]	0,96	[0,65; 1,43]	0,8626
Interaktion p-Wert									0,8530

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	35 (52,2)	2,9 [2,2; 20,3]	83	39 (47,0)	8,5 [4,6; 11,1]	1,34	[0,85; 2,12]	0,1994
Nicht-Asiatisch	170	72 (42,4)	9,4 [6,8; 24,5]	157	63 (40,1)	6,5 [2,8; NE]	0,79	[0,56; 1,11]	0,1834
Interaktion p-Wert									0,0659
Performance status zu baseline									
0	82	41 (50,0)	6,8 [2,9; 24,5]	78	35 (44,9)	3,7 [2,1; NE]	0,90	[0,57; 1,43]	0,6829
1	155	66 (42,6)	8,5 [4,7; 20,3]	162	67 (41,4)	8,5 [5,6; 11,1]	0,94	[0,67; 1,33]	0,7007
Interaktion p-Wert									0,8794

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	55 (44,7)	9,0 [4,7; 20,3]	120	52 (43,3)	6,7 [2,9; NE]	0,90	[0,61; 1,31]	0,5467
Stadium IVB	112	52 (46,4)	6,8 [2,8; 11,2]	120	50 (41,7)	9,3 [3,5; 16,6]	1,00	[0,68; 1,48]	0,9958
Interaktion p-Wert									0,6976
Raucherstatus									
Aktiv	65	24 (36,9)	11,5 [8,3; NE]	49	20 (40,8)	2,9 [1,6; NE]	0,55	[0,30; 1,01]	0,0552
Ehemals	137	69 (50,4)	4,7 [2,8; 8,1]	133	57 (42,9)	8,5 [4,6; 16,6]	1,22	[0,86; 1,73]	0,2643
Nie	35	14 (40,0)	20,3 [4,7; NE]	58	25 (43,1)	6,5 [2,8; NE]	0,70	[0,35; 1,33]	0,2946
Interaktion p-Wert									0,0507

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	56 (40,3)	11,2 [6,8; 24,5]	125	53 (42,4)	4,0 [2,5; NE]	0,73	[0,50; 1,06]	0,1260
Rest of the World	98	51 (52,0)	5,4 [2,8; 9,4]	115	49 (42,6)	9,3 [6,2; 16,6]	1,23	[0,83; 1,82]	0,3013
Interaktion p-Wert									0,0594

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	2,8 [0,8; NE]	12	4 (33,3)	NE [0,8; NE]	1,13	[0,32; 4,42]	0,5276
Pemetrexed-Doublette	142	66 (46,5)	8,5 [6,5; 20,3]	146	68 (46,6)	6,5 [2,9; 10,4]	0,86	[0,61; 1,21]	0,3884
Gemcitabin-Doublette	83	35 (42,2)	5,4 [2,9; 24,5]	82	30 (36,6)	7,7 [3,7; NE]	1,08	[0,66; 1,77]	0,7035
Interaktion p-Wert									0,7228

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	38 (43,2)	5,4 [2,8; 14,4]	90	33 (36,7)	6,2 [3,7; NE]	1,11	[0,69; 1,78]	0,6036
Nicht-Plattenepithelial	149	69 (46,3)	8,5 [6,5; 20,3]	150	69 (46,0)	6,7 [2,9; 11,1]	0,86	[0,61; 1,20]	0,3916
Interaktion p-Wert									0,3861
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	62 (49,6)	6,8 [2,8; 11,3]	130	55 (42,3)	6,7 [2,8; NE]	1,05	[0,73; 1,52]	0,6726
PD-L1 >/=1%	112	45 (40,2)	11,2 [5,3; 32,5]	110	47 (42,7)	6,5 [4,6; 10,4]	0,81	[0,53; 1,22]	0,2348
Interaktion p-Wert									0,3449

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	10 (43,5)	4,7 [1,4; NE]	34	14 (41,2)	9,3 [2,1; NE]	1,17	[0,50; 2,61]	0,7189
Nein	214	97 (45,3)	8,5 [5,2; 15,0]	206	88 (42,7)	6,5 [3,9; 11,1]	0,91	[0,68; 1,22]	0,5334
Interaktion p-Wert									0,5716

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Figure 5.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 dyspnoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs383g.sas Executed : 2022-11-21T220826

Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	90 (46,2)	7,5 [4,0; 9,4]	179	80 (44,7)	6,5 [3,0; 12,9]	0,91	[0,67; 1,23]	0,5526
Weiblich	42	20 (47,6)	9,0 [3,7; 23,3]	61	25 (41,0)	12,7 [3,3; NE]	1,12	[0,61; 2,01]	0,7382
Interaktion p-Wert									0,5311
Alter									
<65 Jahre	130	61 (46,9)	8,1 [4,7; 10,4]	125	45 (36,0)	12,9 [6,5; NE]	1,20	[0,82; 1,78]	0,3404
>/= 65 Jahre	107	49 (45,8)	7,5 [3,0; 13,2]	115	60 (52,2)	4,0 [2,3; 10,3]	0,79	[0,54; 1,15]	0,2082
Interaktion p-Wert									0,1258

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	5,6 [2,2; 9,2]	83	41 (49,4)	7,5 [3,7; 24,3]	1,13	[0,71; 1,80]	0,5397
Nicht-Asiatisch	170	78 (45,9)	8,5 [4,0; 13,2]	157	64 (40,8)	6,7 [2,8; 16,6]	0,90	[0,65; 1,26]	0,5400
Interaktion p-Wert									0,4374
Performance status zu baseline									
0	82	42 (51,2)	4,6 [2,8; 9,0]	78	35 (44,9)	6,5 [2,3; 19,3]	1,07	[0,68; 1,69]	0,7404
1	155	68 (43,9)	9,2 [4,7; 14,6]	162	70 (43,2)	6,9 [3,3; 16,6]	0,91	[0,65; 1,27]	0,5752
Interaktion p-Wert									0,5645

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs293g.sas Executed : 2022-10-17T212346

Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	55 (44,7)	8,5 [4,6; 23,0]	120	58 (48,3)	5,6 [2,7; 19,3]	0,80	[0,55; 1,16]	0,2615
Stadium IVB	112	54 (48,2)	6,0 [3,3; 10,3]	120	47 (39,2)	12,7 [6,5; 16,6]	1,19	[0,80; 1,76]	0,4627
Interaktion p-Wert									0,1561
Raucherstatus									
Aktiv	65	30 (46,2)	8,4 [2,9; 23,0]	49	18 (36,7)	6,5 [2,3; NE]	0,83	[0,47; 1,53]	0,5641
Ehemals	137	63 (46,0)	7,5 [3,9; 9,2]	133	63 (47,4)	6,5 [3,7; 12,9]	0,97	[0,68; 1,37]	0,8818
Nie	35	17 (48,6)	9,0 [2,4; NE]	58	24 (41,4)	12,7 [2,7; NE]	1,06	[0,56; 1,97]	0,8230
Interaktion p-Wert									0,8506

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	62 (44,6)	8,4 [4,0; 14,6]	125	52 (41,6)	6,5 [2,8; 12,7]	0,90	[0,62; 1,30]	0,5471
Rest of the World	98	48 (49,0)	6,1 [3,7; 9,4]	115	53 (46,1)	10,3 [3,7; 19,3]	1,05	[0,71; 1,56]	0,7677
Interaktion p-Wert									0,5579

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs293g.sas Executed : 2022-10-17T212346

Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	5 (41,7)	23,0 [0,8; NE]	12	5 (41,7)	NE [0,8; NE]	0,60	[0,17; 2,16]	0,4976
Pemetrexed-Doublette	142	70 (49,3)	7,7 [4,0; 13,2]	146	68 (46,6)	6,9 [4,0; 12,9]	0,97	[0,69; 1,35]	0,8450
Gemcitabin-Doublette	83	35 (42,2)	6,1 [3,3; 10,4]	82	32 (39,0)	6,5 [2,3; NE]	1,04	[0,64; 1,68]	0,7638
Interaktion p-Wert									0,7236

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs293g.sas Executed : 2022-10-17T212346

Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	36 (40,9)	8,4 [3,3; 10,4]	90	36 (40,0)	6,5 [2,1; NE]	0,95	[0,60; 1,52]	0,9886
Nicht-Plattenepithelial	149	74 (49,7)	7,7 [4,0; 13,2]	150	69 (46,0)	6,9 [4,0; 12,9]	0,97	[0,70; 1,35]	0,8670
Interaktion p-Wert									0,9431
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	62 (49,6)	7,5 [3,3; 11,1]	130	58 (44,6)	6,5 [2,3; 24,3]	0,97	[0,68; 1,39]	0,8936
PD-L1 >/=1%	112	48 (42,9)	8,4 [3,8; 23,0]	110	47 (42,7)	7,5 [3,8; 16,6]	0,96	[0,64; 1,44]	0,8384
Interaktion p-Wert									0,9804

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs293g.sas Executed : 2022-10-17T212346

Table 5.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	3,6 [1,4; 14,6]	34	16 (47,1)	6,0 [1,4; NE]	1,33	[0,61; 2,80]	0,4755
Nein	214	98 (45,8)	8,4 [4,6; 10,4]	206	89 (43,2)	7,5 [3,8; 16,6]	0,94	[0,71; 1,26]	0,6953
Interaktion p-Wert									0,4005

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs293g.sas Executed : 2022-10-17T212346

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs393g.sas Executed : 2022-11-21T221334

Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 insomnia (individual symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	96 (49,2)	5,6 [3,7; 9,2]	179	82 (45,8)	5,6 [2,9; 12,2]	1,01	[0,76; 1,36]	0,9418
Weiblich	42	21 (50,0)	4,0 [1,4; NE]	61	26 (42,6)	7,4 [2,9; NE]	1,26	[0,70; 2,23]	0,3967
Interaktion p-Wert									0,5112
Alter									
<65 Jahre	130	60 (46,2)	6,9 [4,2; 14,4]	125	45 (36,0)	12,2 [4,9; NE]	1,21	[0,82; 1,79]	0,3262
>/= 65 Jahre	107	57 (53,3)	3,7 [2,1; 6,2]	115	63 (54,8)	3,9 [2,2; 7,4]	0,99	[0,69; 1,42]	0,9857
Interaktion p-Wert									0,4574

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	36 (53,7)	3,7 [2,1; 9,4]	83	41 (49,4)	7,6 [3,7; 24,3]	1,38	[0,88; 2,16]	0,1638
Nicht-Asiatisch	170	81 (47,6)	6,1 [3,7; 9,4]	157	67 (42,7)	4,9 [2,8; 12,2]	0,93	[0,68; 1,29]	0,7281
Interaktion p-Wert									0,1679
Performance status zu baseline									
0	82	39 (47,6)	4,9 [2,8; 27,4]	78	36 (46,2)	4,9 [2,9; 17,5]	0,91	[0,58; 1,43]	0,6542
1	155	78 (50,3)	5,6 [2,8; 8,5]	162	72 (44,4)	7,4 [2,9; 12,2]	1,17	[0,85; 1,61]	0,3408
Interaktion p-Wert									0,3682

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	60 (48,8)	6,2 [2,9; 18,1]	120	56 (46,7)	6,7 [3,7; 17,5]	1,02	[0,71; 1,47]	0,9314
Stadium IVB	112	56 (50,0)	3,8 [2,1; 8,5]	120	52 (43,3)	6,2 [2,8; 23,9]	1,12	[0,77; 1,64]	0,5241
Interaktion p-Wert									0,7161
Raucherstatus									
Aktiv	65	26 (40,0)	14,4 [2,8; NE]	49	16 (32,7)	4,9 [2,1; NE]	0,77	[0,42; 1,48]	0,7041
Ehemals	137	72 (52,6)	4,0 [2,2; 6,8]	133	67 (50,4)	6,2 [2,9; 13,9]	1,19	[0,85; 1,66]	0,3238
Nie	35	19 (54,3)	10,4 [2,1; 18,1]	58	25 (43,1)	7,4 [2,8; NE]	1,17	[0,64; 2,12]	0,5926
Interaktion p-Wert									0,4828

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	65 (46,8)	6,1 [3,8; 9,2]	125	52 (41,6)	4,1 [2,2; NE]	0,94	[0,66; 1,37]	0,7754
Rest of the World	98	52 (53,1)	3,7 [2,1; 9,4]	115	56 (48,7)	7,4 [3,8; 17,5]	1,22	[0,84; 1,79]	0,3186
Interaktion p-Wert									0,3338

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	5 (41,7)	9,4 [2,1; NE]	12	4 (33,3)	NE [0,8; NE]	0,71	[0,19; 2,86]	0,6097
Pemetrexed-Doublette	142	84 (59,2)	3,8 [2,1; 6,9]	146	69 (47,3)	7,4 [3,9; 13,9]	1,32	[0,96; 1,81]	0,0926
Gemcitabin-Doublette	83	28 (33,7)	NE [3,7; NE]	82	35 (42,7)	3,9 [2,1; NE]	0,71	[0,43; 1,16]	0,2299
Interaktion p-Wert									0,0991

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	30 (34,1)	9,4 [3,8; NE]	90	37 (41,1)	4,0 [2,1; NE]	0,73	[0,45; 1,18]	0,2492
Nicht-Plattenepithelial	149	87 (58,4)	3,8 [2,1; 6,9]	150	71 (47,3)	7,4 [3,8; 13,9]	1,26	[0,92; 1,73]	0,1461
Interaktion p-Wert									0,0611
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	67 (53,6)	4,8 [3,3; 8,5]	130	60 (46,2)	5,6 [2,8; 13,9]	1,09	[0,77; 1,55]	0,5906
PD-L1 >/=1%	112	50 (44,6)	6,1 [2,2; 27,4]	110	48 (43,6)	7,4 [3,7; 32,6]	1,03	[0,69; 1,54]	0,7926
Interaktion p-Wert									0,8321

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.12.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	13 (56,5)	2,1 [0,8; 4,7]	34	18 (52,9)	1,8 [0,8; NE]	1,25	[0,60; 2,55]	0,5902
Nein	214	104 (48,6)	6,1 [3,8; 9,4]	206	90 (43,7)	6,7 [3,9; 12,2]	1,08	[0,81; 1,43]	0,6128
Interaktion p-Wert									0,7003

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3003g.sas Executed : 2022-11-21T221744

Figure 5.12.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 loss of appetite (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	78 (40,0)	8,4 [4,7; NE]	179	62 (34,6)	10,3 [6,5; NE]	1,12	[0,80; 1,56]	0,5165
Weiblich	42	18 (42,9)	5,8 [2,8; NE]	61	28 (45,9)	3,7 [2,1; NE]	0,88	[0,48; 1,58]	0,6342
Interaktion p-Wert									0,4969
Alter									
<65 Jahre	130	51 (39,2)	12,3 [4,7; NE]	125	40 (32,0)	NE [6,5; NE]	1,17	[0,77; 1,78]	0,4546
>/= 65 Jahre	107	45 (42,1)	5,8 [3,1; NE]	115	50 (43,5)	6,5 [2,8; NE]	0,94	[0,63; 1,41]	0,7619
Interaktion p-Wert									0,4629

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	5,6 [3,3; 12,3]	83	40 (48,2)	6,5 [2,8; NE]	1,11	[0,69; 1,76]	0,6947
Nicht-Asiatisch	170	64 (37,6)	14,4 [4,7; NE]	157	50 (31,8)	NE [4,6; NE]	1,05	[0,72; 1,52]	0,7120
Interaktion p-Wert									0,8534
Performance status zu baseline									
0	82	27 (32,9)	20,5 [6,9; NE]	78	29 (37,2)	15,0 [3,7; NE]	0,77	[0,45; 1,30]	0,2890
1	155	69 (44,5)	4,7 [3,0; 12,3]	162	61 (37,7)	10,3 [6,2; NE]	1,21	[0,86; 1,72]	0,2585
Interaktion p-Wert									0,1518

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	50 (40,7)	8,2 [4,7; NE]	120	51 (42,5)	9,2 [2,8; NE]	0,84	[0,57; 1,24]	0,3755
Stadium IVB	112	45 (40,2)	8,0 [3,3; NE]	120	39 (32,5)	NE [6,5; NE]	1,30	[0,85; 2,01]	0,2281
Interaktion p-Wert									0,1343
Raucherstatus									
Aktiv	65	23 (35,4)	20,5 [5,1; NE]	49	13 (26,5)	NE [3,7; NE]	0,94	[0,48; 1,91]	0,7875
Ehemals	137	58 (42,3)	5,4 [3,1; NE]	133	56 (42,1)	9,2 [4,4; NE]	1,12	[0,77; 1,62]	0,5420
Nie	35	15 (42,9)	14,4 [2,7; NE]	58	21 (36,2)	NE [2,8; NE]	1,06	[0,54; 2,04]	0,8468
Interaktion p-Wert									0,9062

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	46 (33,1)	NE [5,1; NE]	125	37 (29,6)	NE [NE; NE]	0,99	[0,65; 1,54]	0,8866
Rest of the World	98	50 (51,0)	5,4 [2,8; 8,4]	115	53 (46,1)	6,5 [2,8; 15,0]	1,17	[0,79; 1,73]	0,4227
Interaktion p-Wert									0,5771

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	5,1 [0,8; NE]	12	2 (16,7)	NE [0,8; NE]	2,43	[0,56; 16,60]	0,4920
Pemetrexed-Doublette	142	61 (43,0)	8,0 [3,6; NE]	146	64 (43,8)	6,5 [3,7; NE]	0,97	[0,68; 1,38]	0,8975
Gemcitabin-Doublette	83	29 (34,9)	8,2 [4,7; NE]	82	24 (29,3)	15,0 [4,4; NE]	1,11	[0,65; 1,92]	0,7533
Interaktion p-Wert									0,5291

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	32 (36,4)	8,2 [4,7; NE]	90	25 (27,8)	15,0 [15,0; NE]	1,22	[0,72; 2,08]	0,5341
Nicht-Plattenepithelial	149	64 (43,0)	8,0 [3,6; NE]	150	65 (43,3)	6,5 [3,7; NE]	0,97	[0,69; 1,37]	0,8863
Interaktion p-Wert									0,4753
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	52 (41,6)	8,0 [4,5; NE]	130	52 (40,0)	6,2 [2,8; NE]	0,92	[0,63; 1,36]	0,7250
PD-L1 >/=1%	112	44 (39,3)	12,3 [4,7; NE]	110	38 (34,5)	15,0 [6,5; NE]	1,19	[0,77; 1,84]	0,4517
Interaktion p-Wert									0,3958

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.13.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	10 (43,5)	4,7 [1,4; NE]	34	12 (35,3)	NE [2,1; NE]	1,40	[0,59; 3,25]	0,4431
Nein	214	86 (40,2)	8,4 [5,1; NE]	206	78 (37,9)	10,3 [5,6; NE]	1,01	[0,74; 1,37]	0,9795
Interaktion p-Wert									0,4654

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Figure 5.13.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 constipation (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3103g.sas Executed : 2022-11-21T222024

Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	64 (32,8)	25,9 [10,4; NE]	179	50 (27,9)	NE [7,6; NE]	1,02	[0,70; 1,48]	0,9788
Weiblich	42	22 (52,4)	5,7 [2,1; 16,0]	61	15 (24,6)	NE [17,5; NE]	2,31	[1,21; 4,55]	0,0103
Interaktion p-Wert									0,0329
Alter									
<65 Jahre	130	44 (33,8)	28,1 [10,4; NE]	125	35 (28,0)	NE [9,9; NE]	1,03	[0,66; 1,62]	0,8695
>/= 65 Jahre	107	42 (39,3)	9,8 [5,1; NE]	115	30 (26,1)	NE [17,5; NE]	1,48	[0,93; 2,39]	0,0944
Interaktion p-Wert									0,2691

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	29 (43,3)	5,7 [3,7; NE]	83	29 (34,9)	NE [7,4; NE]	1,42	[0,84; 2,38]	0,1746
Nicht-Asiatisch	170	57 (33,5)	22,2 [10,4; NE]	157	36 (22,9)	NE [14,3; NE]	1,18	[0,78; 1,81]	0,4385
Interaktion p-Wert									0,5932
Performance status zu baseline									
0	82	29 (35,4)	25,9 [6,5; NE]	78	22 (28,2)	17,5 [4,9; NE]	1,08	[0,62; 1,91]	0,7927
1	155	57 (36,8)	22,2 [6,5; 32,5]	162	43 (26,5)	NE [14,3; NE]	1,30	[0,88; 1,94]	0,2017
Interaktion p-Wert									0,5961

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	50 (40,7)	10,4 [4,9; NE]	120	29 (24,2)	NE [17,5; NE]	1,58	[1,01; 2,54]	0,0431
Stadium IVB	112	36 (32,1)	22,2 [9,7; NE]	120	36 (30,0)	NE [7,4; NE]	0,95	[0,59; 1,51]	0,7807
Interaktion p-Wert									0,1201
Raucherstatus									
Aktiv	65	17 (26,2)	NE [10,4; NE]	49	9 (18,4)	14,3 [14,3; NE]	1,02	[0,46; 2,40]	0,9577
Ehemals	137	54 (39,4)	22,2 [4,0; 32,5]	133	42 (31,6)	NE [7,4; NE]	1,25	[0,83; 1,88]	0,2585
Nie	35	15 (42,9)	9,8 [5,7; NE]	58	14 (24,1)	NE [17,5; NE]	1,55	[0,74; 3,25]	0,2860
Interaktion p-Wert									0,7520

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2113g.sas Executed : 2022-10-17T213637

Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	45 (32,4)	22,2 [9,8; NE]	125	28 (22,4)	NE [14,3; NE]	1,20	[0,75; 1,96]	0,4140
Rest of the World	98	41 (41,8)	16,0 [4,9; 30,6]	115	37 (32,2)	NE [9,9; NE]	1,30	[0,83; 2,03]	0,2731
Interaktion p-Wert									0,8250

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	7 (58,3)	2,9 [0,8; NE]	12	6 (50,0)	2,4 [0,8; NE]	0,71	[0,23; 2,22]	0,7393
Pemetrexed-Doublette	142	61 (43,0)	9,8 [4,9; 28,1]	146	40 (27,4)	NE [14,3; NE]	1,51	[1,02; 2,27]	0,0395
Gemcitabin-Doublette	83	18 (21,7)	NE [10,4; NE]	82	19 (23,2)	NE [7,4; NE]	0,80	[0,42; 1,54]	0,4617
Interaktion p-Wert									0,1608

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	22 (25,0)	20,2 [10,4; NE]	90	23 (25,6)	NE [7,4; NE]	0,83	[0,46; 1,50]	0,5262
Nicht-Plattenepithelial	149	64 (43,0)	16,0 [5,6; 30,6]	150	42 (28,0)	NE [14,3; NE]	1,45	[0,99; 2,16]	0,0584
Interaktion p-Wert									0,1227
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	41 (32,8)	28,1 [8,3; NE]	130	30 (23,1)	NE [14,3; NE]	1,31	[0,82; 2,11]	0,2685
PD-L1 >/=1%	112	45 (40,2)	20,2 [4,4; 32,5]	110	35 (31,8)	NE [7,4; NE]	1,14	[0,73; 1,79]	0,4969
Interaktion p-Wert									0,6872

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.14.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	2,2 [1,4; NE]	34	8 (23,5)	NE [3,9; NE]	2,49	[1,03; 6,37]	0,0357
Nein	214	74 (34,6)	25,9 [9,7; 32,5]	206	57 (27,7)	NE [14,3; NE]	1,11	[0,79; 1,58]	0,5960
Interaktion p-Wert									0,1002

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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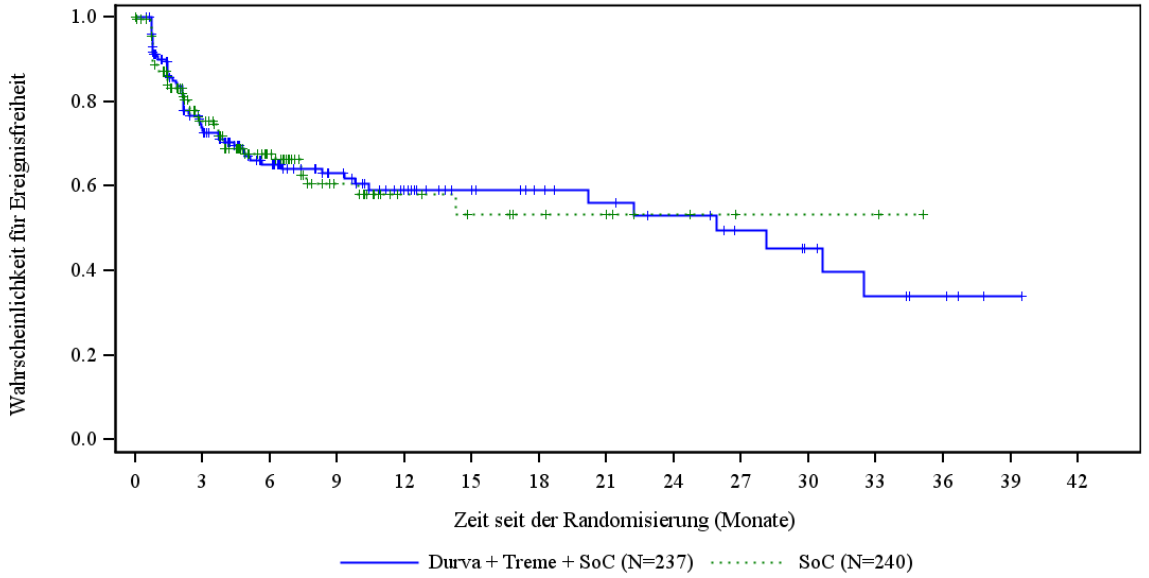
Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	195	109	71	51	35	26	22	19	16	12	9	6	4	1	0
SoC	179	87	49	25	13	10	8	6	4	2	2	2	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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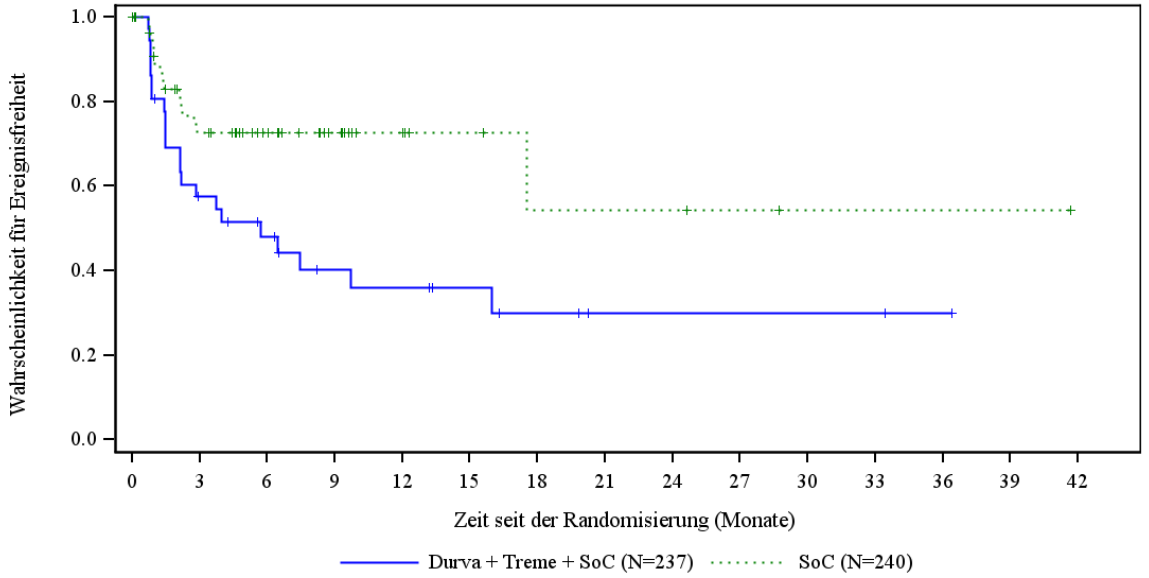
Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	42	19	14	9	8	6	4	2	2	2	2	2	1	0	0
SoC	61	35	24	14	7	5	3	3	3	2	1	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3113g.sas Executed : 2022-11-21T222323

Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.14.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 diarrhoea (individual symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	77 (39,5)	11,4 [5,2; 33,0]	179	61 (34,1)	27,4 [9,2; NE]	1,07	[0,77; 1,51]	0,6819
Weiblich	42	15 (35,7)	18,7 [3,7; NE]	61	17 (27,9)	19,3 [11,1; NE]	1,37	[0,68; 2,76]	0,3828
Interaktion p-Wert									0,5304
Alter									
<65 Jahre	130	51 (39,2)	13,7 [5,2; NE]	125	39 (31,2)	18,4 [9,2; NE]	1,20	[0,79; 1,83]	0,3875
>/= 65 Jahre	107	41 (38,3)	12,1 [4,7; NE]	115	39 (33,9)	19,3 [10,8; NE]	1,11	[0,72; 1,73]	0,5970
Interaktion p-Wert									0,8154

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	26 (38,8)	11,4 [4,5; NE]	83	37 (44,6)	11,2 [6,5; NE]	1,05	[0,63; 1,72]	0,8670
Nicht-Asiatisch	170	66 (38,8)	13,0 [6,2; 33,0]	157	41 (26,1)	NE [11,3; NE]	1,27	[0,86; 1,89]	0,2054
Interaktion p-Wert									0,5529
Performance status zu baseline									
0	82	34 (41,5)	13,7 [4,6; NE]	78	26 (33,3)	19,3 [5,6; NE]	1,17	[0,70; 1,96]	0,5696
1	155	58 (37,4)	12,1 [4,9; NE]	162	52 (32,1)	18,4 [11,1; NE]	1,15	[0,79; 1,68]	0,4695
Interaktion p-Wert									0,9669

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	47 (38,2)	13,1 [6,5; NE]	120	43 (35,8)	11,3 [9,2; 27,4]	0,95	[0,62; 1,44]	0,7294
Stadium IVB	112	45 (40,2)	9,4 [4,0; NE]	120	35 (29,2)	NE [10,8; NE]	1,49	[0,96; 2,33]	0,0647
Interaktion p-Wert									0,1431
Raucherstatus									
Aktiv	65	21 (32,3)	18,7 [11,2; NE]	49	7 (14,3)	NE [NE; NE]	1,58	[0,70; 4,02]	0,3458
Ehemals	137	58 (42,3)	6,2 [4,5; NE]	133	57 (42,9)	10,8 [4,0; NE]	1,09	[0,76; 1,58]	0,6310
Nie	35	13 (37,1)	33,0 [6,5; NE]	58	14 (24,1)	19,3 [11,1; NE]	1,43	[0,66; 3,07]	0,5731
Interaktion p-Wert									0,6494

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	48 (34,5)	13,1 [7,7; NE]	125	33 (26,4)	NE [11,3; NE]	1,09	[0,70; 1,72]	0,6910
Rest of the World	98	44 (44,9)	6,7 [3,1; NE]	115	45 (39,1)	18,4 [9,2; NE]	1,30	[0,86; 1,98]	0,2056
Interaktion p-Wert									0,5761

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	5 (41,7)	4,7 [0,8; NE]	12	5 (41,7)	NE [0,8; NE]	0,59	[0,16; 2,12]	0,5558
Pemetrexed-Doublette	142	56 (39,4)	13,1 [7,7; NE]	146	48 (32,9)	27,4 [11,3; NE]	1,23	[0,83; 1,81]	0,2846
Gemcitabin-Doublette	83	31 (37,3)	5,2 [4,0; NE]	82	25 (30,5)	10,8 [6,5; NE]	1,12	[0,66; 1,92]	0,5701
Interaktion p-Wert									0,5373

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	34 (38,6)	5,1 [4,0; NE]	90	29 (32,2)	9,2 [6,5; NE]	1,08	[0,66; 1,79]	0,6560
Nicht-Plattenepithelial	149	58 (38,9)	13,7 [9,4; NE]	150	49 (32,7)	27,4 [11,3; NE]	1,19	[0,81; 1,75]	0,3503
Interaktion p-Wert									0,7725
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	45 (36,0)	13,0 [6,5; NE]	130	46 (35,4)	19,3 [6,5; NE]	0,97	[0,64; 1,46]	0,9020
PD-L1 >/=1%	112	47 (42,0)	12,1 [4,5; 37,3]	110	32 (29,1)	18,4 [11,2; NE]	1,42	[0,91; 2,25]	0,1188
Interaktion p-Wert									0,2203

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.15.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	9 (39,1)	4,5 [1,4; NE]	34	14 (41,2)	6,5 [2,8; NE]	1,13	[0,47; 2,58]	0,7054
Nein	214	83 (38,8)	13,0 [6,5; NE]	206	64 (31,1)	19,3 [11,1; NE]	1,18	[0,85; 1,64]	0,2993
Interaktion p-Wert									0,9211

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2123g.sas Executed : 2022-10-17T214046

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Figure 5.15.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 financial difficulties (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3123g.sas Executed : 2022-11-21T222619

Anhang 4-G 1.3.2.2: EORTC QLQ-LC13 - Symptomskalen

Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	123 (63,1)	2,8 [2,1; 3,0]	179	113 (63,1)	2,1 [1,4; 2,8]	0,84	[0,65; 1,09]	0,2091
Weiblich	42	23 (54,8)	5,6 [1,2; 29,7]	61	31 (50,8)	5,6 [2,1; 8,8]	1,11	[0,64; 1,89]	0,8195
Interaktion p-Wert									0,3637
Alter									
<65 Jahre	130	79 (60,8)	2,8 [2,1; 4,7]	125	70 (56,0)	2,1 [1,5; 4,2]	0,94	[0,68; 1,30]	0,8600
>/= 65 Jahre	107	67 (62,6)	2,8 [2,1; 3,8]	115	74 (64,3)	2,3 [1,6; 3,7]	0,92	[0,66; 1,28]	0,5934
Interaktion p-Wert									0,9019

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	48 (71,6)	2,2 [1,4; 2,8]	83	56 (67,5)	2,1 [1,4; 3,7]	1,18	[0,80; 1,73]	0,3928
Nicht-Asiatisch	170	98 (57,6)	3,0 [2,1; 5,6]	157	88 (56,1)	2,7 [1,7; 3,8]	0,85	[0,63; 1,13]	0,2486
Interaktion p-Wert									0,1773
Performance status zu baseline									
0	82	54 (65,9)	2,1 [1,4; 2,8]	78	47 (60,3)	2,3 [1,5; 4,2]	1,08	[0,73; 1,61]	0,6578
1	155	92 (59,4)	3,7 [2,4; 5,6]	162	97 (59,9)	2,1 [1,6; 3,7]	0,85	[0,64; 1,14]	0,2911
Interaktion p-Wert									0,3365

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc203g.sas Executed : 2022-10-17T230656

Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	76 (61,8)	3,0 [2,4; 4,7]	120	73 (60,8)	2,1 [1,7; 3,7]	0,88	[0,64; 1,22]	0,4882
Stadium IVB	112	69 (61,6)	2,2 [1,6; 3,9]	120	71 (59,2)	2,4 [1,5; 3,9]	0,97	[0,70; 1,36]	0,8995
Interaktion p-Wert									0,6813
Raucherstatus									
Aktiv	65	35 (53,8)	2,8 [1,5; 9,2]	49	29 (59,2)	1,5 [0,8; 2,4]	0,57	[0,34; 0,93]	0,0665
Ehemals	137	90 (65,7)	2,8 [2,1; 3,3]	133	83 (62,4)	2,7 [1,6; 3,7]	1,09	[0,81; 1,47]	0,5797
Nie	35	21 (60,0)	5,6 [1,6; 15,6]	58	32 (55,2)	3,0 [2,0; 6,5]	0,89	[0,51; 1,54]	0,5621
Interaktion p-Wert									0,0869

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	79 (56,8)	3,0 [2,1; 5,6]	125	74 (59,2)	2,1 [1,5; 3,7]	0,78	[0,57; 1,07]	0,1311
Rest of the World	98	67 (68,4)	2,8 [1,7; 3,8]	115	70 (60,9)	2,4 [1,5; 4,6]	1,14	[0,81; 1,59]	0,4282
Interaktion p-Wert									0,1119

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	8 (66,7)	3,0 [0,8; NE]	12	8 (66,7)	1,8 [0,7; 2,8]	0,60	[0,22; 1,64]	0,1590
Pemetrexed-Doublette	142	92 (64,8)	2,8 [2,2; 5,6]	146	90 (61,6)	2,4 [1,9; 4,2]	0,92	[0,69; 1,23]	0,6022
Gemcitabin-Doublette	83	46 (55,4)	2,1 [1,4; 3,7]	82	46 (56,1)	2,1 [1,5; 3,7]	1,00	[0,66; 1,51]	0,8945
Interaktion p-Wert									0,6476

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	49 (55,7)	2,1 [1,4; 3,3]	90	52 (57,8)	2,1 [1,5; 2,9]	0,97	[0,65; 1,43]	0,9788
Nicht-Plattenepithelial	149	97 (65,1)	2,9 [2,4; 5,6]	150	92 (61,3)	2,7 [1,9; 4,2]	0,91	[0,69; 1,22]	0,5479
Interaktion p-Wert									0,8207
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	78 (62,4)	2,8 [2,1; 4,7]	130	76 (58,5)	2,1 [1,5; 3,9]	0,91	[0,67; 1,26]	0,6465
PD-L1 >/=1%	112	68 (60,7)	2,8 [2,1; 3,9]	110	68 (61,8)	2,4 [1,5; 3,7]	0,94	[0,67; 1,32]	0,7549
Interaktion p-Wert									0,9017

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	14 (60,9)	2,1 [0,8; 3,0]	34	24 (70,6)	1,4 [0,8; 2,1]	0,75	[0,38; 1,43]	0,4301
Nein	214	132 (61,7)	2,8 [2,1; 4,6]	206	120 (58,3)	2,8 [2,1; 3,8]	0,97	[0,76; 1,25]	0,8013
Interaktion p-Wert									0,4703

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Figure 6.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dyspnoea
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc303g.sas Executed : 2022-11-21T223157

Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	70 (35,9)	14,4 [8,5; NE]	179	58 (32,4)	16,6 [8,5; 27,4]	0,99	[0,70; 1,40]	0,9192
Weiblich	42	17 (40,5)	14,1 [5,4; NE]	61	21 (34,4)	18,4 [6,5; NE]	1,12	[0,58; 2,12]	0,7161
Interaktion p-Wert									0,7357
Alter									
<65 Jahre	130	51 (39,2)	14,4 [8,1; 30,8]	125	40 (32,0)	17,6 [7,9; NE]	1,06	[0,70; 1,62]	0,8025
>/= 65 Jahre	107	36 (33,6)	14,1 [7,6; NE]	115	39 (33,9)	16,6 [8,5; NE]	0,97	[0,61; 1,52]	0,8998
Interaktion p-Wert									0,7659

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	26 (38,8)	11,8 [4,8; NE]	83	34 (41,0)	18,4 [6,2; NE]	1,17	[0,69; 1,94]	0,6038
Nicht-Asiatisch	170	61 (35,9)	14,5 [9,3; NE]	157	45 (28,7)	15,6 [8,5; 23,5]	0,97	[0,66; 1,44]	0,9021
Interaktion p-Wert									0,5822
Performance status zu baseline									
0	82	30 (36,6)	14,4 [7,6; NE]	78	33 (42,3)	7,9 [3,7; 30,7]	0,76	[0,46; 1,24]	0,2817
1	155	57 (36,8)	14,1 [8,3; 19,6]	162	46 (28,4)	18,4 [12,2; NE]	1,21	[0,82; 1,79]	0,3535
Interaktion p-Wert									0,1413

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	47 (38,2)	14,4 [8,1; 30,8]	120	39 (32,5)	18,4 [8,5; 30,7]	1,08	[0,71; 1,66]	0,7657
Stadium IVB	112	39 (34,8)	14,6 [8,5; NE]	120	40 (33,3)	15,6 [6,5; NE]	0,94	[0,60; 1,47]	0,9292
Interaktion p-Wert									0,6698
Raucherstatus									
Aktiv	65	20 (30,8)	30,8 [9,3; NE]	49	16 (32,7)	8,5 [2,8; NE]	0,53	[0,27; 1,03]	0,0523
Ehemals	137	50 (36,5)	14,4 [7,6; NE]	133	44 (33,1)	17,6 [8,5; 30,7]	1,13	[0,75; 1,69]	0,5630
Nie	35	17 (48,6)	14,1 [2,2; 17,1]	58	19 (32,8)	15,6 [6,5; NE]	1,48	[0,76; 2,86]	0,2929
Interaktion p-Wert									0,0689

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	47 (33,8)	14,5 [9,3; NE]	125	36 (28,8)	15,6 [6,5; NE]	0,91	[0,59; 1,43]	0,8129
Rest of the World	98	40 (40,8)	11,8 [5,8; 17,1]	115	43 (37,4)	17,6 [8,5; 30,7]	1,16	[0,75; 1,78]	0,5117
Interaktion p-Wert									0,4543

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	1 (8,3)	NE [1,4; NE]	12	3 (25,0)	NE [0,8; NE]	0,15	[0,01; 1,18]	0,2162
Pemetrexed-Doublette	142	56 (39,4)	14,5 [8,1; NE]	146	51 (34,9)	18,4 [8,5; 30,7]	1,11	[0,76; 1,62]	0,5781
Gemcitabin-Doublette	83	30 (36,1)	10,2 [4,8; 19,6]	82	25 (30,5)	11,1 [4,5; NE]	1,01	[0,59; 1,73]	0,8831
Interaktion p-Wert									0,2327

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	30 (34,1)	10,2 [5,6; 19,6]	90	27 (30,0)	11,1 [4,5; NE]	0,95	[0,56; 1,60]	0,6718
Nicht-Plattenepithelial	149	57 (38,3)	14,6 [8,3; NE]	150	52 (34,7)	18,4 [8,5; 30,7]	1,05	[0,72; 1,53]	0,7707
Interaktion p-Wert									0,7542
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	44 (35,2)	14,4 [8,5; 30,8]	130	34 (26,2)	27,4 [12,2; NE]	1,23	[0,79; 1,93]	0,3634
PD-L1 >/=1%	112	43 (38,4)	13,5 [4,8; NE]	110	45 (40,9)	11,1 [4,7; 18,4]	0,86	[0,56; 1,31]	0,5623
Interaktion p-Wert									0,2525

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc213g.sas Executed : 2022-10-17T231148

Table 6.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	10 (43,5)	4,8 [1,4; NE]	34	12 (35,3)	NE [2,2; NE]	1,47	[0,62; 3,41]	0,4278
Nein	214	77 (36,0)	14,4 [9,3; NE]	206	67 (32,5)	16,6 [8,5; 27,4]	0,99	[0,72; 1,38]	0,9345
Interaktion p-Wert									0,3951

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc213g.sas Executed : 2022-10-17T231148

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Figure 6.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (chest) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc313g.sas Executed : 2022-11-21T223413

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	74 (37,9)	8,9 [6,2; 14,4]	179	60 (33,5)	12,0 [6,2; NE]	1,02	[0,73; 1,44]	0,9148
Weiblich	42	20 (47,6)	4,4 [2,2; NE]	61	22 (36,1)	11,1 [4,7; NE]	1,50	[0,81; 2,75]	0,1832
Interaktion p-Wert									0,2810
Alter									
<65 Jahre	130	53 (40,8)	8,4 [5,6; NE]	125	43 (34,4)	11,1 [5,6; NE]	1,07	[0,72; 1,61]	0,6920
>/= 65 Jahre	107	41 (38,3)	8,9 [4,9; NE]	115	39 (33,9)	12,0 [5,6; NE]	1,15	[0,74; 1,78]	0,5495
Interaktion p-Wert									0,8210

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	5,5 [3,7; 8,4]	83	37 (44,6)	10,2 [4,6; NE]	1,35	[0,83; 2,17]	0,2335
Nicht-Asiatisch	170	62 (36,5)	10,6 [6,5; NE]	157	45 (28,7)	12,0 [8,6; NE]	1,05	[0,72; 1,56]	0,7883
Interaktion p-Wert									0,4314
Performance status zu baseline									
0	82	29 (35,4)	14,4 [5,6; NE]	78	26 (33,3)	12,0 [4,6; NE]	0,90	[0,53; 1,54]	0,6809
1	155	65 (41,9)	6,8 [4,7; 9,3]	162	56 (34,6)	11,1 [6,2; NE]	1,24	[0,87; 1,78]	0,2451
Interaktion p-Wert									0,3259

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	51 (41,5)	8,9 [5,1; NE]	120	39 (32,5)	18,4 [7,5; NE]	1,24	[0,82; 1,90]	0,2890
Stadium IVB	112	43 (38,4)	8,5 [4,9; 11,3]	120	43 (35,8)	9,4 [4,6; NE]	1,00	[0,66; 1,53]	0,9772
Interaktion p-Wert									0,4765
Raucherstatus									
Aktiv	65	24 (36,9)	8,4 [4,7; NE]	49	17 (34,7)	5,6 [2,4; NE]	0,76	[0,41; 1,44]	0,3456
Ehemals	137	52 (38,0)	9,3 [5,7; 14,4]	133	47 (35,3)	18,4 [7,4; NE]	1,09	[0,73; 1,62]	0,6891
Nie	35	18 (51,4)	5,6 [3,3; NE]	58	18 (31,0)	NE [4,7; NE]	1,73	[0,89; 3,34]	0,0910
Interaktion p-Wert									0,2006

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	50 (36,0)	9,3 [5,8; NE]	125	33 (26,4)	12,0 [8,6; NE]	1,21	[0,78; 1,89]	0,4461
Rest of the World	98	44 (44,9)	6,7 [4,6; 14,1]	115	49 (42,6)	10,2 [4,6; NE]	1,09	[0,72; 1,63]	0,7173
Interaktion p-Wert									0,7276

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	5 (41,7)	5,5 [0,8; NE]	12	3 (25,0)	NE [0,9; NE]	1,19	[0,29; 5,82]	0,6542
Pemetrexed-Doublette	142	59 (41,5)	8,9 [5,6; NE]	146	58 (39,7)	9,4 [4,9; NE]	1,01	[0,70; 1,45]	0,9642
Gemcitabin-Doublette	83	30 (36,1)	6,8 [4,7; NE]	82	21 (25,6)	NE [10,2; NE]	1,36	[0,78; 2,41]	0,2874
Interaktion p-Wert									0,6702

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	31 (35,2)	8,4 [4,7; NE]	90	22 (24,4)	NE [10,2; NE]	1,36	[0,79; 2,39]	0,2814
Nicht-Plattenepithelial	149	63 (42,3)	8,9 [5,6; NE]	150	60 (40,0)	9,4 [4,9; NE]	1,01	[0,71; 1,44]	0,9395
Interaktion p-Wert									0,3694
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	46 (36,8)	10,6 [5,7; NE]	130	45 (34,6)	12,0 [5,6; NE]	0,97	[0,64; 1,47]	0,9178
PD-L1 >/=1%	112	48 (42,9)	6,7 [4,6; 9,3]	110	37 (33,6)	11,1 [7,4; NE]	1,27	[0,83; 1,97]	0,2684
Interaktion p-Wert									0,3747

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Table 6.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	14 (60,9)	2,1 [0,8; 3,9]	34	15 (44,1)	5,6 [2,1; NE]	2,13	[1,02; 4,45]	0,0609
Nein	214	80 (37,4)	9,0 [6,5; NE]	206	67 (32,5)	18,4 [7,5; NE]	1,06	[0,77; 1,47]	0,7391
Interaktion p-Wert									0,0874

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc223g.sas Executed : 2022-10-17T231619

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Figure 6.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (arm/shoulder) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc323g.sas Executed : 2022-11-21T223633

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	80 (41,0)	8,5 [5,6; 21,7]	179	72 (40,2)	8,8 [5,6; 13,8]	0,90	[0,65; 1,24]	0,5423
Weiblich	42	23 (54,8)	6,5 [1,9; 19,8]	61	26 (42,6)	9,3 [4,5; 27,7]	1,28	[0,73; 2,25]	0,4282
Interaktion p-Wert									0,2772
Alter									
<65 Jahre	130	53 (40,8)	9,5 [5,7; 21,7]	125	52 (41,6)	8,5 [4,6; 22,4]	0,81	[0,55; 1,19]	0,3363
>/= 65 Jahre	107	50 (46,7)	5,8 [3,9; 19,8]	115	46 (40,0)	9,3 [5,6; 19,4]	1,20	[0,80; 1,79]	0,3664
Interaktion p-Wert									0,1648

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	25 (37,3)	14,6 [5,7; NE]	83	41 (49,4)	7,5 [4,6; 22,4]	0,80	[0,48; 1,30]	0,3779
Nicht-Asiatisch	170	78 (45,9)	7,7 [4,6; 9,5]	157	57 (36,3)	8,8 [5,6; 10,3]	1,04	[0,74; 1,48]	0,8022
Interaktion p-Wert									0,3826
Performance status zu baseline									
0	82	42 (51,2)	6,8 [3,7; 11,3]	78	33 (42,3)	5,6 [3,3; 27,7]	0,99	[0,63; 1,58]	0,9810
1	155	61 (39,4)	8,5 [5,2; 25,4]	162	65 (40,1)	9,2 [5,8; 16,3]	0,95	[0,67; 1,35]	0,7083
Interaktion p-Wert									0,8660

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	58 (47,2)	6,5 [4,7; 20,5]	120	46 (38,3)	16,3 [4,6; 27,4]	1,16	[0,79; 1,72]	0,4309
Stadium IVB	112	45 (40,2)	8,5 [5,3; 19,8]	120	52 (43,3)	7,5 [5,6; 9,5]	0,82	[0,55; 1,23]	0,3215
Interaktion p-Wert									0,2211
Raucherstatus									
Aktiv	65	20 (30,8)	20,5 [5,6; NE]	49	20 (40,8)	4,6 [2,2; 10,3]	0,45	[0,24; 0,84]	0,0164
Ehemals	137	62 (45,3)	6,8 [3,8; 9,5]	133	56 (42,1)	9,0 [5,6; 16,3]	1,13	[0,79; 1,63]	0,4330
Nie	35	21 (60,0)	6,5 [2,2; 19,8]	58	22 (37,9)	9,3 [5,6; 27,7]	1,39	[0,76; 2,53]	0,4284
Interaktion p-Wert									0,0182

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	61 (43,9)	8,3 [4,6; 9,5]	125	44 (35,2)	8,8 [5,6; 10,3]	1,07	[0,72; 1,58]	0,8176
Rest of the World	98	42 (42,9)	11,3 [5,2; 25,4]	115	54 (47,0)	7,5 [4,6; 16,3]	0,88	[0,58; 1,31]	0,5157
Interaktion p-Wert									0,4901

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	5 (41,7)	NE [0,8; NE]	12	3 (25,0)	4,5 [0,7; NE]	1,12	[0,27; 5,48]	0,5348
Pemetrexed-Doublette	142	67 (47,2)	7,7 [5,2; 20,5]	146	69 (47,3)	8,8 [5,6; 10,6]	0,92	[0,66; 1,29]	0,5999
Gemcitabin-Doublette	83	31 (37,3)	8,3 [4,7; 9,5]	82	26 (31,7)	NE [3,7; NE]	1,10	[0,65; 1,87]	0,7682
Interaktion p-Wert									0,8424

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	32 (36,4)	8,5 [4,7; NE]	90	29 (32,2)	5,8 [3,9; NE]	1,02	[0,62; 1,70]	0,9911
Nicht-Plattenepithelial	149	71 (47,7)	6,8 [4,7; 20,5]	150	69 (46,0)	9,0 [5,6; 13,8]	0,95	[0,68; 1,33]	0,7577
Interaktion p-Wert									0,8113
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	51 (40,8)	8,5 [5,2; 25,4]	130	52 (40,0)	8,8 [3,9; 22,4]	0,85	[0,58; 1,25]	0,4003
PD-L1 >/=1%	112	52 (46,4)	5,8 [3,4; 20,5]	110	46 (41,8)	9,0 [5,6; 16,3]	1,13	[0,76; 1,68]	0,5067
Interaktion p-Wert									0,3162

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Table 6.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	13 (56,5)	4,8 [0,8; 14,6]	34	20 (58,8)	5,6 [2,1; 9,3]	0,97	[0,47; 1,93]	0,5627
Nein	214	90 (42,1)	8,5 [5,6; 20,5]	206	78 (37,9)	9,2 [5,8; 22,4]	1,01	[0,75; 1,37]	0,8852
Interaktion p-Wert									0,9080

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc233g.sas Executed : 2022-10-17T232107

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
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+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

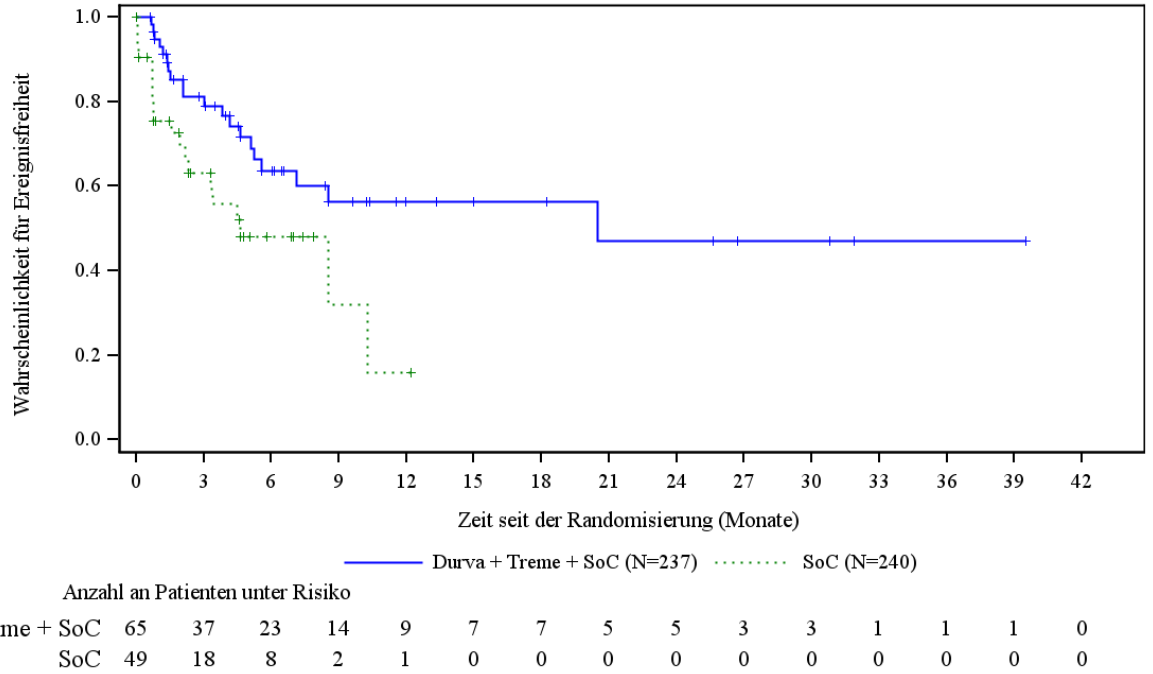
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv



Anzahl an Patienten unter Risiko

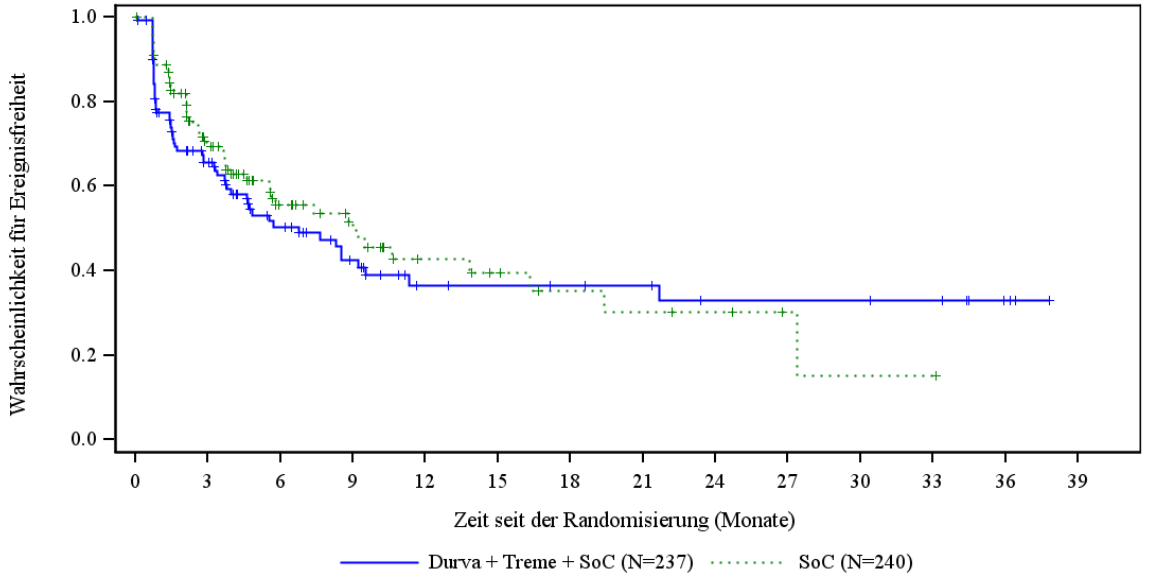
Durva + Treme + SoC	65	37	23	14	9	7	7	5	5	3	3	1	1	1	0
SoC	49	18	8	2	1	0	0	0	0	0	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	137	68	37	25	14	13	12	11	8	8	8	7	3	0
SoC	133	66	34	25	13	10	7	6	5	2	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
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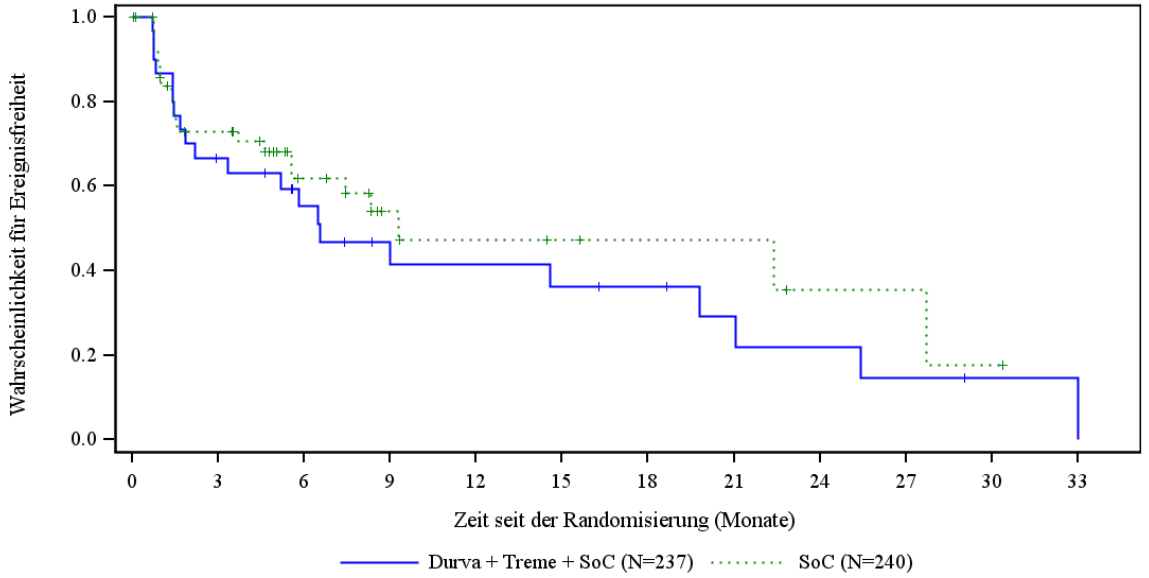
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	35	19	13	9	8	7	6	4	3	2	1	0
SoC	58	33	18	8	6	5	4	4	2	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Figure 6.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 pain (other) (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc333g.sas Executed : 2022-11-21T223904

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	77 (39,5)	9,4 [6,6; NE]	179	59 (33,0)	20,1 [6,3; NE]	1,13	[0,81; 1,59]	0,4505
Weiblich	42	14 (33,3)	34,6 [4,2; NE]	61	23 (37,7)	18,4 [4,5; NE]	0,95	[0,48; 1,83]	0,7863
Interaktion p-Wert									0,6480
Alter									
<65 Jahre	130	53 (40,8)	9,4 [6,6; NE]	125	36 (28,8)	NE [18,4; NE]	1,36	[0,89; 2,09]	0,1448
>/= 65 Jahre	107	38 (35,5)	11,8 [5,4; NE]	115	46 (40,0)	6,5 [4,5; 20,1]	0,88	[0,57; 1,36]	0,5445
Interaktion p-Wert									0,1624

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	24 (35,8)	11,8 [6,7; NE]	83	29 (34,9)	18,4 [6,5; NE]	1,25	[0,72; 2,15]	0,4042
Nicht-Asiatisch	170	67 (39,4)	9,2 [6,5; NE]	157	53 (33,8)	11,0 [4,5; NE]	0,99	[0,69; 1,43]	0,9791
Interaktion p-Wert									0,4843
Performance status zu baseline									
0	82	33 (40,2)	9,2 [4,7; NE]	78	28 (35,9)	20,1 [4,8; NE]	1,07	[0,65; 1,79]	0,8197
1	155	58 (37,4)	10,6 [6,0; NE]	162	54 (33,3)	18,4 [6,2; NE]	1,11	[0,76; 1,61]	0,5809
Interaktion p-Wert									0,9227

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	46 (37,4)	12,0 [7,4; NE]	120	41 (34,2)	18,4 [6,2; NE]	1,03	[0,67; 1,57]	0,9493
Stadium IVB	112	44 (39,3)	8,5 [3,8; NE]	120	41 (34,2)	NE [5,6; NE]	1,19	[0,78; 1,83]	0,3864
Interaktion p-Wert									0,6289
Raucherstatus									
Aktiv	65	28 (43,1)	8,3 [3,1; NE]	49	14 (28,6)	6,3 [4,5; NE]	1,26	[0,67; 2,46]	0,5164
Ehemals	137	48 (35,0)	12,0 [7,4; NE]	133	46 (34,6)	20,1 [6,5; NE]	1,02	[0,68; 1,53]	0,9706
Nie	35	15 (42,9)	10,6 [1,4; NE]	58	22 (37,9)	18,4 [3,7; NE]	1,19	[0,61; 2,28]	0,5895
Interaktion p-Wert									0,8315

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	52 (37,4)	9,2 [6,5; NE]	125	44 (35,2)	11,0 [3,9; NE]	0,87	[0,58; 1,30]	0,4889
Rest of the World	98	39 (39,8)	10,6 [3,7; NE]	115	38 (33,0)	20,1 [6,6; NE]	1,41	[0,90; 2,21]	0,1331
Interaktion p-Wert									0,1141

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	4 (33,3)	NE [2,9; NE]	12	5 (41,7)	4,5 [0,8; NE]	0,39	[0,10; 1,48]	0,0957
Pemetrexed-Doublette	142	56 (39,4)	10,6 [6,7; NE]	146	51 (34,9)	18,4 [6,6; NE]	1,15	[0,79; 1,68]	0,4743
Gemcitabin-Doublette	83	31 (37,3)	7,3 [4,2; NE]	82	26 (31,7)	NE [4,8; NE]	1,16	[0,69; 1,97]	0,5433
Interaktion p-Wert									0,2918

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	33 (37,5)	7,3 [4,2; NE]	90	29 (32,2)	6,5 [4,8; NE]	1,11	[0,67; 1,84]	0,6574
Nicht-Plattenepithelial	149	58 (38,9)	11,8 [8,3; NE]	150	53 (35,3)	18,4 [6,3; NE]	1,08	[0,74; 1,57]	0,6830
Interaktion p-Wert									0,9292
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	54 (43,2)	8,3 [5,1; 13,1]	130	51 (39,2)	6,6 [3,7; NE]	1,08	[0,73; 1,58]	0,6550
PD-L1 >/=1%	112	37 (33,0)	28,8 [6,6; NE]	110	31 (28,2)	NE [16,3; NE]	1,14	[0,71; 1,85]	0,6205
Interaktion p-Wert									0,8588

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Table 6.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	4 (17,4)	NE [4,5; NE]	34	15 (44,1)	6,3 [1,4; NE]	0,34	[0,10; 0,93]	0,0557
Nein	214	87 (40,7)	9,2 [6,6; 28,8]	206	67 (32,5)	20,1 [11,0; NE]	1,24	[0,90; 1,71]	0,1882
Interaktion p-Wert									0,0262

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc243g.sas Executed : 2022-10-17T232517

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

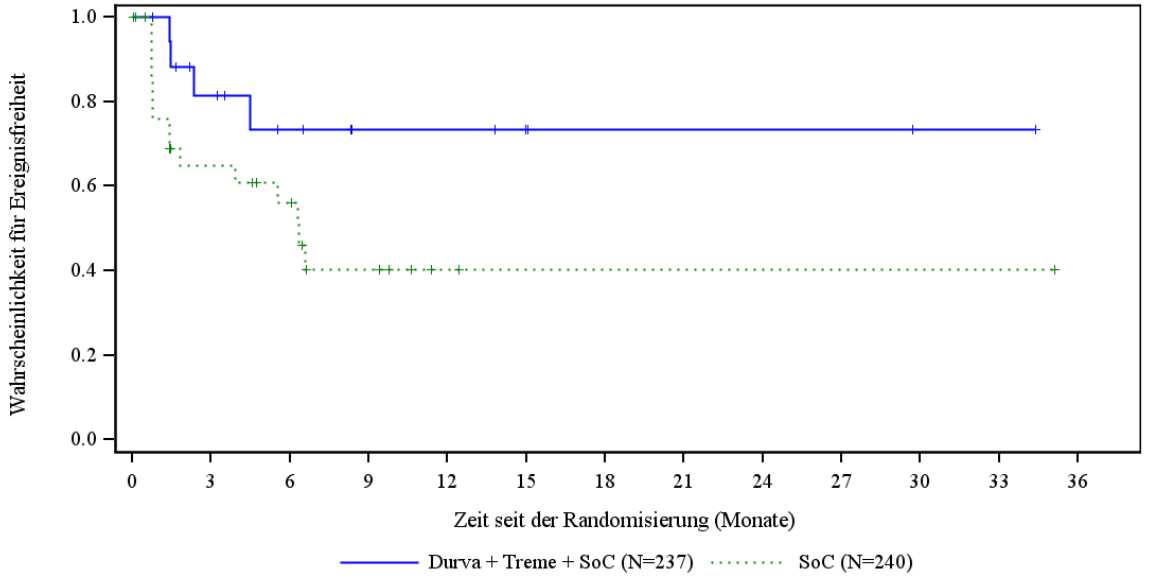
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja



Anzahl an Patienten unter Risiko

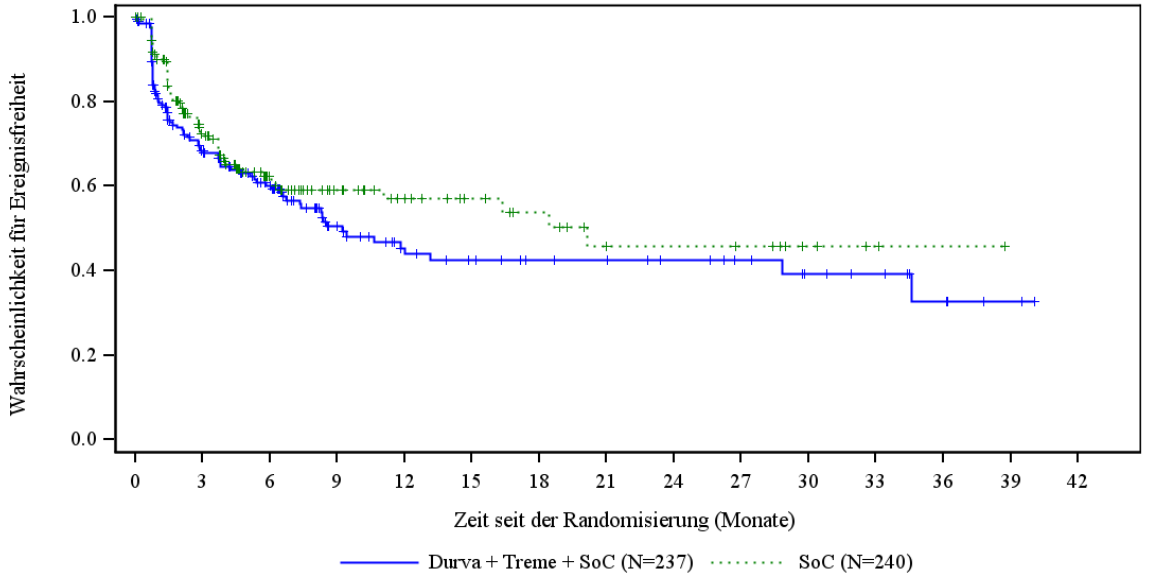
Durva + Treme + SoC	23	12	8	5	5	3	2	2	2	2	1	1	0
SoC	34	16	12	6	2	1	1	1	1	1	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc343g.sas Executed : 2022-11-21T224157

Figure 6.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 in cough (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	214	111	76	44	30	26	22	21	18	15	11	9	5	2	0
SoC	206	103	57	37	25	19	15	9	9	8	4	2	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	23 (11,8)	NE [NE; NE]	179	24 (13,4)	NE [NE; NE]	0,71	[0,40; 1,27]	0,2594
Weiblich	42	4 (9,5)	NE [31,3; NE]	61	8 (13,1)	NE [NE; NE]	0,64	[0,17; 2,03]	0,4416
Interaktion p-Wert									0,8738
Alter									
<65 Jahre	130	16 (12,3)	NE [NE; NE]	125	14 (11,2)	NE [NE; NE]	0,91	[0,44; 1,89]	0,8414
>/= 65 Jahre	107	11 (10,3)	NE [28,8; NE]	115	18 (15,7)	NE [13,1; NE]	0,56	[0,26; 1,17]	0,1206
Interaktion p-Wert									0,3652

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	7 (10,4)	NE [NE; NE]	83	16 (19,3)	NE [14,8; NE]	0,58	[0,22; 1,37]	0,2254
Nicht-Asiatisch	170	20 (11,8)	NE [NE; NE]	157	16 (10,2)	NE [NE; NE]	0,85	[0,44; 1,67]	0,6101
Interaktion p-Wert									0,5079
Performance status zu baseline									
0	82	11 (13,4)	NE [NE; NE]	78	13 (16,7)	NE [13,1; NE]	0,65	[0,28; 1,46]	0,3340
1	155	16 (10,3)	NE [31,3; NE]	162	19 (11,7)	NE [NE; NE]	0,75	[0,38; 1,46]	0,3605
Interaktion p-Wert									0,7833

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	12 (9,8)	NE [NE; NE]	120	14 (11,7)	NE [NE; NE]	0,68	[0,31; 1,47]	0,3750
Stadium IVB	112	15 (13,4)	NE [31,3; NE]	120	18 (15,0)	NE [14,8; NE]	0,78	[0,39; 1,55]	0,4382
Interaktion p-Wert									0,7893
Raucherstatus									
Aktiv	65	10 (15,4)	NE [NE; NE]	49	5 (10,2)	NE [NE; NE]	1,03	[0,36; 3,33]	0,7489
Ehemals	137	14 (10,2)	NE [NE; NE]	133	18 (13,5)	NE [NE; NE]	0,67	[0,33; 1,35]	0,2544
Nie	35	3 (8,6)	31,3 [NE; NE]	58	9 (15,5)	NE [NE; NE]	0,44	[0,10; 1,48]	0,2055
Interaktion p-Wert									0,6106

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	15 (10,8)	NE [31,3; NE]	125	12 (9,6)	NE [NE; NE]	0,85	[0,40; 1,87]	0,7150
Rest of the World	98	12 (12,2)	NE [NE; NE]	115	20 (17,4)	NE [NE; NE]	0,64	[0,31; 1,30]	0,2476
Interaktion p-Wert									0,6005

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	1 (8,3) NE	[4,5; NE]	12	1 (8,3) NE	[0,8; NE]	0,48	[0,02; 12,13]	0,5878
Pemetrexed-Doublette	142	19 (13,4) NE	[NE; NE]	146	20 (13,7) NE	[NE; NE]	0,85	[0,45; 1,59]	0,5700
Gemcitabin-Doublette	83	7 (8,4) NE	[NE; NE]	82	11 (13,4) NE	[13,1; NE]	0,52	[0,19; 1,34]	0,2268
Interaktion p-Wert									0,6825

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	8 (9,1)	NE [NE; NE]	90	12 (13,3)	NE [13,1; NE]	0,56	[0,22; 1,36]	0,2567
Nicht-Plattenepithelial	149	19 (12,8)	NE [NE; NE]	150	20 (13,3)	NE [NE; NE]	0,80	[0,42; 1,52]	0,4720
Interaktion p-Wert									0,5177
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	17 (13,6)	NE [28,8; NE]	130	16 (12,3)	NE [NE; NE]	0,91	[0,46; 1,82]	0,7087
PD-L1 >/=1%	112	10 (8,9)	NE [NE; NE]	110	16 (14,5)	NE [NE; NE]	0,52	[0,23; 1,14]	0,1615
Interaktion p-Wert									0,3000

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Table 6.7.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	3 (13,0)	NE [NE; NE]	34	7 (20,6)	NE [8,3; NE]	0,66	[0,14; 2,39]	0,6014
Nein	214	24 (11,2)	NE [NE; NE]	206	25 (12,1)	NE [NE; NE]	0,76	[0,43; 1,33]	0,3036
Interaktion p-Wert									0,8643

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc253g.sas Executed : 2022-10-17T232936

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Figure 6.7.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 hemoptysis (symptom) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc353g.sas Executed : 2022-11-21T224442

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	62 (31,8)	NE [11,3; NE]	179	52 (29,1)	23,9 [8,3; NE]	0,95	[0,66; 1,38]	0,7917
Weiblich	42	14 (33,3)	NE [2,2; NE]	61	21 (34,4)	14,2 [5,6; NE]	1,06	[0,53; 2,07]	0,8168
Interaktion p-Wert									0,7839
Alter									
<65 Jahre	130	33 (25,4)	NE [NE; NE]	125	36 (28,8)	NE [8,0; NE]	0,75	[0,47; 1,21]	0,2278
>/= 65 Jahre	107	43 (40,2)	9,3 [4,5; NE]	115	37 (32,2)	23,9 [8,5; NE]	1,25	[0,81; 1,95]	0,3312
Interaktion p-Wert									0,1216

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	4,5 [2,3; NE]	83	34 (41,0)	10,3 [4,7; NE]	1,37	[0,84; 2,22]	0,1873
Nicht-Asiatisch	170	44 (25,9)	NE [18,6; NE]	157	39 (24,8)	NE [14,2; NE]	0,84	[0,55; 1,31]	0,4961
Interaktion p-Wert									0,1449
Performance status zu baseline									
0	82	23 (28,0)	NE [10,1; NE]	78	26 (33,3)	8,5 [4,9; NE]	0,71	[0,40; 1,24]	0,2165
1	155	53 (34,2)	19,9 [5,8; NE]	162	47 (29,0)	23,9 [10,3; NE]	1,13	[0,76; 1,68]	0,5286
Interaktion p-Wert									0,1755

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	38 (30,9)	NE [11,3; NE]	120	40 (33,3)	10,3 [7,4; NE]	0,80	[0,51; 1,25]	0,3023
Stadium IVB	112	37 (33,0)	NE [5,1; NE]	120	33 (27,5)	23,9 [8,3; NE]	1,16	[0,72; 1,86]	0,5386
Interaktion p-Wert									0,2657
Raucherstatus									
Aktiv	65	13 (20,0)	NE [NE; NE]	49	13 (26,5)	8,3 [3,3; NE]	0,50	[0,23; 1,09]	0,0619
Ehemals	137	48 (35,0)	19,9 [5,8; NE]	133	43 (32,3)	23,9 [8,3; NE]	1,09	[0,72; 1,65]	0,6958
Nie	35	15 (42,9)	6,5 [2,2; NE]	58	17 (29,3)	NE [5,6; NE]	1,44	[0,71; 2,89]	0,3054
Interaktion p-Wert									0,1149

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	37 (26,6)	NE [18,6; NE]	125	30 (24,0)	NE [8,3; NE]	0,92	[0,57; 1,50]	0,7559
Rest of the World	98	39 (39,8)	10,1 [3,3; NE]	115	43 (37,4)	14,2 [5,7; NE]	1,08	[0,70; 1,66]	0,7366
Interaktion p-Wert									0,6375

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	3 (25,0)	NE [1,5; NE]	12	5 (41,7)	NE [0,8; NE]	0,31	[0,06; 1,26]	0,2109
Pemetrexed-Doublette	142	56 (39,4)	18,6 [5,7; NE]	146	51 (34,9)	23,9 [8,3; NE]	1,08	[0,74; 1,58]	0,6992
Gemcitabin-Doublette	83	17 (20,5)	NE [11,3; NE]	82	17 (20,7)	NE [7,4; NE]	0,90	[0,46; 1,78]	0,7585
Interaktion p-Wert									0,2480

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	19 (21,6)	NE [11,3; NE]	90	21 (23,3)	NE [7,4; NE]	0,82	[0,44; 1,53]	0,5349
Nicht-Plattenepithelial	149	57 (38,3)	19,9 [5,8; NE]	150	52 (34,7)	23,9 [8,3; NE]	1,03	[0,71; 1,50]	0,8673
Interaktion p-Wert									0,5407
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	37 (29,6)	NE [9,3; NE]	130	39 (30,0)	14,2 [8,3; NE]	0,83	[0,53; 1,31]	0,4714
PD-L1 >/=1%	112	39 (34,8)	19,9 [4,9; NE]	110	34 (30,9)	23,9 [8,3; NE]	1,12	[0,71; 1,79]	0,6021
Interaktion p-Wert									0,3640

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Table 6.8.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	9 (39,1)	3,3 [2,2; NE]	34	15 (44,1)	8,3 [2,8; 23,9]	0,99	[0,41; 2,22]	0,9931
Nein	214	67 (31,3)	NE [11,3; NE]	206	58 (28,2)	NE [10,3; NE]	1,00	[0,70; 1,43]	0,9488
Interaktion p-Wert									0,9721

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc263g.sas Executed : 2022-10-17T233345

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
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Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Figure 6.8.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 sore mouth (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc363g.sas Executed : 2022-11-21T224706

Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	63 (32,3)	23,2 [11,3; NE]	179	48 (26,8)	NE [26,7; NE]	1,09	[0,75; 1,59]	0,6104
Weiblich	42	15 (35,7)	31,5 [5,6; NE]	61	19 (31,1)	14,2 [7,9; NE]	1,11	[0,56; 2,19]	0,9010
Interaktion p-Wert									0,9598
Alter									
<65 Jahre	130	39 (30,0)	25,9 [14,1; NE]	125	31 (24,8)	NE [14,2; NE]	1,03	[0,65; 1,67]	0,9357
>/= 65 Jahre	107	39 (36,4)	31,5 [5,6; NE]	115	36 (31,3)	26,7 [8,3; NE]	1,18	[0,75; 1,87]	0,4467
Interaktion p-Wert									0,6819

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	28 (41,8)	9,2 [3,6; NE]	83	29 (34,9)	26,7 [8,3; NE]	1,43	[0,85; 2,40]	0,1638
Nicht-Asiatisch	170	50 (29,4)	31,5 [14,1; NE]	157	38 (24,2)	NE [14,2; NE]	0,98	[0,64; 1,50]	0,8803
Interaktion p-Wert									0,2701
Performance status zu baseline									
0	82	27 (32,9)	25,9 [8,0; NE]	78	22 (28,2)	NE [7,9; NE]	1,02	[0,58; 1,81]	0,9560
1	155	51 (32,9)	23,2 [9,1; NE]	162	45 (27,8)	NE [14,2; NE]	1,13	[0,76; 1,69]	0,5491
Interaktion p-Wert									0,7745

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	44 (35,8)	25,9 [9,5; NE]	120	31 (25,8)	NE [26,7; NE]	1,31	[0,83; 2,09]	0,2141
Stadium IVB	112	34 (30,4)	23,2 [8,7; NE]	120	36 (30,0)	14,2 [8,3; NE]	0,92	[0,57; 1,47]	0,6634
Interaktion p-Wert									0,2906
Raucherstatus									
Aktiv	65	15 (23,1)	NE [14,9; NE]	49	11 (22,4)	NE [3,5; NE]	0,66	[0,30; 1,48]	0,3361
Ehemals	137	53 (38,7)	11,3 [6,3; 25,9]	133	39 (29,3)	NE [14,2; NE]	1,41	[0,93; 2,14]	0,1021
Nie	35	10 (28,6)	31,5 [5,7; NE]	58	17 (29,3)	NE [7,9; NE]	0,85	[0,38; 1,83]	0,6890
Interaktion p-Wert									0,1818

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	40 (28,8)	NE [14,1; NE]	125	28 (22,4)	NE [NE; NE]	1,11	[0,69; 1,82]	0,6295
Rest of the World	98	38 (38,8)	23,2 [5,6; NE]	115	39 (33,9)	26,7 [12,0; NE]	1,12	[0,72; 1,76]	0,6216
Interaktion p-Wert									0,9767

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	3,7 [0,8; NE]	12	4 (33,3)	NE [0,8; NE]	0,98	[0,28; 3,87]	0,6329
Pemetrexed-Doublette	142	52 (36,6)	23,2 [9,1; NE]	146	44 (30,1)	NE [13,9; NE]	1,16	[0,78; 1,74]	0,4925
Gemcitabin-Doublette	83	20 (24,1)	NE [9,5; NE]	82	19 (23,2)	NE [NE; NE]	0,94	[0,50; 1,77]	0,8633
Interaktion p-Wert									0,8459

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	23 (26,1)	NE [9,5; NE]	90	22 (24,4)	NE [5,8; NE]	0,96	[0,53; 1,73]	0,9145
Nicht-Plattenepithelial	149	55 (36,9)	23,2 [9,1; NE]	150	45 (30,0)	NE [13,9; NE]	1,16	[0,78; 1,72]	0,4844
Interaktion p-Wert									0,5945
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	38 (30,4)	31,5 [9,7; NE]	130	35 (26,9)	NE [12,0; NE]	1,02	[0,65; 1,63]	0,9925
PD-L1 >/=1%	112	40 (35,7)	23,2 [5,7; NE]	110	32 (29,1)	NE [26,7; NE]	1,16	[0,73; 1,86]	0,4544
Interaktion p-Wert									0,7096

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.9.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	5 (21,7)	NE [2,8; NE]	34	12 (35,3)	14,2 [4,7; NE]	0,59	[0,19; 1,58]	0,3034
Nein	214	73 (34,1)	23,2 [9,7; NE]	206	55 (26,7)	NE [26,7; NE]	1,18	[0,83; 1,69]	0,3412
Interaktion p-Wert									0,2109

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc373g.sas Executed : 2022-11-21T224948

Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc373g.sas Executed : 2022-11-21T224948

Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc373g.sas Executed : 2022-11-21T224948

Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc373g.sas Executed : 2022-11-21T224948

Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc373g.sas Executed : 2022-11-21T224948

Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.9.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 dysphagia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	88 (45,1)	6,4 [4,7; 10,2]	179	77 (43,0)	6,6 [4,6; 9,9]	0,97	[0,72; 1,33]	0,8440
Weiblich	42	17 (40,5)	6,4 [2,8; NE]	61	25 (41,0)	9,4 [3,7; NE]	1,03	[0,55; 1,90]	0,8463
Interaktion p-Wert									0,8713
Alter									
<65 Jahre	130	58 (44,6)	6,4 [4,2; 11,3]	125	54 (43,2)	6,5 [3,7; 9,4]	0,92	[0,64; 1,34]	0,6726
>/= 65 Jahre	107	47 (43,9)	6,8 [4,7; 11,3]	115	48 (41,7)	7,0 [4,6; 18,5]	1,11	[0,74; 1,66]	0,6735
Interaktion p-Wert									0,5101

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	5,7 [2,8; 10,2]	83	39 (47,0)	7,2 [4,6; 29,1]	1,22	[0,76; 1,95]	0,3793
Nicht-Asiatisch	170	73 (42,9)	7,7 [4,9; 12,1]	157	63 (40,1)	6,5 [4,4; 10,0]	0,91	[0,65; 1,28]	0,5572
Interaktion p-Wert									0,3091
Performance status zu baseline									
0	82	37 (45,1)	7,9 [5,7; 14,4]	78	33 (42,3)	6,5 [3,4; NE]	0,94	[0,59; 1,52]	0,8078
1	155	68 (43,9)	5,6 [4,2; 10,2]	162	69 (42,6)	6,7 [4,7; 10,0]	1,04	[0,74; 1,46]	0,8101
Interaktion p-Wert									0,7395

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	56 (45,5)	7,7 [4,7; 12,2]	120	53 (44,2)	6,7 [4,6; 10,3]	0,92	[0,63; 1,35]	0,6474
Stadium IVB	112	48 (42,9)	5,6 [3,0; 10,2]	120	49 (40,8)	6,5 [3,9; 18,5]	1,12	[0,75; 1,67]	0,5907
Interaktion p-Wert									0,4916
Raucherstatus									
Aktiv	65	31 (47,7)	5,6 [2,4; 12,1]	49	18 (36,7)	6,2 [2,9; NE]	0,95	[0,54; 1,74]	0,9911
Ehemals	137	59 (43,1)	5,8 [4,9; 11,3]	133	61 (45,9)	6,7 [4,6; 10,0]	1,01	[0,70; 1,44]	0,9623
Nie	35	15 (42,9)	10,7 [3,7; NE]	58	23 (39,7)	10,6 [3,5; NE]	0,93	[0,47; 1,76]	0,8489
Interaktion p-Wert									0,9725

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	57 (41,0)	7,9 [4,7; 14,4]	125	48 (38,4)	6,7 [3,9; 10,6]	0,95	[0,64; 1,40]	0,8170
Rest of the World	98	48 (49,0)	5,7 [3,7; 8,7]	115	54 (47,0)	6,6 [4,6; 10,3]	1,09	[0,74; 1,61]	0,6226
Interaktion p-Wert									0,6168

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	7 (58,3)	2,5 [1,4; NE]	12	6 (50,0)	2,1 [0,8; NE]	0,75	[0,25; 2,33]	0,7221
Pemetrexed-Doublette	142	69 (48,6)	6,4 [4,9; 10,2]	146	68 (46,6)	6,7 [4,6; 10,6]	1,04	[0,75; 1,46]	0,8063
Gemcitabin-Doublette	83	29 (34,9)	14,4 [3,7; NE]	82	28 (34,1)	7,4 [3,9; NE]	0,95	[0,56; 1,60]	0,8506
Interaktion p-Wert									0,8288

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	32 (36,4)	8,4 [3,5; NE]	90	33 (36,7)	6,5 [3,9; 9,9]	0,90	[0,55; 1,46]	0,6930
Nicht-Plattenepithelial	149	73 (49,0)	6,4 [4,9; 10,2]	150	69 (46,0)	6,7 [4,6; 10,6]	1,06	[0,76; 1,47]	0,7346
Interaktion p-Wert									0,5762
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	54 (43,2)	6,8 [4,9; 14,4]	130	48 (36,9)	8,1 [6,2; NE]	1,08	[0,73; 1,60]	0,6583
PD-L1 >/=1%	112	51 (45,5)	6,4 [3,0; 11,3]	110	54 (49,1)	5,1 [3,7; 9,9]	0,94	[0,64; 1,38]	0,7242
Interaktion p-Wert									0,6241

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.10.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	11 (47,8)	2,8 [1,6; NE]	34	13 (38,2)	9,4 [2,9; NE]	1,75	[0,77; 3,92]	0,1651
Nein	214	94 (43,9)	6,8 [5,1; 10,7]	206	89 (43,2)	6,6 [4,6; 10,0]	0,95	[0,71; 1,27]	0,7021
Interaktion p-Wert									0,1575

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Figure 6.10.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 peripheral neuropathy (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc383g.sas Executed : 2022-11-21T225207

Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	89 (45,6)	4,6 [3,4; 18,4]	179	70 (39,1)	8,3 [4,5; NE]	1,17	[0,86; 1,60]	0,3075
Weiblich	42	24 (57,1)	2,8 [1,2; 8,4]	61	32 (52,5)	6,2 [2,3; 10,2]	1,36	[0,79; 2,30]	0,2348
Interaktion p-Wert									0,6280
Alter									
<65 Jahre	130	60 (46,2)	4,2 [2,8; 28,8]	125	53 (42,4)	8,3 [3,7; 11,1]	1,06	[0,74; 1,55]	0,7562
>/= 65 Jahre	107	53 (49,5)	4,1 [2,4; 10,2]	115	49 (42,6)	6,5 [3,9; NE]	1,30	[0,88; 1,92]	0,1861
Interaktion p-Wert									0,4715

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	32 (47,8)	4,6 [2,2; NE]	83	40 (48,2)	9,1 [2,8; NE]	1,18	[0,74; 1,88]	0,4690
Nicht-Asiatisch	170	81 (47,6)	4,2 [2,8; 10,2]	157	62 (39,5)	5,7 [3,7; 10,2]	1,15	[0,83; 1,61]	0,4087
Interaktion p-Wert									0,9289
Performance status zu baseline									
0	82	44 (53,7)	4,0 [2,1; 6,7]	78	31 (39,7)	9,9 [3,9; NE]	1,43	[0,91; 2,29]	0,1300
1	155	69 (44,5)	4,2 [2,9; 20,0]	162	71 (43,8)	5,7 [3,7; 9,2]	1,05	[0,75; 1,46]	0,7624
Interaktion p-Wert									0,2827

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	67 (54,5)	3,6 [2,1; 6,7]	120	47 (39,2)	9,8 [4,7; 23,0]	1,52	[1,05; 2,22]	0,0298
Stadium IVB	112	45 (40,2)	8,6 [3,7; NE]	120	55 (45,8)	5,0 [2,8; 9,1]	0,86	[0,58; 1,28]	0,4507
Interaktion p-Wert									0,0406
Raucherstatus									
Aktiv	65	33 (50,8)	4,6 [1,6; 15,9]	49	18 (36,7)	7,9 [2,1; 9,8]	1,21	[0,69; 2,20]	0,5368
Ehemals	137	64 (46,7)	4,2 [3,0; 9,7]	133	57 (42,9)	6,5 [3,7; NE]	1,19	[0,84; 1,71]	0,3288
Nie	35	16 (45,7)	8,4 [1,4; NE]	58	27 (46,6)	6,5 [3,7; 10,2]	1,00	[0,52; 1,83]	0,9993
Interaktion p-Wert									0,8692

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	66 (47,5)	3,8 [2,1; 8,6]	125	48 (38,4)	8,3 [3,1; NE]	1,26	[0,87; 1,84]	0,1761
Rest of the World	98	47 (48,0)	5,8 [3,0; 18,4]	115	54 (47,0)	7,9 [4,6; 11,8]	1,06	[0,71; 1,56]	0,7979
Interaktion p-Wert									0,5145

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	11 (91,7)	0,8 [0,8; 0,8]	12	9 (75,0)	1,2 [0,8; 2,1]	2,96	[1,20; 7,45]	0,0100
Pemetrexed-Doublette	142	69 (48,6)	5,6 [3,6; 15,9]	146	57 (39,0)	9,9 [6,5; NE]	1,30	[0,92; 1,85]	0,1453
Gemcitabin-Doublette	83	33 (39,8)	4,2 [2,1; NE]	82	36 (43,9)	4,5 [2,8; 7,9]	0,89	[0,55; 1,42]	0,6585
Interaktion p-Wert									0,0608

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc293g.sas Executed : 2022-10-17T234659

Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	38 (43,2)	4,2 [1,7; NE]	90	42 (46,7)	4,1 [2,1; 5,7]	0,91	[0,58; 1,41]	0,7232
Nicht-Plattenepithelial	149	75 (50,3)	4,6 [3,0; 10,2]	150	60 (40,0)	9,8 [6,2; NE]	1,34	[0,96; 1,89]	0,0888
Interaktion p-Wert									0,1711
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	57 (45,6)	5,6 [3,4; 18,4]	130	55 (42,3)	6,5 [3,9; 23,0]	1,11	[0,76; 1,61]	0,6016
PD-L1 >/=1%	112	56 (50,0)	4,0 [2,2; 10,2]	110	47 (42,7)	7,9 [3,5; 11,1]	1,24	[0,84; 1,83]	0,2807
Interaktion p-Wert									0,6842

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc293g.sas Executed : 2022-10-17T234659

Table 6.11.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	9 (39,1)	3,0 [0,8; NE]	34	20 (58,8)	3,5 [1,4; 8,3]	0,67	[0,29; 1,44]	0,3554
Nein	214	104 (48,6)	4,2 [3,1; 8,6]	206	82 (39,8)	8,3 [5,3; 11,8]	1,28	[0,96; 1,72]	0,0972
Interaktion p-Wert									0,1324

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc293g.sas Executed : 2022-10-17T234659

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

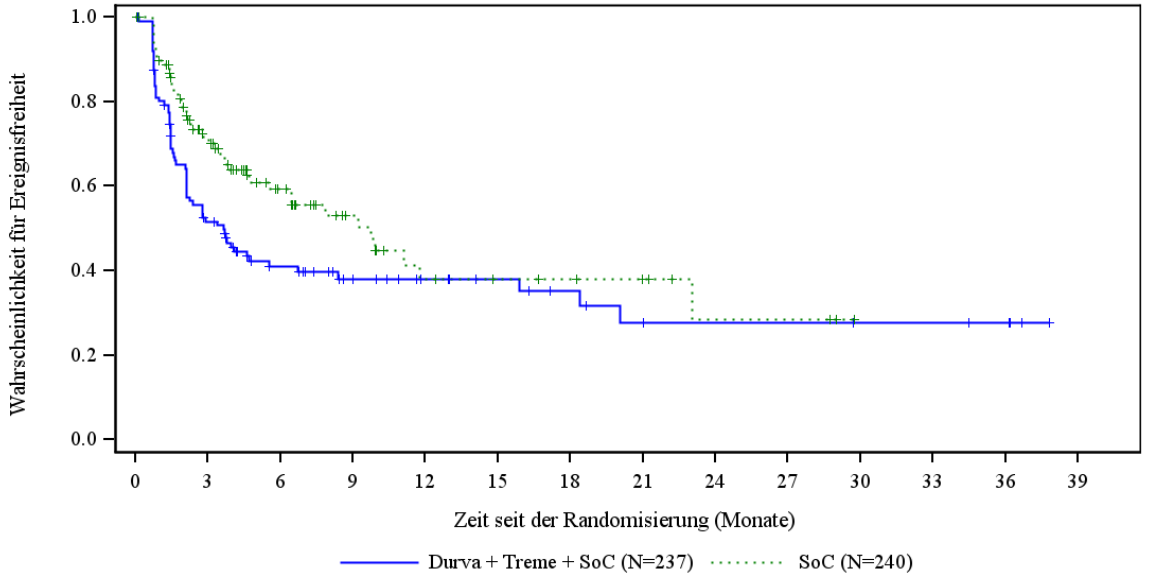
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA



Anzahl an Patienten unter Risiko

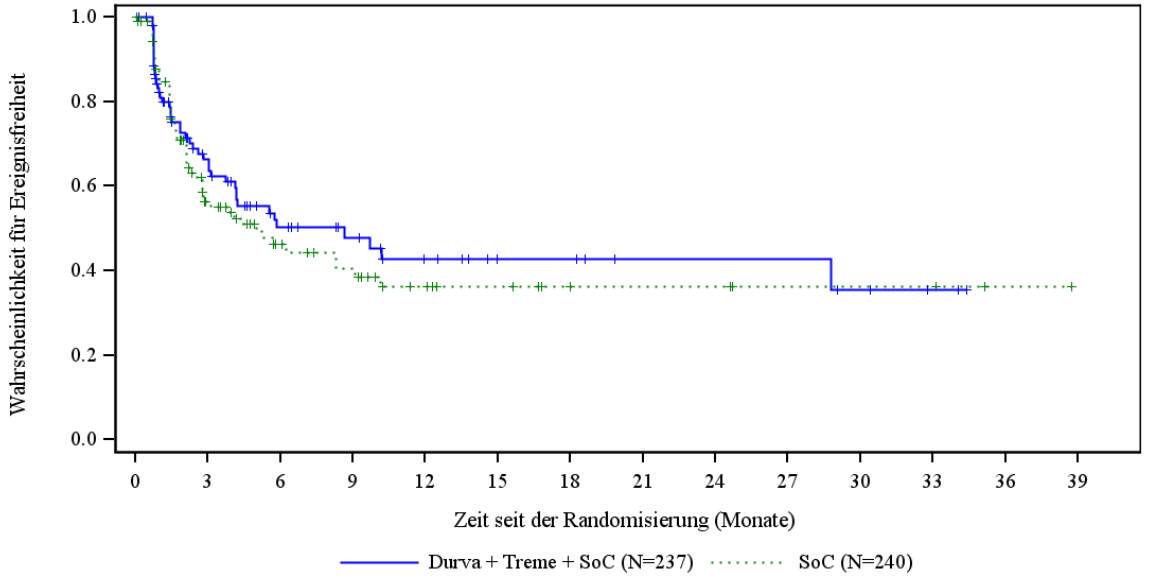
Durva + Treme + SoC	123	53	32	22	16	13	10	7	6	6	5	5	4	0
SoC	120	62	33	19	11	9	8	6	3	3	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	112	50	29	20	14	9	9	6	6	6	4	2	0	0
SoC	120	46	27	21	13	9	6	5	5	3	3	3	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\lc393g.sas Executed : 2022-11-21T225450

Figure 6.11.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-LC13 alopecia (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Anhang 4-G 1.3.2.3: EQ-5D-5L VAS - Gesundheitszustand

Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	57 (29,2)	NE [11,8; NE]	179	48 (26,8)	26,8 [14,8; NE]	0,98	[0,67; 1,45]	0,9524
Weiblich	42	13 (31,0)	NE [8,1; NE]	61	18 (29,5)	NE [7,4; NE]	0,99	[0,48; 2,02]	0,9704
Interaktion p-Wert									0,9818
Alter									
<65 Jahre	130	40 (30,8)	21,6 [11,3; NE]	125	36 (28,8)	26,8 [26,8; NE]	0,94	[0,60; 1,49]	0,8330
>/= 65 Jahre	107	30 (28,0)	NE [9,0; NE]	115	30 (26,1)	NE [10,3; NE]	1,02	[0,61; 1,70]	0,9246
Interaktion p-Wert									0,8153

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	22 (32,8)	NE [6,5; NE]	83	27 (32,5)	NE [10,3; NE]	1,18	[0,67; 2,07]	0,5893
Nicht-Asiatisch	170	48 (28,2)	NE [11,8; NE]	157	39 (24,8)	26,8 [14,8; NE]	0,91	[0,60; 1,40]	0,6039
Interaktion p-Wert									0,4713
Performance status zu baseline									
0	82	21 (25,6)	NE [11,6; NE]	78	16 (20,5)	NE [NE; NE]	1,13	[0,59; 2,20]	0,7313
1	155	49 (31,6)	19,4 [9,0; NE]	162	50 (30,9)	26,8 [10,3; NE]	0,95	[0,64; 1,41]	0,8057
Interaktion p-Wert									0,6491

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	41 (33,3)	19,4 [10,7; NE]	120	31 (25,8)	26,8 [26,8; NE]	1,24	[0,78; 1,99]	0,4166
Stadium IVB	112	28 (25,0)	NE [NE; NE]	120	35 (29,2)	NE [14,8; NE]	0,75	[0,45; 1,23]	0,3108
Interaktion p-Wert									0,1517
Raucherstatus									
Aktiv	65	18 (27,7)	NE [7,9; NE]	49	8 (16,3)	NE [NE; NE]	1,43	[0,64; 3,50]	0,3073
Ehemals	137	44 (32,1)	19,4 [10,7; NE]	133	39 (29,3)	26,8 [14,8; NE]	1,09	[0,71; 1,69]	0,6857
Nie	35	8 (22,9)	NE [8,1; NE]	58	19 (32,8)	NE [2,8; NE]	0,51	[0,21; 1,13]	0,1039
Interaktion p-Wert									0,1823

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va203g.sas Executed : 2022-10-18T081835

Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	37 (26,6)	NE [11,6; NE]	125	28 (22,4)	26,8 [26,8; NE]	1,03	[0,63; 1,69]	0,9821
Rest of the World	98	33 (33,7)	NE [6,9; NE]	115	38 (33,0)	NE [10,3; NE]	0,99	[0,62; 1,58]	0,9911
Interaktion p-Wert									0,9168

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	9,0 [0,8; NE]	12	3 (25,0)	NE [0,8; NE]	1,57	[0,41; 7,45]	0,8690
Pemetrexed-Doublette	142	48 (33,8)	NE [9,0; NE]	146	46 (31,5)	26,8 [10,3; NE]	1,02	[0,68; 1,53]	0,9053
Gemcitabin-Doublette	83	16 (19,3)	NE [11,8; NE]	82	17 (20,7)	NE [NE; NE]	0,81	[0,41; 1,61]	0,5873
Interaktion p-Wert									0,6799

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	17 (19,3)	NE [11,8; NE]	90	19 (21,1)	NE [NE; NE]	0,80	[0,41; 1,54]	0,5375
Nicht-Plattenepithelial	149	53 (35,6)	21,6 [8,1; NE]	150	47 (31,3)	26,8 [10,3; NE]	1,07	[0,72; 1,59]	0,7356
Interaktion p-Wert									0,4461
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	41 (32,8)	21,6 [7,9; NE]	130	33 (25,4)	26,8 [26,8; NE]	1,27	[0,80; 2,01]	0,3241
PD-L1 >/=1%	112	29 (25,9)	NE [11,6; NE]	110	33 (30,0)	NE [10,3; NE]	0,73	[0,44; 1,21]	0,2201
Interaktion p-Wert									0,1143

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va203g.sas Executed : 2022-10-18T081835

Table 7.2.2.1 Summary of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	3 (13,0)	NE [5,4; NE]	34	8 (23,5)	NE [4,6; NE]	0,52	[0,11; 1,80]	0,3798
Nein	214	67 (31,3)	21,6 [11,3; NE]	206	58 (28,2)	26,8 [14,8; NE]	1,01	[0,71; 1,44]	0,9475
Interaktion p-Wert									0,3459

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=10) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va203g.sas Executed : 2022-10-18T081835

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\va303g.sas Executed : 2022-11-21T225959

Figure 7.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EQ-5D VAS
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase from baseline score of >=15) in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Anhang 4-G 1.3.2.4: PGIC – Gesundheitszustand

Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	15 (7,7)	NE [NE; NE]	179	21 (11,7)	NE [26,1; NE]	0,50	[0,25; 0,98]	0,0403
Weiblich	42	5 (11,9)	NE [NE; NE]	61	2 (3,3)	NE [NE; NE]	3,32	[0,71; 23,18]	0,1339
Interaktion p-Wert									0,0370
Alter									
<65 Jahre	130	7 (5,4)	NE [NE; NE]	125	11 (8,8)	NE [NE; NE]	0,48	[0,18; 1,22]	0,1510
>/= 65 Jahre	107	13 (12,1)	NE [NE; NE]	115	12 (10,4)	NE [26,1; NE]	1,00	[0,45; 2,22]	0,9507
Interaktion p-Wert									0,2428

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	9 (13,4)	NE [27,4; NE]	83	7 (8,4)	NE [26,1; NE]	1,90	[0,71; 5,34]	0,2260
Nicht-Asiatisch	170	11 (6,5)	NE [NE; NE]	157	16 (10,2)	NE [NE; NE]	0,42	[0,19; 0,91]	0,0306
Interaktion p-Wert									0,0192
Performance status zu baseline									
0	82	8 (9,8)	NE [NE; NE]	78	8 (10,3)	NE [NE; NE]	0,74	[0,27; 2,02]	0,4718
1	155	12 (7,7)	NE [NE; NE]	162	15 (9,3)	NE [26,1; NE]	0,70	[0,32; 1,50]	0,4086
Interaktion p-Wert									0,9330

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	12 (9,8)	NE [NE; NE]	120	9 (7,5)	NE [26,1; NE]	1,06	[0,45; 2,60]	0,8742
Stadium IVB	112	8 (7,1)	NE [NE; NE]	120	14 (11,7)	NE [NE; NE]	0,51	[0,20; 1,18]	0,1426
Interaktion p-Wert									0,2367
Raucherstatus									
Aktiv	65	4 (6,2)	NE [NE; NE]	49	3 (6,1)	NE [NE; NE]	0,56	[0,12; 2,86]	0,4248
Ehemals	137	15 (10,9)	NE [NE; NE]	133	19 (14,3)	NE [26,1; NE]	0,69	[0,35; 1,36]	0,2951
Nie	35	1 (2,9)	NE [NE; NE]	58	1 (1,7)	NE [NE; NE]	1,31	[0,05; 33,21]	0,8979
Interaktion p-Wert									0,8688

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	8 (5,8)	NE [NE; NE]	125	14 (11,2)	NE [14,8; NE]	0,34	[0,14; 0,81]	0,0146
Rest of the World	98	12 (12,2)	NE [NE; NE]	115	9 (7,8)	NE [26,1; NE]	1,52	[0,64; 3,72]	0,3735
Interaktion p-Wert									0,0178

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	1 (8,3)	NE [NE; NE]	12	3 (25,0)	NE [0,8; NE]	0,12	[0,01; 0,98]	0,2243
Pemetrexed-Doublette	142	13 (9,2)	NE [NE; NE]	146	15 (10,3)	NE [NE; NE]	0,76	[0,36; 1,60]	0,4575
Gemcitabin-Doublette	83	6 (7,2)	NE [NE; NE]	82	5 (6,1)	NE [10,8; NE]	0,95	[0,28; 3,31]	0,8707
Interaktion p-Wert									0,2786

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	7 (8,0)	NE [NE; NE]	90	7 (7,8)	NE [10,8; NE]	0,82	[0,28; 2,41]	0,7082
Nicht-Plattenepithelial	149	13 (8,7)	NE [NE; NE]	150	16 (10,7)	NE [NE; NE]	0,67	[0,32; 1,39]	0,2816
Interaktion p-Wert									0,7525
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	12 (9,6)	NE [NE; NE]	130	14 (10,8)	NE [26,1; NE]	0,74	[0,34; 1,61]	0,4596
PD-L1 >/=1%	112	8 (7,1)	NE [NE; NE]	110	9 (8,2)	NE [NE; NE]	0,70	[0,26; 1,83]	0,4790
Interaktion p-Wert									0,9162

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 8.2.2.1 Summary of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	2 (8,7)	NE [9,1; NE]	34	4 (11,8)	NE [18,0; NE]	0,76	[0,11; 3,92]	0,8312
Nein	214	18 (8,4)	NE [NE; NE]	206	19 (9,2)	NE [NE; NE]	0,73	[0,38; 1,39]	0,3323
Interaktion p-Wert									0,9560

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of much worse or "very much worse") in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach.
[c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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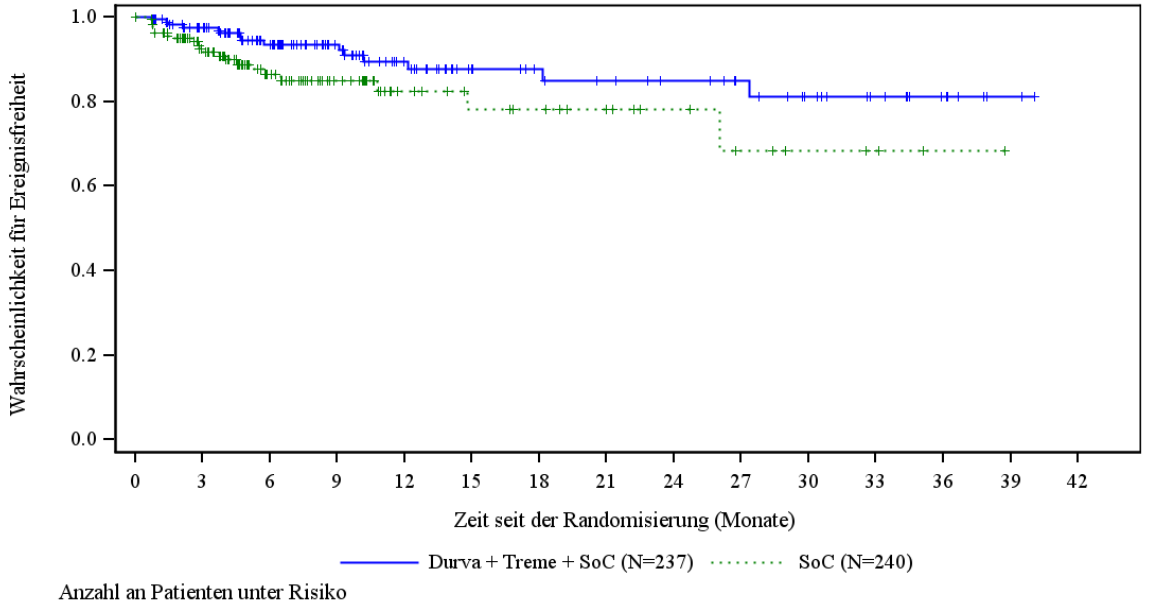
Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	195	145	103	73	51	36	32	29	26	22	17	12	7	2	0
SoC	179	110	65	42	25	19	16	12	9	6	4	3	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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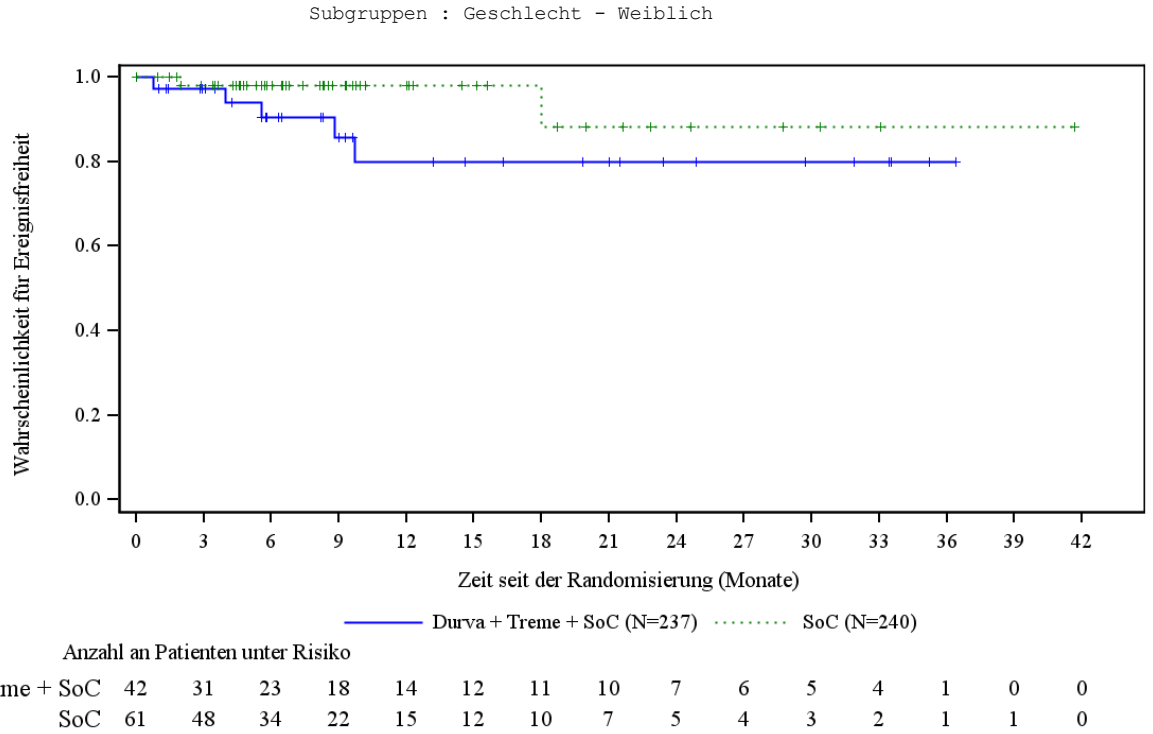
Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

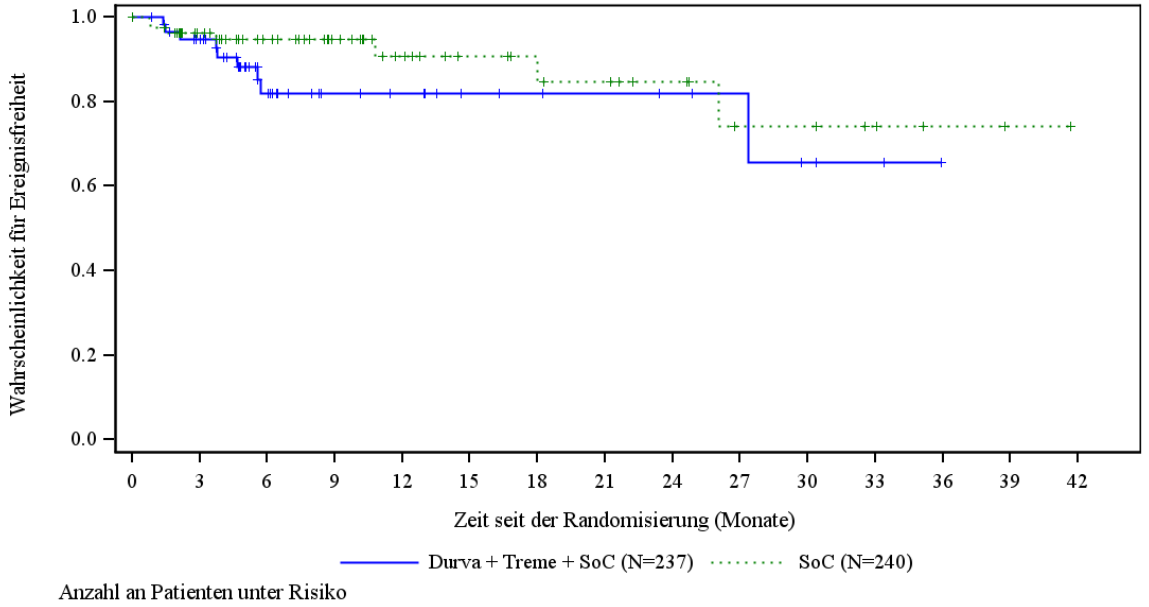
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	67	50	26	15	13	9	8	7	6	5	3	2	0	0	0
SoC	83	62	43	32	22	17	15	13	10	6	6	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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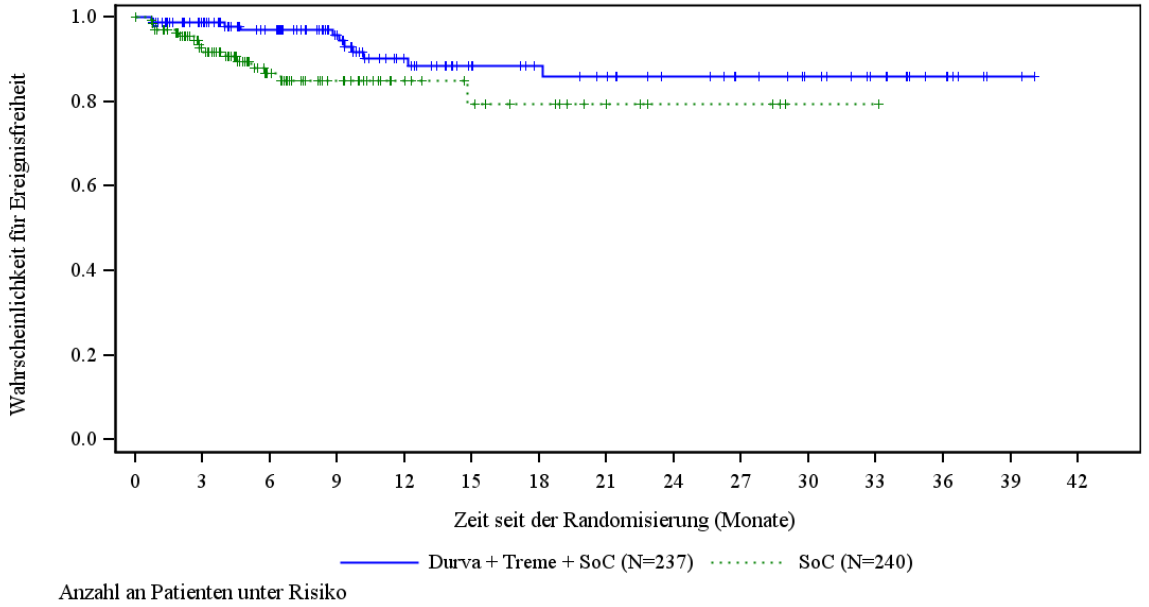
Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	170	126	100	76	52	39	35	32	27	23	19	14	8	2	0
SoC	157	96	56	32	18	14	11	6	4	4	1	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
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+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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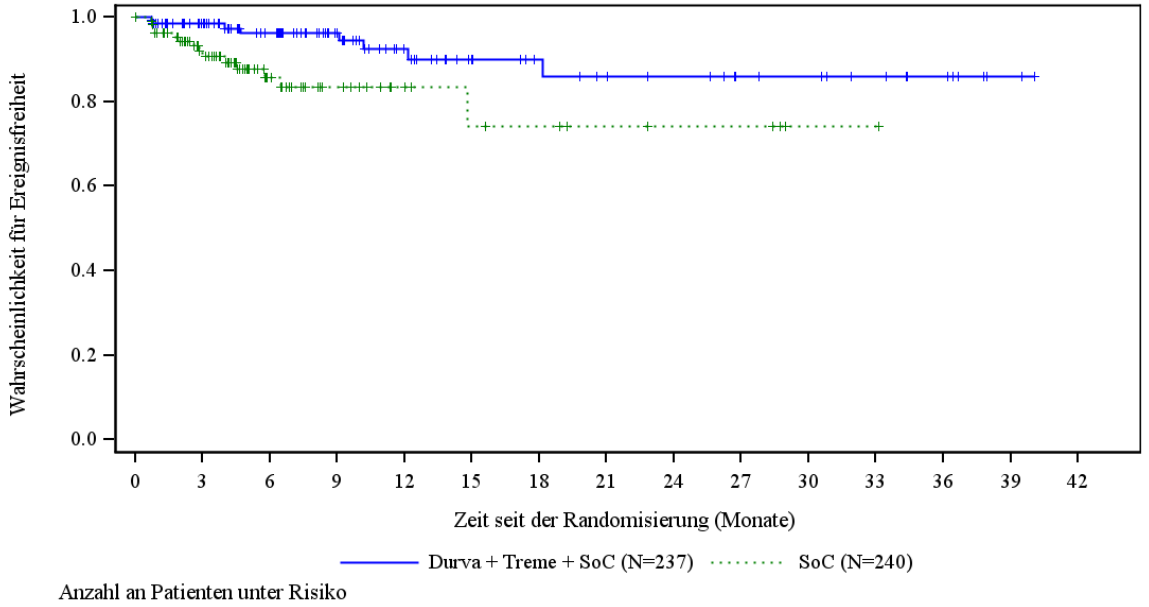
Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	139	101	77	57	38	27	23	20	18	14	13	10	7	2	0
SoC	125	74	38	18	10	8	7	5	4	4	1	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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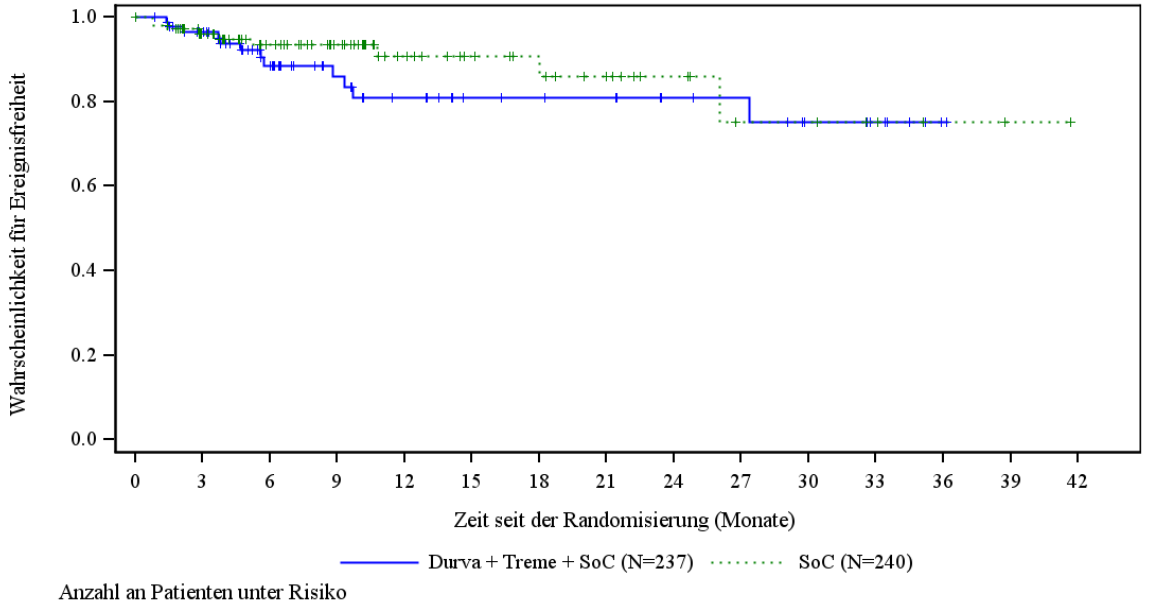
Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	98	75	49	34	27	21	20	19	15	14	9	6	1	0	0
SoC	115	84	61	46	30	23	19	14	10	6	6	4	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\pg303g.sas Executed : 2022-11-21T225728

Figure 8.2.2.2 Kaplan-Meier of subgroup analyses of time to first worsening of PGIC
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to worsening is defined as the time from date of randomization until the earliest of the dates of a worsening (any rating of "much worse" or "very much worse") in score.
For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Anhang 4-G 1.3.3: Gesundheitsbezogene Lebensqualität

Anhang 4-G 1.3.3.1: EORTC QLQ-C30 – Globaler Gesundheitsstatus

Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	87 (44,6)	6,2 [3,6; 13,9]	179	84 (46,9)	4,9 [3,1; 7,5]	0,90	[0,66; 1,21]	0,4667
Weiblich	42	20 (47,6)	3,9 [1,7; NE]	61	26 (42,6)	8,7 [2,2; NE]	1,15	[0,63; 2,05]	0,6374
Interaktion p-Wert									0,4629
Alter									
<65 Jahre	130	55 (42,3)	10,0 [3,6; NE]	125	49 (39,2)	7,5 [3,3; NE]	1,02	[0,69; 1,50]	0,8581
>/= 65 Jahre	107	52 (48,6)	4,0 [2,2; 9,3]	115	61 (53,0)	3,9 [2,2; 6,6]	0,91	[0,62; 1,31]	0,5929
Interaktion p-Wert									0,6668

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	37 (55,2)	3,3 [2,1; 5,7]	83	48 (57,8)	6,2 [2,2; 11,8]	1,11	[0,72; 1,70]	0,6084
Nicht-Asiatisch	170	70 (41,2)	9,3 [5,1; 22,8]	157	62 (39,5)	5,8 [3,1; NE]	0,91	[0,65; 1,29]	0,6618
Interaktion p-Wert									0,4821
Performance status zu baseline									
0	82	43 (52,4)	3,6 [1,5; 8,3]	78	36 (46,2)	7,4 [3,3; 16,7]	1,28	[0,83; 2,01]	0,2771
1	155	64 (41,3)	9,3 [3,8; 20,3]	162	74 (45,7)	4,9 [2,8; 16,3]	0,80	[0,57; 1,12]	0,2239
Interaktion p-Wert									0,0968

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	58 (47,2)	6,1 [3,0; 13,9]	120	57 (47,5)	7,2 [2,8; 16,3]	0,95	[0,66; 1,37]	0,7641
Stadium IVB	112	49 (43,8)	6,2 [2,3; 22,8]	120	53 (44,2)	4,5 [2,8; 16,7]	0,97	[0,66; 1,44]	0,9539
Interaktion p-Wert									0,9253
Raucherstatus									
Aktiv	65	27 (41,5)	8,3 [2,1; NE]	49	19 (38,8)	3,7 [1,9; NE]	0,87	[0,48; 1,58]	0,7232
Ehemals	137	65 (47,4)	3,9 [2,8; 9,3]	133	71 (53,4)	4,7 [2,8; 7,2]	0,90	[0,64; 1,26]	0,5200
Nie	35	15 (42,9)	19,8 [1,7; NE]	58	20 (34,5)	24,6 [2,9; NE]	1,14	[0,57; 2,22]	0,7483
Interaktion p-Wert									0,7992

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	55 (39,6)	13,9 [4,0; NE]	125	53 (42,4)	4,2 [2,8; NE]	0,84	[0,58; 1,23]	0,4076
Rest of the World	98	52 (53,1)	3,8 [2,2; 8,3]	115	57 (49,6)	7,2 [2,9; 16,3]	1,10	[0,76; 1,61]	0,6044
Interaktion p-Wert									0,3176

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	3,8 [1,4; NE]	12	5 (41,7)	NE [0,8; NE]	0,75	[0,22; 2,60]	0,8800
Pemetrexed-Doublette	142	70 (49,3)	5,7 [2,3; 19,8]	146	71 (48,6)	6,5 [2,8; 16,3]	0,96	[0,69; 1,33]	0,8341
Gemcitabin-Doublette	83	31 (37,3)	9,3 [5,1; 14,4]	82	34 (41,5)	4,7 [2,8; NE]	0,97	[0,59; 1,58]	0,8281
Interaktion p-Wert									0,9217

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	34 (38,6)	9,3 [3,8; 13,9]	90	38 (42,2)	4,7 [2,8; NE]	0,97	[0,61; 1,54]	0,8200
Nicht-Plattenepithelial	149	73 (49,0)	5,7 [2,8; 19,8]	150	72 (48,0)	6,5 [2,8; 16,3]	0,94	[0,68; 1,31]	0,7798
Interaktion p-Wert									0,9286
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	60 (48,0)	5,3 [2,2; 13,9]	130	58 (44,6)	7,2 [2,2; 24,6]	0,99	[0,69; 1,42]	0,9883
PD-L1 >/=1%	112	47 (42,0)	6,1 [3,0; 20,3]	110	52 (47,3)	4,9 [2,9; 11,8]	0,90	[0,61; 1,34]	0,6864
Interaktion p-Wert									0,7329

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.16.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	2,2 [0,8; NE]	34	23 (67,6)	2,1 [1,4; 2,8]	0,73	[0,35; 1,44]	0,5437
Nein	214	95 (44,4)	6,5 [3,8; 14,4]	206	87 (42,2)	7,4 [4,5; 16,7]	1,03	[0,77; 1,38]	0,8683
Interaktion p-Wert									0,3731

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs2133g.sas Executed : 2022-10-17T214444

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Figure 5.16.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 global health status (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs3133g.sas Executed : 2022-11-21T222921

Anhang 4-G 1.3.3.2: EORTC QLQ-C30 – Funktionsskalen

Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	105 (53,8)	4,9 [3,7; 6,7]	179	89 (49,7)	3,7 [2,8; 8,0]	0,98	[0,74; 1,30]	0,8923
Weiblich	42	22 (52,4)	4,0 [2,1; 33,2]	61	33 (54,1)	3,5 [2,0; 14,8]	0,88	[0,50; 1,50]	0,6389
Interaktion p-Wert									0,7280
Alter									
<65 Jahre	130	72 (55,4)	5,5 [2,8; 8,5]	125	60 (48,0)	4,5 [2,8; 12,2]	1,05	[0,75; 1,48]	0,7922
>/= 65 Jahre	107	55 (51,4)	4,2 [3,0; 6,0]	115	62 (53,9)	3,4 [2,2; 6,2]	0,86	[0,60; 1,24]	0,4902
Interaktion p-Wert									0,4321

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	44 (65,7)	3,0 [2,1; 4,2]	83	50 (60,2)	4,6 [2,1; 8,0]	1,41	[0,94; 2,12]	0,0806
Nicht-Asiatisch	170	83 (48,8)	6,3 [4,2; 9,3]	157	72 (45,9)	3,7 [2,8; 7,9]	0,82	[0,59; 1,12]	0,2135
Interaktion p-Wert									0,0383
Performance status zu baseline									
0	82	42 (51,2)	5,9 [2,8; 11,3]	78	39 (50,0)	3,5 [2,1; 9,1]	0,86	[0,56; 1,34]	0,5411
1	155	85 (54,8)	4,7 [3,7; 6,1]	162	83 (51,2)	3,7 [2,8; 8,0]	1,00	[0,74; 1,36]	0,9971
Interaktion p-Wert									0,5812

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	68 (55,3)	4,7 [2,8; 7,1]	120	64 (53,3)	3,7 [2,6; 6,4]	0,95	[0,67; 1,34]	0,7929
Stadium IVB	112	58 (51,8)	4,7 [3,7; 6,8]	120	58 (48,3)	4,2 [2,4; 12,7]	0,98	[0,68; 1,41]	0,9259
Interaktion p-Wert									0,8893
Raucherstatus									
Aktiv	65	26 (40,0)	9,2 [3,8; NE]	49	24 (49,0)	2,3 [1,5; 3,7]	0,46	[0,26; 0,80]	0,0100
Ehemals	137	79 (57,7)	4,2 [2,8; 6,1]	133	72 (54,1)	4,2 [2,8; 8,0]	1,08	[0,78; 1,49]	0,6468
Nie	35	22 (62,9)	3,7 [2,1; 7,1]	58	26 (44,8)	7,5 [2,8; 18,4]	1,42	[0,80; 2,51]	0,2040
Interaktion p-Wert									0,0101

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	66 (47,5)	6,2 [4,2; 9,2]	125	58 (46,4)	3,7 [2,7; 5,8]	0,80	[0,56; 1,15]	0,2346
Rest of the World	98	61 (62,2)	3,7 [2,2; 4,9]	115	64 (55,7)	4,6 [2,2; 8,0]	1,19	[0,84; 1,70]	0,3263
Interaktion p-Wert									0,1186

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	7 (58,3)	3,7 [1,4; NE]	12	5 (41,7)	NE [0,8; NE]	0,94	[0,30; 3,17]	0,8004
Pemetrexed-Doublette	142	81 (57,0)	4,9 [3,0; 6,7]	146	74 (50,7)	5,8 [2,8; 12,7]	1,11	[0,81; 1,52]	0,5437
Gemcitabin-Doublette	83	39 (47,0)	6,1 [2,8; 10,4]	82	43 (52,4)	2,8 [2,1; 3,7]	0,69	[0,44; 1,06]	0,0999
Interaktion p-Wert									0,2194

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	42 (47,7)	4,7 [2,8; 10,0]	90	47 (52,2)	2,8 [2,1; 3,7]	0,70	[0,46; 1,07]	0,1078
Nicht-Plattenepi-thelial	149	85 (57,0)	4,9 [3,7; 6,3]	150	75 (50,0)	6,2 [2,8; 12,7]	1,11	[0,81; 1,52]	0,5334
Interaktion p-Wert									0,0841
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	67 (53,6)	6,0 [3,8; 8,5]	130	68 (52,3)	3,7 [2,4; 7,5]	0,89	[0,63; 1,24]	0,5115
PD-L1 >/=1%	112	60 (53,6)	4,2 [2,8; 5,6]	110	54 (49,1)	3,7 [2,7; 12,9]	1,04	[0,72; 1,51]	0,8038
Interaktion p-Wert									0,5247

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.2.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	2,3 [0,8; NE]	34	19 (55,9)	3,5 [1,4; 9,1]	0,96	[0,45; 1,97]	0,9983
Nein	214	115 (53,7)	5,5 [3,7; 6,3]	206	103 (50,0)	3,7 [2,8; 7,9]	0,97	[0,74; 1,27]	0,7801
Interaktion p-Wert									0,9925

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
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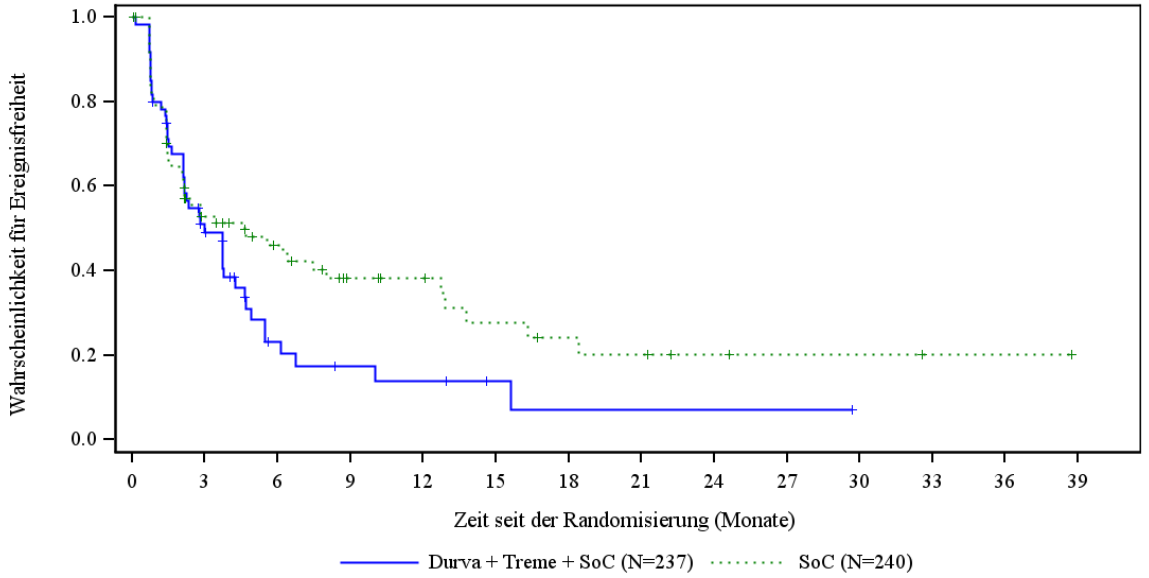
Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	67	25	8	5	4	2	1	1	1	1	0	0	0	0
SoC	83	37	24	15	12	8	6	5	3	2	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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+ indicates a censored observation.

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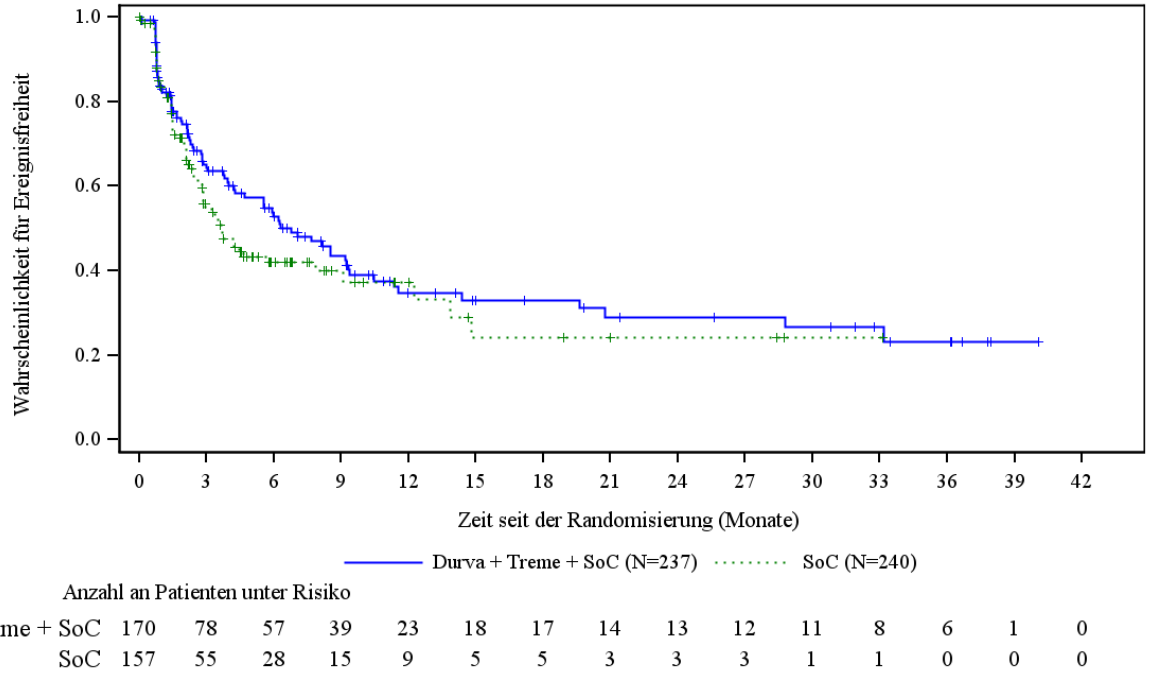
Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	170	78	57	39	23	18	17	14	13	12	11	8	6	1	0
SoC	157	55	28	15	9	5	5	3	3	3	1	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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+ indicates a censored observation.

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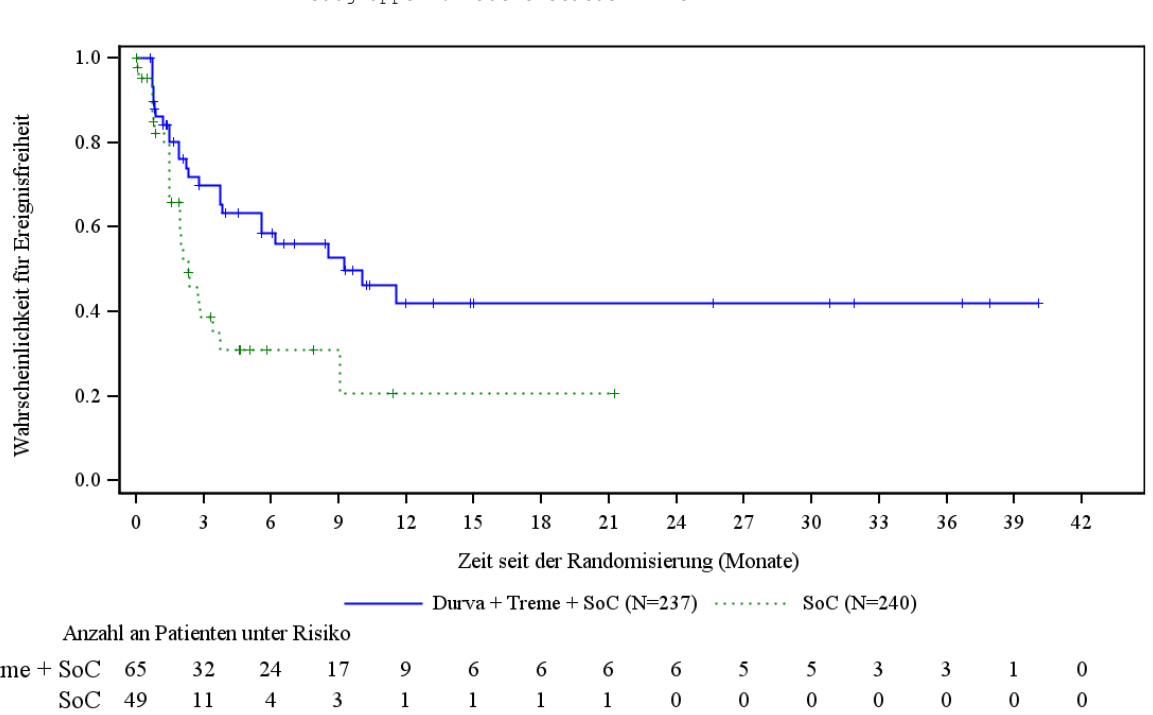
Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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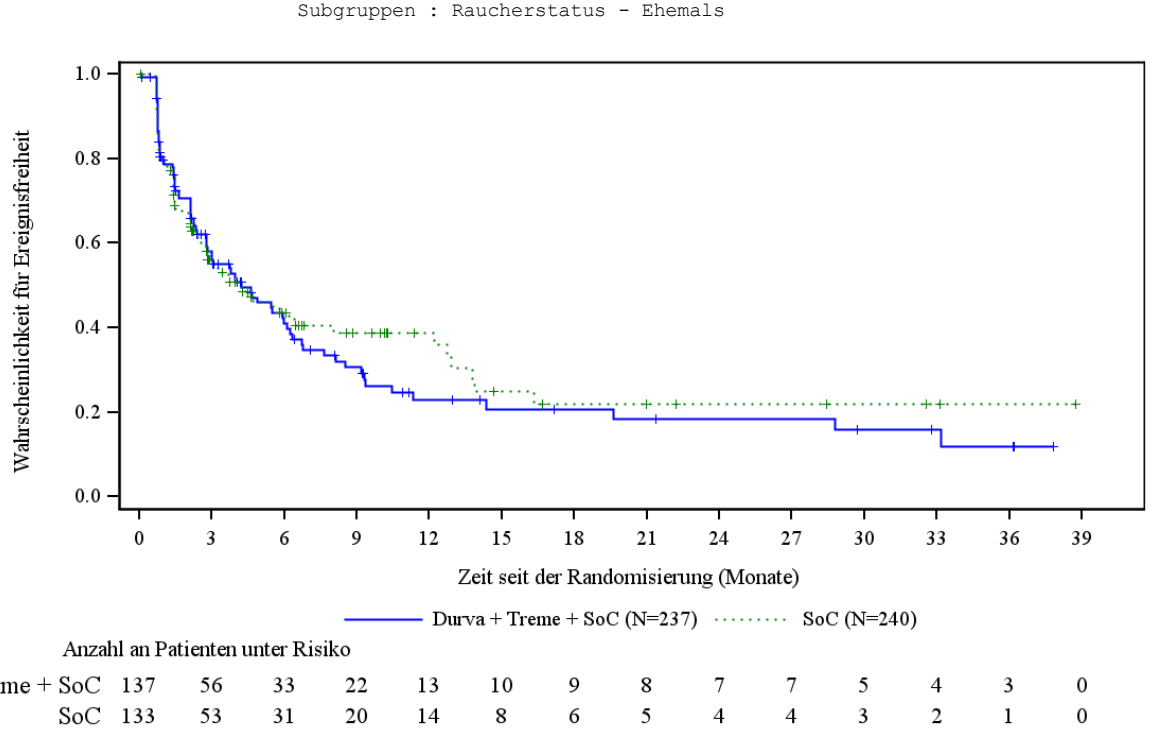
Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
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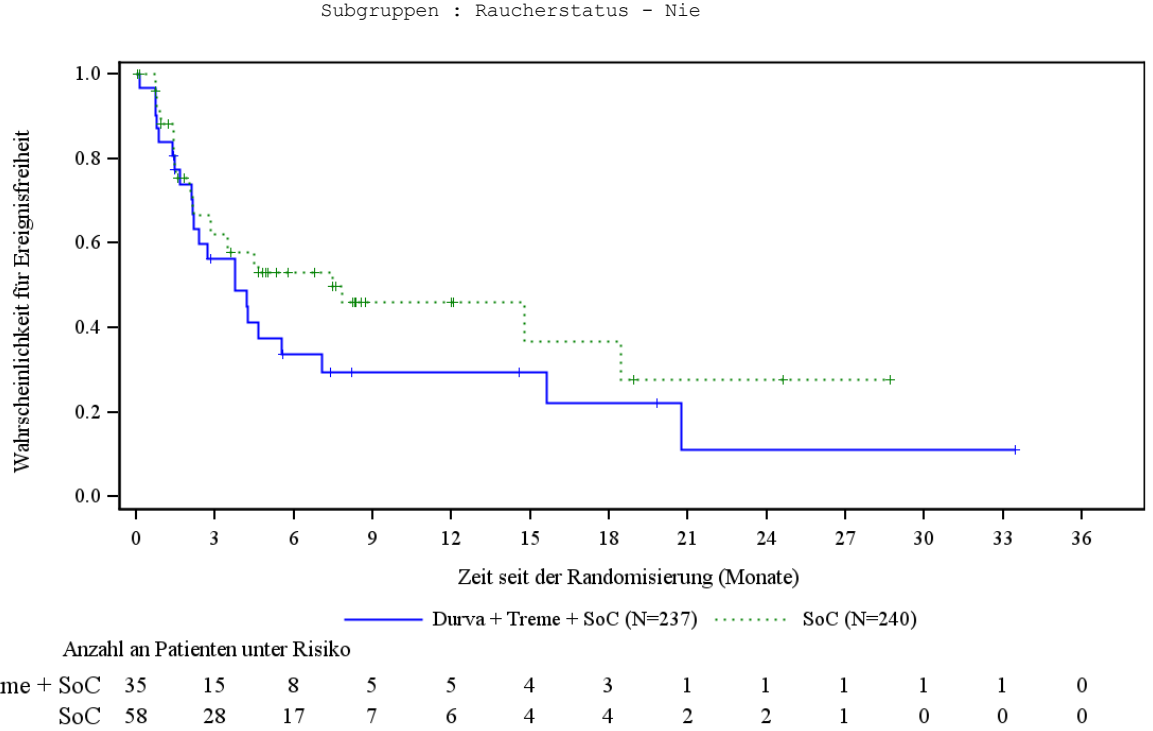
Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Figure 5.2.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 physical (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs303g.sas Executed : 2022-11-21T214505

Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	106 (54,4)	3,0 [2,1; 5,5]	179	96 (53,6)	3,5 [2,1; 4,6]	0,95	[0,72; 1,26]	0,7436
Weiblich	42	20 (47,6)	5,6 [1,6; NE]	61	29 (47,5)	8,5 [2,2; NE]	1,06	[0,59; 1,86]	0,9013
Interaktion p-Wert									0,7417
Alter									
<65 Jahre	130	63 (48,5)	6,2 [3,1; 15,6]	125	56 (44,8)	5,6 [2,2; 12,7]	0,98	[0,69; 1,41]	0,9399
>/= 65 Jahre	107	63 (58,9)	2,1 [1,4; 3,0]	115	69 (60,0)	3,7 [2,1; 4,6]	1,07	[0,76; 1,51]	0,6811
Interaktion p-Wert									0,7385

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	37 (55,2)	3,3 [2,1; 5,5]	83	55 (66,3)	2,2 [1,5; 5,6]	0,96	[0,63; 1,44]	0,8626
Nicht-Asiatisch	170	89 (52,4)	3,8 [2,1; 9,2]	157	70 (44,6)	4,4 [3,0; 7,7]	1,07	[0,78; 1,47]	0,7318
Interaktion p-Wert									0,6788
Performance status zu baseline									
0	82	49 (59,8)	2,1 [1,4; 5,6]	78	40 (51,3)	3,5 [2,0; 13,9]	1,17	[0,77; 1,79]	0,3628
1	155	77 (49,7)	4,6 [2,8; 8,1]	162	85 (52,5)	3,9 [2,2; 6,7]	0,92	[0,67; 1,25]	0,5394
Interaktion p-Wert									0,3516

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	69 (56,1)	3,0 [1,5; 6,2]	120	64 (53,3)	3,8 [2,2; 8,5]	1,02	[0,73; 1,44]	0,8744
Stadium IVB	112	57 (50,9)	3,3 [2,1; 10,4]	120	61 (50,8)	3,9 [2,1; 7,4]	1,00	[0,70; 1,44]	0,9878
Interaktion p-Wert									0,9327
Raucherstatus									
Aktiv	65	30 (46,2)	5,6 [0,9; NE]	49	20 (40,8)	4,4 [1,7; 8,5]	0,94	[0,54; 1,68]	0,9914
Ehemals	137	75 (54,7)	3,1 [1,4; 5,5]	133	78 (58,6)	3,5 [1,7; 4,6]	0,92	[0,67; 1,27]	0,6427
Nie	35	21 (60,0)	3,8 [1,6; 10,3]	58	27 (46,6)	8,5 [2,2; NE]	1,39	[0,78; 2,45]	0,2325
Interaktion p-Wert									0,4569

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	71 (51,1)	2,9 [1,4; 9,2]	125	54 (43,2)	5,6 [3,1; 12,7]	1,19	[0,84; 1,71]	0,3199
Rest of the World	98	55 (56,1)	3,9 [2,1; 8,1]	115	71 (61,7)	2,2 [1,7; 4,6]	0,86	[0,60; 1,22]	0,3900
Interaktion p-Wert									0,1968

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	6 (50,0)	24,9 [0,8; NE]	12	5 (41,7)	NE [0,8; NE]	0,66	[0,20; 2,30]	0,5851
Pemetrexed-Doublette	142	86 (60,6)	2,8 [1,6; 4,9]	146	85 (58,2)	3,5 [2,2; 6,0]	1,03	[0,76; 1,39]	0,8838
Gemcitabin-Doublette	83	34 (41,0)	5,6 [1,4; NE]	82	35 (42,7)	3,9 [2,1; NE]	1,01	[0,63; 1,63]	0,7968
Interaktion p-Wert									0,7794

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	36 (40,9)	5,6 [1,4; NE]	90	39 (43,3)	3,9 [2,1; NE]	0,96	[0,61; 1,51]	0,9850
Nicht-Plattenepithelial	149	90 (60,4)	2,8 [2,1; 4,9]	150	86 (57,3)	3,8 [2,2; 6,5]	1,02	[0,76; 1,37]	0,9391
Interaktion p-Wert									0,8209
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	64 (51,2)	3,9 [2,2; 8,1]	130	67 (51,5)	3,9 [2,1; 7,7]	0,98	[0,70; 1,39]	0,9333
PD-L1 >/=1%	112	62 (55,4)	2,8 [1,4; 6,2]	110	58 (52,7)	3,8 [2,1; 7,4]	1,02	[0,71; 1,47]	0,8469
Interaktion p-Wert									0,8756

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.3.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	14 (60,9)	1,4 [0,8; 3,8]	34	21 (61,8)	2,1 [1,4; 10,2]	1,23	[0,61; 2,40]	0,5716
Nein	214	112 (52,3)	3,9 [2,2; 7,7]	206	104 (50,5)	3,9 [2,4; 6,5]	1,00	[0,76; 1,31]	0,9780
Interaktion p-Wert									0,5793

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Figure 5.3.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 role (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs313g.sas Executed : 2022-11-21T214810

Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	98 (50,3)	4,7 [3,3; 7,7]	179	80 (44,7)	5,7 [3,7; 12,2]	1,08	[0,80; 1,45]	0,6094
Weiblich	42	24 (57,1)	2,8 [1,4; 9,7]	61	29 (47,5)	6,5 [2,9; NE]	1,51	[0,87; 2,60]	0,1311
Interaktion p-Wert									0,2840
Alter									
<65 Jahre	130	67 (51,5)	4,7 [2,9; 8,5]	125	52 (41,6)	6,5 [3,7; 12,2]	1,21	[0,84; 1,75]	0,3011
>/= 65 Jahre	107	55 (51,4)	4,0 [2,8; 7,7]	115	57 (49,6)	4,6 [2,2; 13,1]	1,11	[0,76; 1,61]	0,5451
Interaktion p-Wert									0,7381

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	40 (59,7)	2,8 [2,1; 4,7]	83	46 (55,4)	5,6 [2,2; 13,8]	1,45	[0,94; 2,22]	0,0966
Nicht-Asiatisch	170	82 (48,2)	5,8 [3,3; 9,7]	157	63 (40,1)	6,1 [4,0; 11,6]	1,07	[0,77; 1,50]	0,6743
Interaktion p-Wert									0,2776
Performance status zu baseline									
0	82	37 (45,1)	6,5 [3,3; NE]	78	35 (44,9)	5,8 [2,9; NE]	0,95	[0,60; 1,52]	0,8661
1	155	85 (54,8)	3,7 [2,3; 5,6]	162	74 (45,7)	6,1 [3,7; 11,6]	1,27	[0,93; 1,74]	0,1318
Interaktion p-Wert									0,3114

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs223g.sas Executed : 2022-10-17T205435

Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	69 (56,1)	3,7 [2,7; 5,6]	120	56 (46,7)	5,6 [2,8; 12,2]	1,22	[0,86; 1,74]	0,2881
Stadium IVB	112	52 (46,4)	5,8 [3,0; 9,7]	120	53 (44,2)	6,1 [3,9; 13,1]	1,06	[0,72; 1,55]	0,8745
Interaktion p-Wert									0,5988
Raucherstatus									
Aktiv	65	23 (35,4)	NE [4,3; NE]	49	15 (30,6)	9,1 [2,8; NE]	0,81	[0,42; 1,58]	0,7440
Ehemals	137	78 (56,9)	3,7 [2,8; 5,8]	133	65 (48,9)	5,8 [2,9; 13,1]	1,31	[0,94; 1,82]	0,1038
Nie	35	21 (60,0)	2,8 [1,4; 4,7]	58	29 (50,0)	5,0 [2,9; 11,6]	1,44	[0,81; 2,52]	0,1900
Interaktion p-Wert									0,3596

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	63 (45,3)	7,7 [3,3; 12,1]	125	49 (39,2)	6,1 [3,7; NE]	1,04	[0,71; 1,52]	0,7721
Rest of the World	98	59 (60,2)	3,3 [2,1; 5,6]	115	60 (52,2)	5,7 [2,2; 12,2]	1,36	[0,95; 1,96]	0,0877
Interaktion p-Wert									0,3049

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs223g.sas Executed : 2022-10-17T205435

Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	4 (33,3)	31,5 [1,4; NE]	12	5 (41,7)	3,7 [0,8; NE]	0,46	[0,11; 1,74]	0,3645
Pemetrexed-Doublette	142	86 (60,6)	3,7 [2,4; 5,6]	146	73 (50,0)	6,1 [2,9; 9,4]	1,31	[0,96; 1,79]	0,0813
Gemcitabin-Doublette	83	32 (38,6)	6,2 [2,9; NE]	82	31 (37,8)	10,3 [3,7; NE]	1,00	[0,61; 1,64]	0,9178
Interaktion p-Wert									0,2431

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs223g.sas Executed : 2022-10-17T205435

Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	34 (38,6)	6,2 [2,8; NE]	90	34 (37,8)	5,7 [3,7; NE]	1,00	[0,62; 1,61]	0,9253
Nicht-Plattenepithelial	149	88 (59,1)	3,9 [2,8; 5,8]	150	75 (50,0)	5,8 [2,9; 9,4]	1,23	[0,90; 1,67]	0,1900
Interaktion p-Wert									0,4760
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	63 (50,4)	5,1 [2,8; 9,2]	130	58 (44,6)	5,8 [3,7; 10,3]	1,08	[0,75; 1,54]	0,6580
PD-L1 >/=1%	112	59 (52,7)	4,2 [2,3; 5,8]	110	51 (46,4)	6,5 [2,8; 13,8]	1,25	[0,86; 1,82]	0,2396
Interaktion p-Wert									0,5802

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs223g.sas Executed : 2022-10-17T205435

Table 5.4.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	10 (43,5)	3,3 [1,4; NE]	34	18 (52,9)	6,5 [1,4; NE]	0,87	[0,39; 1,85]	0,6609
Nein	214	112 (52,3)	4,3 [2,9; 6,5]	206	91 (44,2)	6,1 [3,7; 11,6]	1,20	[0,91; 1,59]	0,1893
Interaktion p-Wert									0,4357

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie – Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs323g.sas Executed : 2022-11-21T215033

Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.4.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 cognitive (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	70 (35,9)	14,3 [7,6; NE]	179	67 (37,4)	9,2 [5,0; NE]	0,80	[0,57; 1,13]	0,1998
Weiblich	42	19 (45,2)	5,7 [2,1; NE]	61	24 (39,3)	12,7 [4,8; NE]	1,32	[0,71; 2,40]	0,4258
Interaktion p-Wert									0,1612
Alter									
<65 Jahre	130	50 (38,5)	12,2 [5,7; NE]	125	38 (30,4)	18,0 [9,2; NE]	1,18	[0,77; 1,81]	0,4860
>/= 65 Jahre	107	39 (36,4)	15,0 [6,1; NE]	115	53 (46,1)	4,6 [2,8; NE]	0,69	[0,46; 1,05]	0,1141
Interaktion p-Wert									0,0786

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	25 (37,3)	9,2 [3,7; NE]	83	38 (45,8)	12,0 [3,7; 26,1]	0,89	[0,53; 1,46]	0,6422
Nicht-Asiatisch	170	64 (37,6)	14,3 [6,1; NE]	157	53 (33,8)	9,2 [5,6; NE]	0,91	[0,63; 1,32]	0,6200
Interaktion p-Wert									0,9250
Performance status zu baseline									
0	82	33 (40,2)	11,7 [4,2; NE]	78	26 (33,3)	NE [4,8; NE]	1,17	[0,70; 1,97]	0,5143
1	155	56 (36,1)	14,3 [6,1; NE]	162	65 (40,1)	11,0 [5,6; 18,1]	0,79	[0,55; 1,13]	0,1745
Interaktion p-Wert									0,2201

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	54 (43,9)	6,8 [4,6; NE]	120	45 (37,5)	18,4 [5,0; NE]	1,09	[0,74; 1,63]	0,6320
Stadium IVB	112	35 (31,3)	26,4 [9,2; NE]	120	46 (38,3)	8,5 [4,8; 18,1]	0,72	[0,46; 1,11]	0,1060
Interaktion p-Wert									0,1658
Raucherstatus									
Aktiv	65	15 (23,1)	NE [11,7; NE]	49	15 (30,6)	8,5 [2,9; NE]	0,50	[0,24; 1,03]	0,0541
Ehemals	137	57 (41,6)	7,7 [4,2; NE]	133	55 (41,4)	11,0 [3,9; NE]	0,97	[0,67; 1,42]	0,9874
Nie	35	17 (48,6)	6,1 [2,8; NE]	58	21 (36,2)	12,7 [5,6; NE]	1,30	[0,68; 2,46]	0,6699
Interaktion p-Wert									0,1310

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	45 (32,4)	34,4 [8,3; NE]	125	42 (33,6)	12,7 [5,0; NE]	0,79	[0,52; 1,21]	0,2831
Rest of the World	98	44 (44,9)	6,8 [4,2; 26,4]	115	49 (42,6)	11,0 [5,6; 26,1]	1,06	[0,70; 1,59]	0,8190
Interaktion p-Wert									0,3325

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	1 (8,3)	NE [2,1; NE]	12	4 (33,3)	NE [0,8; NE]	0,11	[0,01; 0,76]	0,0905
Pemetrexed-Doublette	142	65 (45,8)	7,7 [4,2; 26,4]	146	62 (42,5)	12,0 [5,8; 18,4]	1,07	[0,75; 1,52]	0,7111
Gemcitabin-Doublette	83	23 (27,7)	14,3 [5,7; NE]	82	25 (30,5)	NE [3,7; NE]	0,76	[0,43; 1,34]	0,3918
Interaktion p-Wert									0,0956

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	23 (26,1)	NE [6,1; NE]	90	27 (30,0)	NE [4,8; NE]	0,71	[0,40; 1,24]	0,2615
Nicht-Plattenepithelial	149	66 (44,3)	8,3 [4,9; 34,4]	150	64 (42,7)	11,0 [5,6; 18,4]	0,99	[0,70; 1,41]	0,9686
Interaktion p-Wert									0,3163
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	49 (39,2)	9,4 [5,9; NE]	130	48 (36,9)	9,2 [5,6; 26,1]	0,93	[0,62; 1,38]	0,6700
PD-L1 >/=1%	112	40 (35,7)	15,0 [5,7; NE]	110	43 (39,1)	12,7 [4,8; NE]	0,87	[0,56; 1,33]	0,5026
Interaktion p-Wert									0,8262

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.5.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	9 (39,1)	12,2 [1,4; NE]	34	16 (47,1)	6,3 [1,4; NE]	0,75	[0,32; 1,68]	0,3909
Nein	214	80 (37,4)	11,7 [6,1; NE]	206	75 (36,4)	12,0 [6,5; 26,1]	0,94	[0,68; 1,29]	0,7050
Interaktion p-Wert									0,6285

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Figure 5.5.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 emotional (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs333g.sas Executed : 2022-11-21T215318

Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	195	94 (48,2)	5,6 [3,9; 10,2]	179	81 (45,3)	4,6 [2,9; 10,0]	0,94	[0,70; 1,27]	0,7499
Weiblich	42	21 (50,0)	6,5 [3,7; 18,7]	61	24 (39,3)	11,1 [3,7; NE]	1,25	[0,69; 2,25]	0,4909
Interaktion p-Wert									0,4007
Alter									
<65 Jahre	130	59 (45,4)	8,5 [4,8; 14,4]	125	47 (37,6)	NE [3,7; NE]	1,06	[0,73; 1,57]	0,7063
>/= 65 Jahre	107	56 (52,3)	4,2 [2,2; 6,5]	115	58 (50,4)	3,9 [2,7; 6,0]	1,02	[0,70; 1,47]	0,9699
Interaktion p-Wert									0,8656

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs243g.sas Executed : 2022-10-17T210242

Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung									
Asiatisch	67	31 (46,3)	5,6 [2,2; NE]	83	44 (53,0)	5,6 [2,9; 11,1]	0,90	[0,56; 1,41]	0,6533
Nicht-Asiatisch	170	84 (49,4)	6,2 [3,9; 9,2]	157	61 (38,9)	5,8 [2,9; NE]	1,10	[0,79; 1,53]	0,6415
Interaktion p-Wert									0,4842
Performance status zu baseline									
0	82	47 (57,3)	4,7 [2,3; 10,4]	78	31 (39,7)	5,6 [3,7; NE]	1,31	[0,84; 2,08]	0,2366
1	155	68 (43,9)	6,3 [4,6; 10,2]	162	74 (45,7)	5,6 [2,8; 11,1]	0,89	[0,64; 1,24]	0,5220
Interaktion p-Wert									0,1792

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs243g.sas Executed : 2022-10-17T210242

Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	123	63 (51,2)	6,5 [3,7; 10,6]	120	54 (45,0)	5,6 [3,1; NE]	1,02	[0,71; 1,48]	0,8850
Stadium IVB	112	52 (46,4)	4,7 [2,8; 10,2]	120	51 (42,5)	5,6 [2,8; NE]	1,04	[0,71; 1,54]	0,7699
Interaktion p-Wert									0,9497
Raucherstatus									
Aktiv	65	24 (36,9)	14,8 [7,8; NE]	49	15 (30,6)	NE [2,3; NE]	0,74	[0,39; 1,45]	0,2816
Ehemals	137	71 (51,8)	3,9 [2,2; 5,6]	133	65 (48,9)	4,6 [2,9; 10,0]	1,11	[0,79; 1,56]	0,5124
Nie	35	20 (57,1)	6,3 [1,4; 13,1]	58	25 (43,1)	8,3 [2,9; NE]	1,31	[0,72; 2,35]	0,3876
Interaktion p-Wert									0,4209

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region									
Europa und Nordamerika	139	63 (45,3)	6,5 [4,6; 10,4]	125	46 (36,8)	10,0 [3,7; NE]	1,07	[0,73; 1,58]	0,7793
Rest of the World	98	52 (53,1)	4,7 [2,2; 10,2]	115	59 (51,3)	4,6 [2,8; 8,3]	1,01	[0,69; 1,46]	0,9151
Interaktion p-Wert									0,8209

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie									
Paclitaxel-Doublette	12	4 (33,3)	NE [2,1; NE]	12	5 (41,7)	2,9 [0,7; NE]	0,45	[0,11; 1,72]	0,4110
Pemetrexed-Doublette	142	82 (57,7)	4,6 [2,3; 6,5]	146	67 (45,9)	6,0 [3,1; NE]	1,25	[0,90; 1,73]	0,1752
Gemcitabin-Doublette	83	29 (34,9)	14,4 [4,7; 16,1]	82	33 (40,2)	4,6 [2,7; NE]	0,75	[0,45; 1,23]	0,2097
Interaktion p-Wert									0,1081

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	88	31 (35,2)	14,4 [4,7; 16,1]	90	37 (41,1)	3,7 [2,8; NE]	0,73	[0,45; 1,17]	0,1624
Nicht-Plattenepithelial	149	84 (56,4)	4,6 [2,4; 6,5]	150	68 (45,3)	6,0 [3,1; NE]	1,20	[0,87; 1,65]	0,2637
Interaktion p-Wert									0,0909
PD-L1-Status (1% cut-off)									
PD-L1 <1%	125	58 (46,4)	7,8 [4,6; 10,4]	130	63 (48,5)	3,7 [2,8; 8,3]	0,83	[0,58; 1,19]	0,3039
PD-L1 >/=1%	112	57 (50,9)	4,7 [2,3; 10,2]	110	42 (38,2)	10,0 [3,7; NE]	1,31	[0,88; 1,97]	0,1578
Interaktion p-Wert									0,0922

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 5.6.2.1 Summary of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function)
(modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

	Durva + Treme + SoC (N=237)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen									
Ja	23	12 (52,2)	3,9 [0,8; 5,6]	34	17 (50,0)	6,0 [0,8; NE]	1,22	[0,57; 2,53]	0,5546
Nein	214	103 (48,1)	6,3 [4,6; 10,2]	206	88 (42,7)	5,6 [3,7; NE]	1,02	[0,77; 1,36]	0,8905
Interaktion p-Wert									0,6566

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
N Number of patients in treatment group. n Number of patients in category or analysis. Percentages are out of n. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 for symptom scales and decrease of >=10 for functional items) in score. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. For certain subgroups there are patients with missing status so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Männlich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Geschlecht - Weiblich

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Abstammung - Nicht-Asiatisch

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 0

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Performance status zu baseline - 1

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Aktiv

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Ehemals

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Raucherstatus - Nie

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\qs343g.sas Executed : 2022-11-21T215544

Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Ja

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Figure 5.6.2.2 Kaplan-Meier of subgroup analyses of time to first deterioration of EORTC QLQ-C30 social (function) (modified Full analysis set - Patients with PD-L1<50%)
Data Cut-off: 12th March 2021

Subgruppen : Hirnmetastasen - Nein

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to deterioration is defined as the time from date of randomization until the earliest of the dates of a deterioration (increase of >=10 in symptom scales and decrease of >=10 in function items) in score. For certain subgroups there are patients with missing status and so are not included in the analysis.
A curve is only presented for subgroup analyses with a statistically significant interaction term.
+ indicates a censored observation.

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Anhang 4-G 1.3.4: Gesamtraten unerwünschter Ereignisse

Anhang 4-G 1.3.4.1: Unerwünschte Ereignisse

Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse (UE)	191	184 (96,3)	0,2 [0,2; 0,3]	181	173 (95,6)	0,3 [0,2; 0,3]	1,13	[0,92; 1,39]	0,2372
Weiblich	Unerwünschte Ereignisse (UE)	40	39 (97,5)	0,1 [0,1; 0,1]	59	59 (100)	0,2 [0,1; 0,2]	1,08	[0,72; 1,61]	0,6931
Interaktion p-Wert										0,8486

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse (UE)	127	122 (96,1)	0,3 [0,2; 0,3]	125	121 (96,8)	0,3 [0,2; 0,3]	1,08	[0,84; 1,39]	0,4810
>/= 65 Jahre	Unerwünschte Ereignisse (UE)	104	101 (97,1)	0,2 [0,1; 0,2]	115	111 (96,5)	0,2 [0,1; 0,3]	1,11	[0,84; 1,45]	0,4763
Interaktion p-Wert										0,9097

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Unerwünschte Ereignisse (UE)	65	64 (98,5)	0,2 [0,1; 0,3]	83	81 (97,6)	0,2 [0,1; 0,3]	1,15	[0,82; 1,59]	0,5184
Nicht-Asiatisch	Unerwünschte Ereignisse (UE)	166	159 (95,8)	0,2 [0,2; 0,3]	157	151 (96,2)	0,3 [0,2; 0,3]	1,09	[0,87; 1,37]	0,4217
Interaktion p-Wert										0,8079

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Unerwünschte Ereignisse (UE)	81	77 (95,1)	0,3 [0,2; 0,5]	79	77 (97,5)	0,3 [0,2; 0,6]	1,06	[0,77; 1,45]	0,7059
1	Unerwünschte Ereignisse (UE)	150	146 (97,3)	0,2 [0,1; 0,3]	161	155 (96,3)	0,2 [0,1; 0,3]	1,12	[0,90; 1,41]	0,3214
Interaktion p-Wert										0,7649

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse (UE)	122	118 (96,7)	0,2 [0,2; 0,3]	119	114 (95,8)	0,3 [0,1; 0,3]	1,12	[0,87; 1,46]	0,3965
Stadium IVB	Unerwünschte Ereignisse (UE)	108	104 (96,3)	0,2 [0,1; 0,3]	121	118 (97,5)	0,2 [0,1; 0,3]	1,06	[0,81; 1,38]	0,6746
Interaktion p-Wert										0,7547

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Unerwünschte Ereignisse (UE)	65	62 (95,4)	0,3 [0,2; 0,5]	49	47 (95,9)	0,3 [0,1; 0,4]	0,96	[0,66; 1,40]	0,8131
Ehemals	Unerwünschte Ereignisse (UE)	133	128 (96,2)	0,1 [0,1; 0,2]	134	129 (96,3)	0,2 [0,1; 0,3]	1,12	[0,88; 1,43]	0,4202
Nie	Unerwünschte Ereignisse (UE)	33	33 (100)	0,3 [0,2; 0,5]	57	56 (98,2)	0,3 [0,1; 0,7]	1,19	[0,77; 1,82]	0,2570
Interaktion p-Wert										0,7168

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse (UE)	136	129 (94,9)	0,3 [0,2; 0,3]	124	118 (95,2)	0,3 [0,3; 0,7]	1,14	[0,89; 1,47]	0,2725
Rest of the World	Unerwünschte Ereignisse (UE)	95	94 (98,9)	0,1 [0,1; 0,2]	116	114 (98,3)	0,1 [0,1; 0,2]	1,11	[0,84; 1,45]	0,6056
Interaktion p-Wert										0,8647

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Unerwünschte Ereignisse (UE)	12	12 (100)	0,1 [0,0; 0,2]	12	12 (100)	0,1 [0,0; 0,5]	1,11	[0,49; 2,50]	0,6654
Pemetrexed-Doublette	Unerwünschte Ereignisse (UE)	139	134 (96,4)	0,2 [0,2; 0,3]	145	138 (95,2)	0,2 [0,2; 0,3]	1,06	[0,84; 1,35]	0,6232
Gemcitabin-Doublette	Unerwünschte Ereignisse (UE)	80	77 (96,3)	0,2 [0,1; 0,3]	83	82 (98,8)	0,3 [0,1; 0,5]	1,14	[0,84; 1,56]	0,3487
Interaktion p-Wert										0,9348

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse (UE)	85	82 (96,5)	0,2 [0,1; 0,3]	91	90 (98,9)	0,3 [0,1; 0,4]	1,11	[0,82; 1,50]	0,4659
Nicht-Plattenepithelial	Unerwünschte Ereignisse (UE)	146	141 (96,6)	0,2 [0,2; 0,3]	149	142 (95,3)	0,2 [0,1; 0,3]	1,08	[0,86; 1,37]	0,5249
Interaktion p-Wert										0,8817

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Unerwünschte Ereignisse (UE)	120	115 (95,8)	0,2 [0,2; 0,3]	130	127 (97,7)	0,2 [0,1; 0,3]	1,03	[0,80; 1,32]	0,8058
PD-L1 >/=1%	Unerwünschte Ereignisse (UE)	111	108 (97,3)	0,2 [0,1; 0,3]	110	105 (95,5)	0,2 [0,1; 0,3]	1,17	[0,89; 1,53]	0,2609
Interaktion p-Wert										0,4869

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Unerwünschte Ereignisse (UE)	22	19 (86,4)	0,2 [0,1; 0,5]	34	32 (94,1)	0,2 [0,1; 0,3]	0,86	[0,48; 1,49]	0,6815
Nein	Unerwünschte Ereignisse (UE)	209	204 (97,6)	0,2 [0,1; 0,3]	206	200 (97,1)	0,3 [0,2; 0,3]	1,12	[0,92; 1,37]	0,2389
Interaktion p-Wert										0,3747

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from first dose until the first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Asiatisch
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Nicht-Asiatisch
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 0
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 1
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Aktiv
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Ehemals
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Nie
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Ja
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae303g.sas Executed : 2022-11-21T155640

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Nein
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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Anhang 4-G 1.3.4.2: Behandlungsabbruch aufgrund unerwünschter Ereignisse

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Therapieabbrüche aufgrund von UE	191	34 (17,8)	NE [36,3; NE]	181	29 (16,0)	NE [22,9; NE]	0,88	[0,53; 1,46]	0,6195
Weiblich	Therapieabbrüche aufgrund von UE	40	10 (25,0)	NE [12,9; NE]	59	6 (10,2)	NE [17,1; NE]	2,14	[0,79; 6,32]	0,1321
Interaktion p-Wert										0,1205

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae223g.sas Executed : 2022-09-13T154435

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Therapieabbrüche aufgrund von UE	127	15 (11,8)	NE [NE; NE]	125	16 (12,8)	NE [31,7; NE]	0,75	[0,37; 1,53]	0,4754
>/= 65 Jahre	Therapieabbrüche aufgrund von UE	104	29 (27,9)	NE [17,1; NE]	115	19 (16,5)	NE [17,1; NE]	1,40	[0,79; 2,55]	0,2772
Interaktion p-Wert										0,1799

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae223g.sas Executed : 2022-09-13T154435

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Therapieabbrüche aufgrund von UE	65	11 (16,9)	NE [NE; NE]	83	9 (10,8)	NE [NE; NE]	1,49	[0,62; 3,69]	0,3356
Nicht-Asiatisch	Therapieabbrüche aufgrund von UE	166	33 (19,9)	NE [35,7; NE]	157	26 (16,6)	31,7 [22,9; NE]	0,92	[0,55; 1,57]	0,6604
Interaktion p-Wert										0,3620

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae223g.sas Executed : 2022-09-13T154435

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Therapieabbrüche aufgrund von UE	81	17 (21,0)	NE [22,5; NE]	79	12 (15,2)	NE [17,1; NE]	1,08	[0,51; 2,32]	0,9930
1	Therapieabbrüche aufgrund von UE	150	27 (18,0)	NE [35,7; NE]	161	23 (14,3)	NE [31,7; NE]	1,07	[0,61; 1,89]	0,7438
Interaktion p-Wert										0,9908

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Therapieabbrüche aufgrund von UE	122	20 (16,4)	NE [36,3; NE]	119	12 (10,1)	NE [NE; NE]	1,31	[0,65; 2,78]	0,3109
Stadium IVB	Therapieabbrüche aufgrund von UE	108	24 (22,2)	NE [22,5; NE]	121	23 (19,0)	31,7 [17,1; NE]	1,00	[0,56; 1,78]	0,8623
Interaktion p-Wert										0,5574

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Therapieabbrüche aufgrund von UE	65	13 (20,0)	NE [22,5; NE]	49	8 (16,3)	NE [NE; NE]	0,83	[0,34; 2,11]	0,3890
Ehemals	Therapieabbrüche aufgrund von UE	133	27 (20,3)	NE [NE; NE]	134	21 (15,7)	NE [22,9; NE]	1,09	[0,62; 1,96]	0,5967
Nie	Therapieabbrüche aufgrund von UE	33	4 (12,1)	35,7 [NE; NE]	57	6 (10,5)	NE [17,1; NE]	0,97	[0,25; 3,41]	0,9841
Interaktion p-Wert										0,8743

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Therapieabbrüche aufgrund von UE	136	27 (19,9)	NE [35,7; NE]	124	20 (16,1)	31,7 [NE; NE]	0,97	[0,54; 1,76]	0,8105
Rest of the World	Therapieabbrüche aufgrund von UE	95	17 (17,9)	NE [NE; NE]	116	15 (12,9)	NE [22,9; NE]	1,18	[0,59; 2,39]	0,5965
Interaktion p-Wert										0,6718

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Therapieabbrüche aufgrund von UE	12	3 (25,0)	NE [3,9; NE]	12	2 (16,7)	NE [3,0; NE]	0,89	[0,15; 6,80]	0,8608
Pemetrexed-Doublette	Therapieabbrüche aufgrund von UE	139	29 (20,9)	NE [35,7; NE]	145	18 (12,4)	NE [31,7; NE]	1,43	[0,80; 2,64]	0,2600
Gemcitabin-Doublette	Therapieabbrüche aufgrund von UE	80	12 (15,0)	NE [NE; NE]	83	15 (18,1)	NE [NE; NE]	0,65	[0,30; 1,39]	0,4189
Interaktion p-Wert										0,2669

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Therapieabbrüche aufgrund von UE	85	14 (16,5)	NE [NE; NE]	91	17 (18,7)	NE [NE; NE]	0,70	[0,34; 1,42]	0,4918
Nicht-Plattenepithelial	Therapieabbrüche aufgrund von UE	146	30 (20,5)	NE [35,7; NE]	149	18 (12,1)	NE [31,7; NE]	1,41	[0,79; 2,58]	0,2885
Interaktion p-Wert										0,1339

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Therapieabbrüche aufgrund von UE	120	21 (17,5)	36,3 [36,3; NE]	130	20 (15,4)	NE [17,1; NE]	0,94	[0,50; 1,74]	0,8483
PD-L1 >/=1%	Therapieabbrüche aufgrund von UE	111	23 (20,7)	NE [35,7; NE]	110	15 (13,6)	31,7 [22,9; NE]	1,26	[0,65; 2,48]	0,4925
Interaktion p-Wert										0,5220

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Therapieabbrüche aufgrund von UE	22	7 (31,8)	12,9 [12,2; NE]	34	2 (5,9)	NE [NE; NE]	5,44	[1,31; 36,54]	0,0465
Nein	Therapieabbrüche aufgrund von UE	209	37 (17,7)	NE [NE; NE]	206	33 (16,0)	NE [22,9; NE]	0,89	[0,55; 1,44]	0,6942
Interaktion p-Wert										0,0306

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Asiatisch
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Nicht-Asiatisch
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 0
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 1
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Aktiv
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Ehemals
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Nie
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Ja
Therapieabbrüche aufgrund von UE

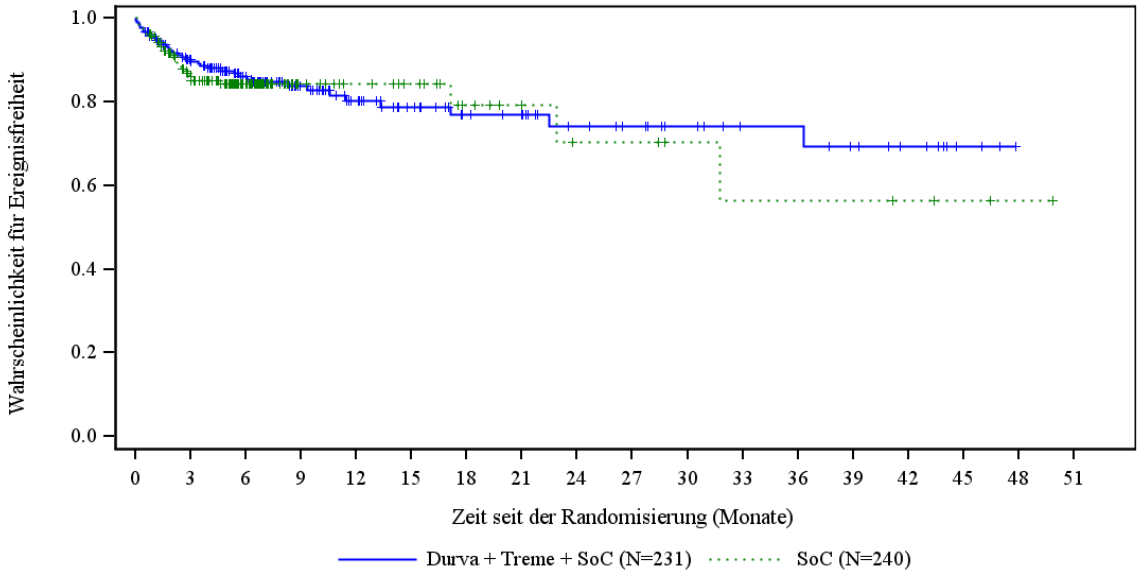
PLOT IS NOT CREATED BECAUSE FEWER THAN 10 EVENTS OCCUR

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae323g.sas Executed : 2022-11-21T165659

Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Nein
Therapieabbrüche aufgrund von UE



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	209	168	125	85	60	47	37	34	26	23	19	15	15	11	8	3	0	0
SoC	206	151	88	30	24	20	13	9	7	7	5	4	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Anhang 4-G 1.3.4.3: Schwere unerwünschte Ereignisse (CTCAE-Grad $\geq$ 3)

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	UE mit max. CTCAE Grad >/=3	191	121 (63,4)	2,5 [2,0; 5,6]	181	108 (59,7)	2,7 [1,9; 4,9]	1,00	[0,77; 1,30]	0,9440
Weiblich	UE mit max. CTCAE Grad >/=3	40	30 (75,0)	2,6 [1,3; 9,2]	59	37 (62,7)	2,1 [1,0; 11,1]	1,04	[0,64; 1,68]	0,7760
Interaktion p-Wert										0,8853

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	UE mit max. CTCAE Grad >/=3	127	81 (63,8)	2,6 [2,1; 9,2]	125	69 (55,2)	2,8 [2,0; NE]	1,09	[0,79; 1,51]	0,5933
>/= 65 Jahre	UE mit max. CTCAE Grad >/=3	104	70 (67,3)	2,1 [1,4; 5,4]	115	76 (66,1)	2,1 [1,4; 3,2]	0,92	[0,67; 1,28]	0,6532
Interaktion p-Wert										0,4723

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	UE mit max. CTCAE Grad >/=3	65	53 (81,5)	1,2 [0,9; 2,0]	83	49 (59,0)	2,3 [1,4; 11,1]	1,72	[1,16; 2,54]	0,0064
Nicht-Asiatisch	UE mit max. CTCAE Grad >/=3	166	98 (59,0)	5,6 [2,5; 11,7]	157	96 (61,1)	2,3 [1,7; 3,9]	0,81	[0,61; 1,07]	0,1239
Interaktion p-Wert										0,0022

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	UE mit max. CTCAE Grad >/=3	81	47 (58,0)	9,2 [2,6; 17,1]	79	42 (53,2)	4,1 [1,6; NE]	0,92	[0,61; 1,40]	0,5838
1	UE mit max. CTCAE Grad >/=3	150	104 (69,3)	2,0 [1,4; 2,8]	161	103 (64,0)	2,3 [1,7; 2,8]	1,07	[0,81; 1,40]	0,6239
Interaktion p-Wert										0,5586

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	UE mit max. CTCAE Grad >/=3	122	77 (63,1)	3,9 [1,5; 11,6]	119	69 (58,0)	2,7 [1,6; 11,1]	0,99	[0,72; 1,38]	0,9992
Stadium IVB	UE mit max. CTCAE Grad >/=3	108	73 (67,6)	2,3 [1,6; 3,1]	121	76 (62,8)	2,1 [1,4; 4,1]	1,03	[0,75; 1,42]	0,8748
Interaktion p-Wert										0,8730

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	UE mit max. CTCAE Grad >/=3	65	41 (63,1)	2,6 [1,3; 11,7]	49	31 (63,3)	2,1 [1,2; 3,9]	0,81	[0,51; 1,31]	0,3300
Ehemals	UE mit max. CTCAE Grad >/=3	133	89 (66,9)	2,3 [1,5; 3,8]	134	81 (60,4)	2,3 [1,6; 5,7]	1,07	[0,79; 1,45]	0,6443
Nie	UE mit max. CTCAE Grad >/=3	33	21 (63,6)	4,6 [1,4; 29,9]	57	33 (57,9)	3,2 [1,6; NE]	0,96	[0,55; 1,64]	0,8585
Interaktion p-Wert										0,6175

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae213g.sas Executed : 2022-09-13T153103

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	UE mit max. CTCAE Grad >/=3	136	76 (55,9)	9,2 [2,6; 16,1]	124	73 (58,9)	2,3 [1,6; 6,8]	0,80	[0,58; 1,10]	0,1449
Rest of the World	UE mit max. CTCAE Grad >/=3	95	75 (78,9)	1,6 [1,0; 2,3]	116	72 (62,1)	2,3 [1,6; 4,9]	1,37	[0,99; 1,89]	0,0472
Interaktion p-Wert										0,0206

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	UE mit max. CTCAE Grad >/=3	12	9 (75,0)	1,0 [0,2; NE]	12	10 (83,3)	1,0 [0,0; 2,8]	0,82	[0,33; 2,05]	0,8953
Pemetrexed-Doublette	UE mit max. CTCAE Grad >/=3	139	92 (66,2)	3,0 [2,0; 6,2]	145	74 (51,0)	6,9 [2,3; 31,7]	1,27	[0,94; 1,73]	0,1270
Gemcitabin-Doublette	UE mit max. CTCAE Grad >/=3	80	50 (62,5)	2,4 [1,1; 9,2]	83	61 (73,5)	1,3 [0,9; 2,1]	0,68	[0,46; 0,99]	0,0556
Interaktion p-Wert										0,0369

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	UE mit max. CTCAE Grad >/=3	85	53 (62,4)	2,3 [1,0; 9,2]	91	67 (73,6)	1,3 [0,9; 2,1]	0,68	[0,47; 0,97]	0,0466
Nicht-Plattenepithelial	UE mit max. CTCAE Grad >/=3	146	98 (67,1)	2,8 [1,8; 5,6]	149	78 (52,3)	6,8 [2,3; 31,7]	1,27	[0,94; 1,71]	0,1142
Interaktion p-Wert										0,0084

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	UE mit max. CTCAE Grad >/=3	120	78 (65,0)	3,4 [2,3; 9,2]	130	82 (63,1)	2,2 [1,6; 3,2]	0,89	[0,65; 1,22]	0,3838
PD-L1 >/=1%	UE mit max. CTCAE Grad >/=3	111	73 (65,8)	1,8 [1,1; 5,4]	110	63 (57,3)	3,0 [1,6; 11,1]	1,15	[0,82; 1,62]	0,3980
Interaktion p-Wert										0,2708

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	UE mit max. CTCAE Grad >/=3	22	17 (77,3)	2,6 [0,3; 5,6]	34	19 (55,9)	2,3 [1,0; NE]	1,44	[0,74; 2,78]	0,2962
Nein	UE mit max. CTCAE Grad >/=3	209	134 (64,1)	2,4 [1,8; 5,9]	206	126 (61,2)	2,3 [1,9; 3,2]	0,96	[0,75; 1,23]	0,8011
Interaktion p-Wert										0,2600

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AE G>=3 Adverse event with maximum CTCAE grade >= 3. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis only performed if at least 10 patients in each subgroup level and at least 10 events in at least one subgroup level across both treatment arms.
NE Not estimable as median (or 95% CI) not reached. Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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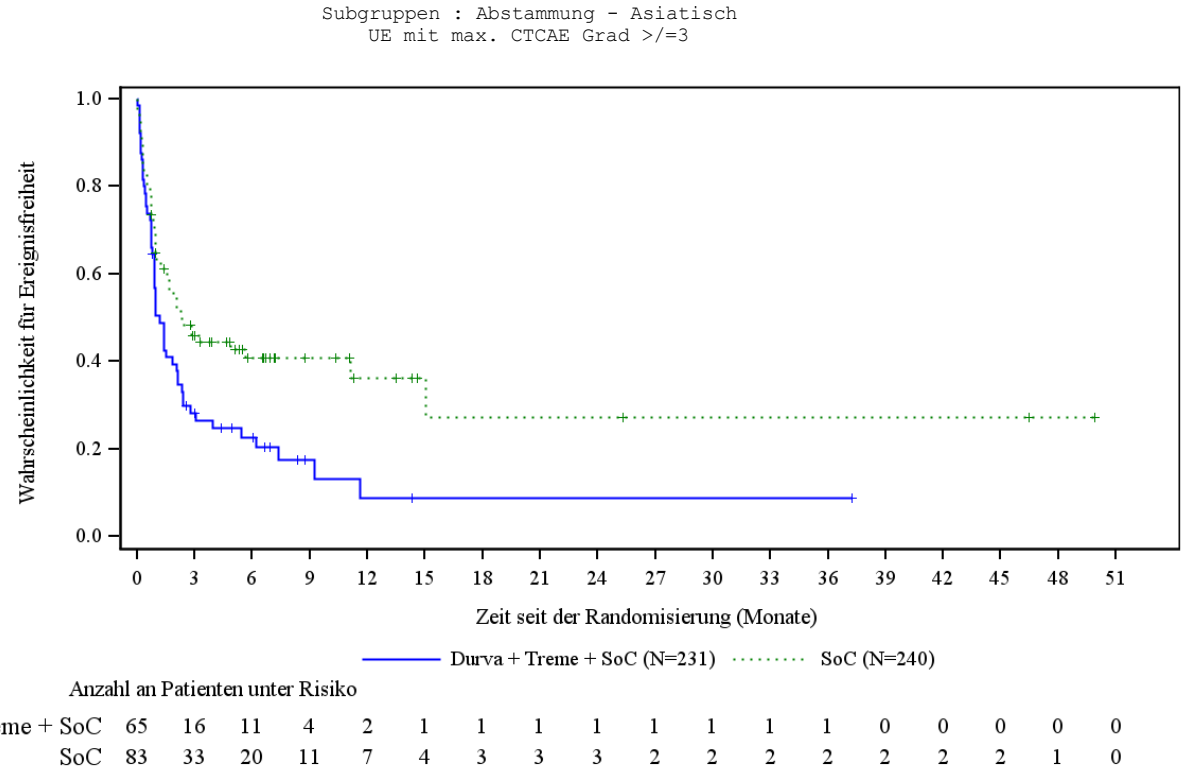
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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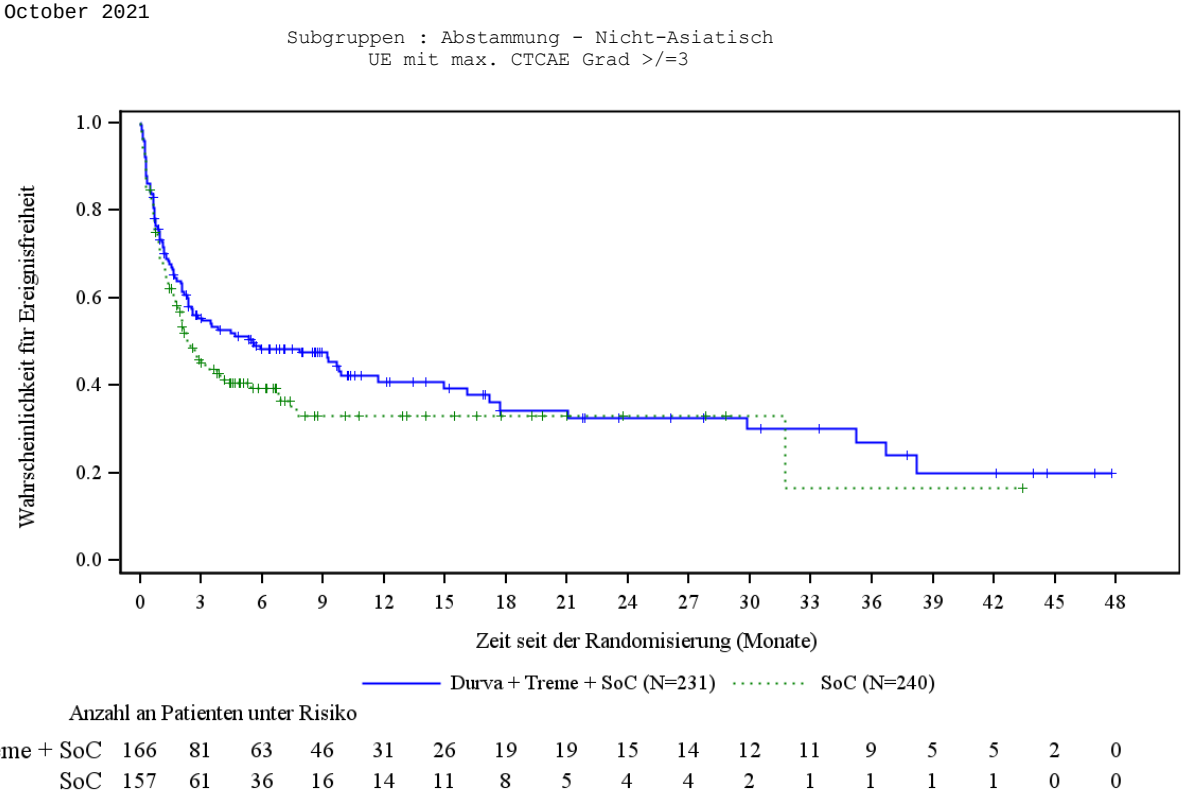
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	166	81	63	46	31	26	19	19	15	14	12	11	9	5	5	2	0
SoC	157	61	36	16	14	11	8	5	4	4	2	1	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 0
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 1
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Aktiv
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Ehemals
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Nie
UE mit max. CTCAE Grad >/=3

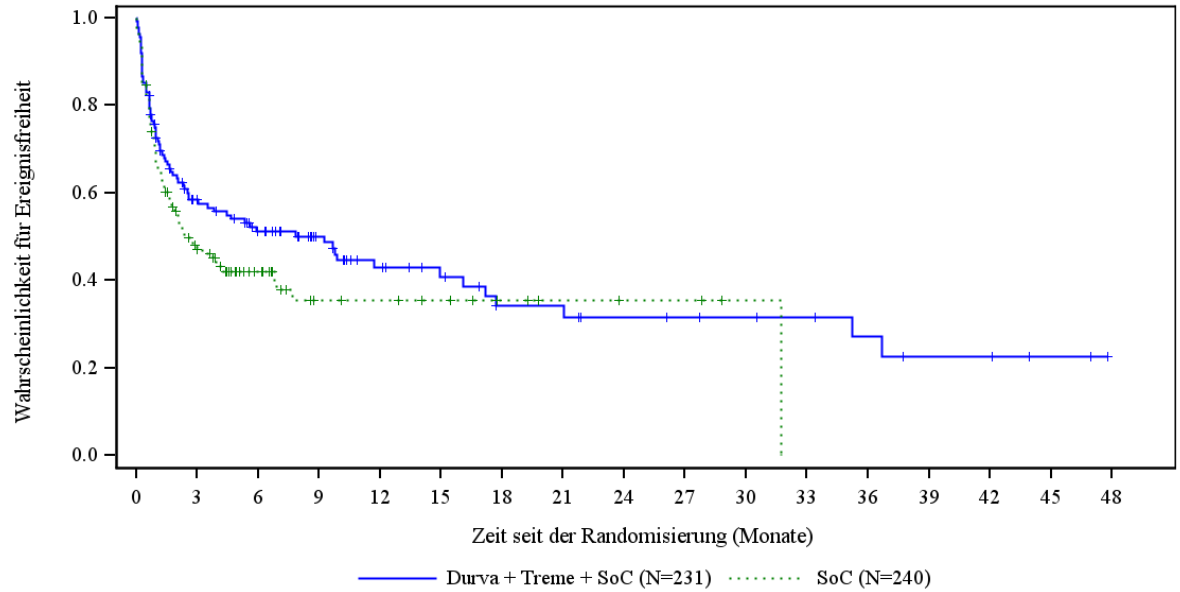
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
UE mit max. CTCAE Grad >/=3



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	136	68	52	37	25	20	14	14	11	10	9	8	6	4	4	2	0
SoC	124	50	29	12	11	9	6	4	3	3	1	0	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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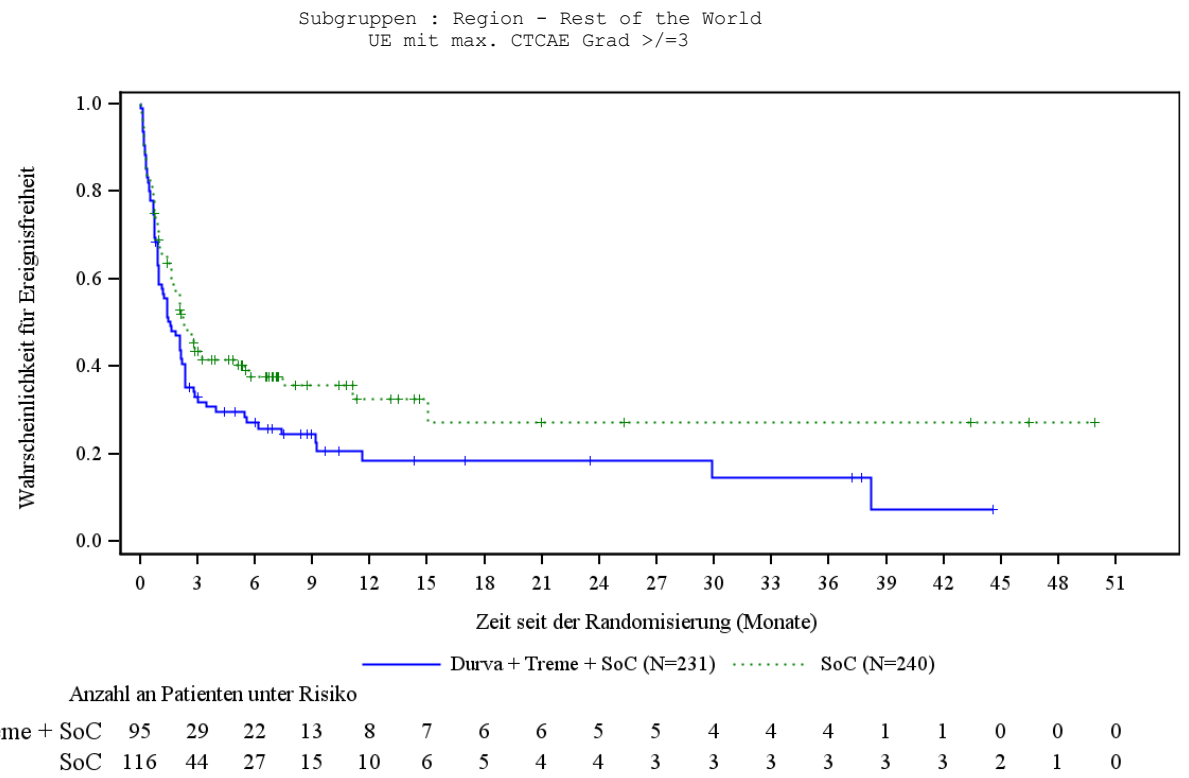
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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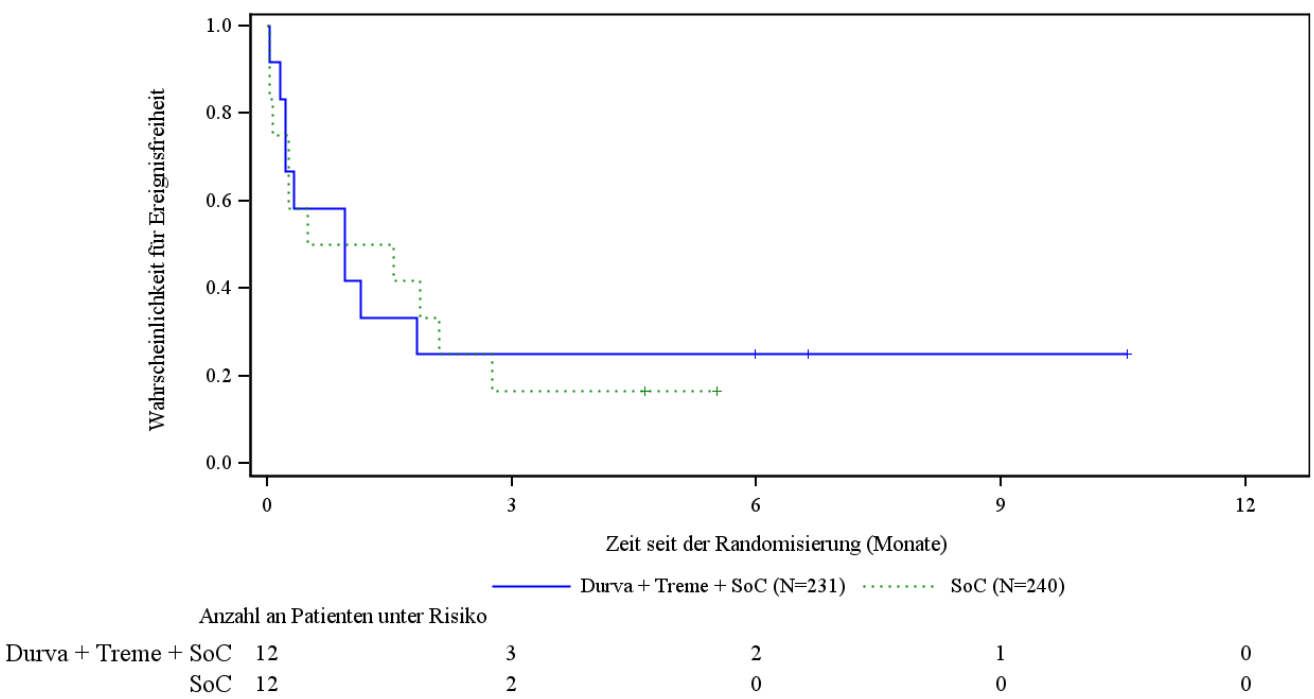
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



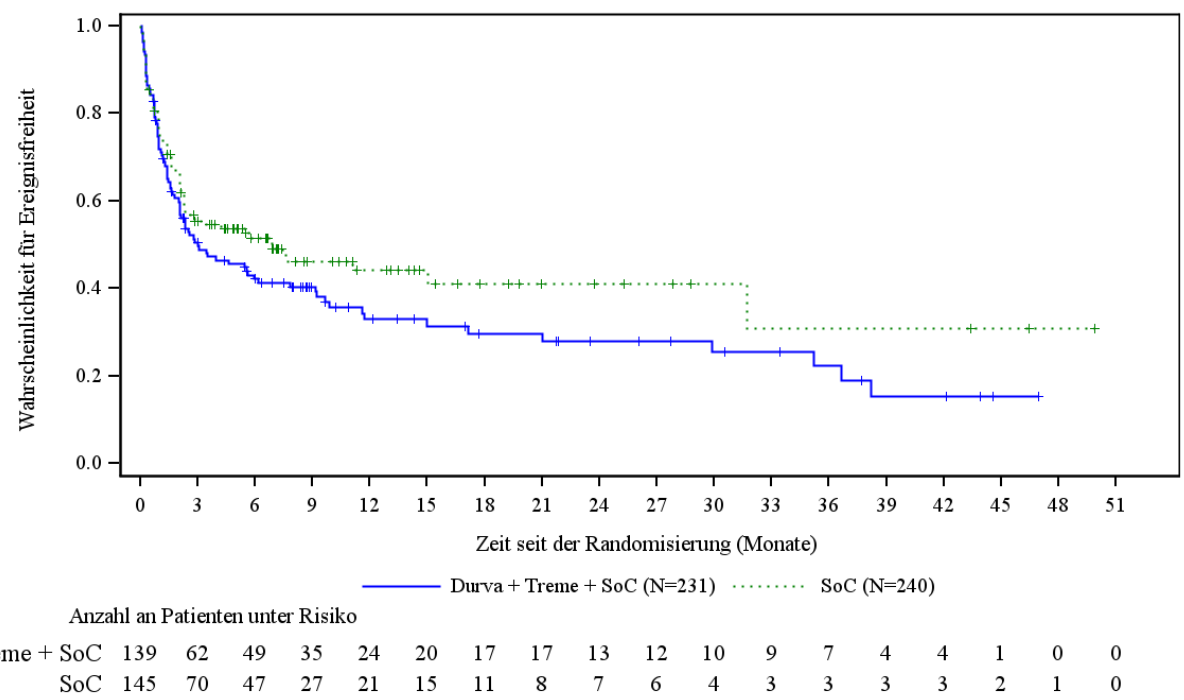
Anzahl an Patienten unter Risiko

Durva + Treme + SoC	12	3	2	1	0
SoC	12	2	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

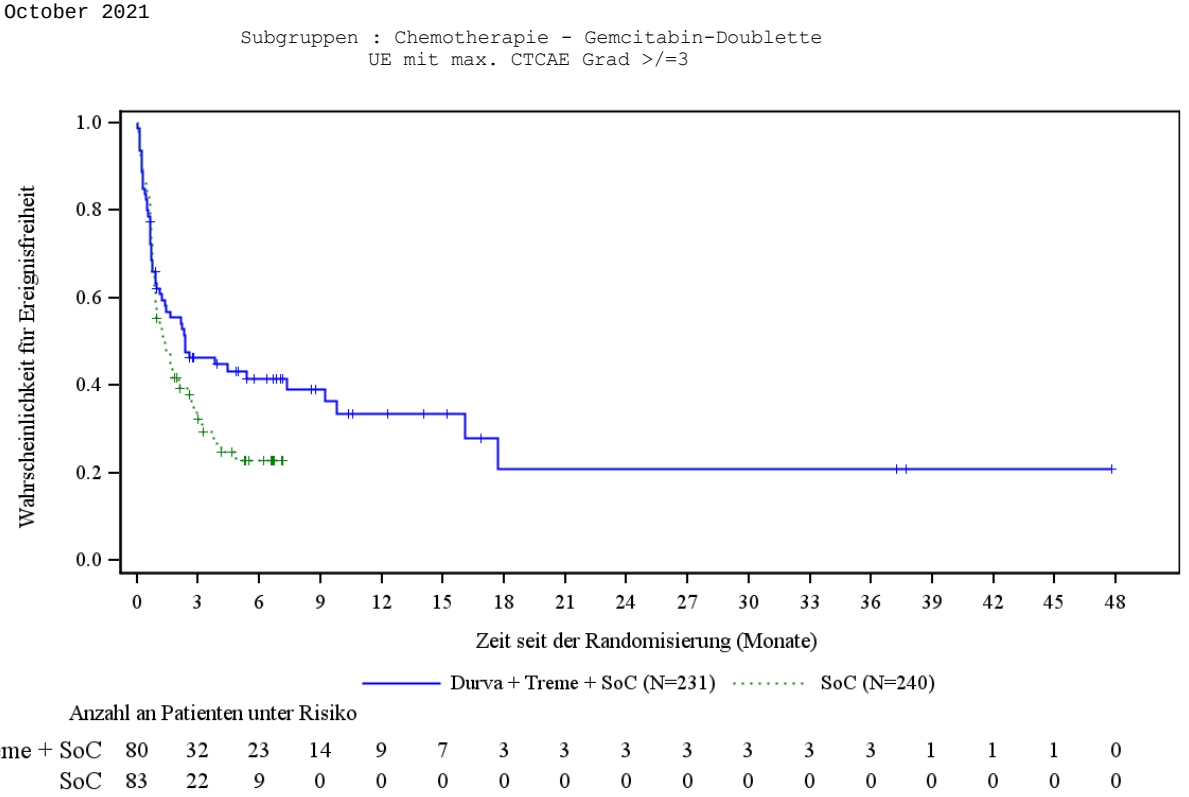
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

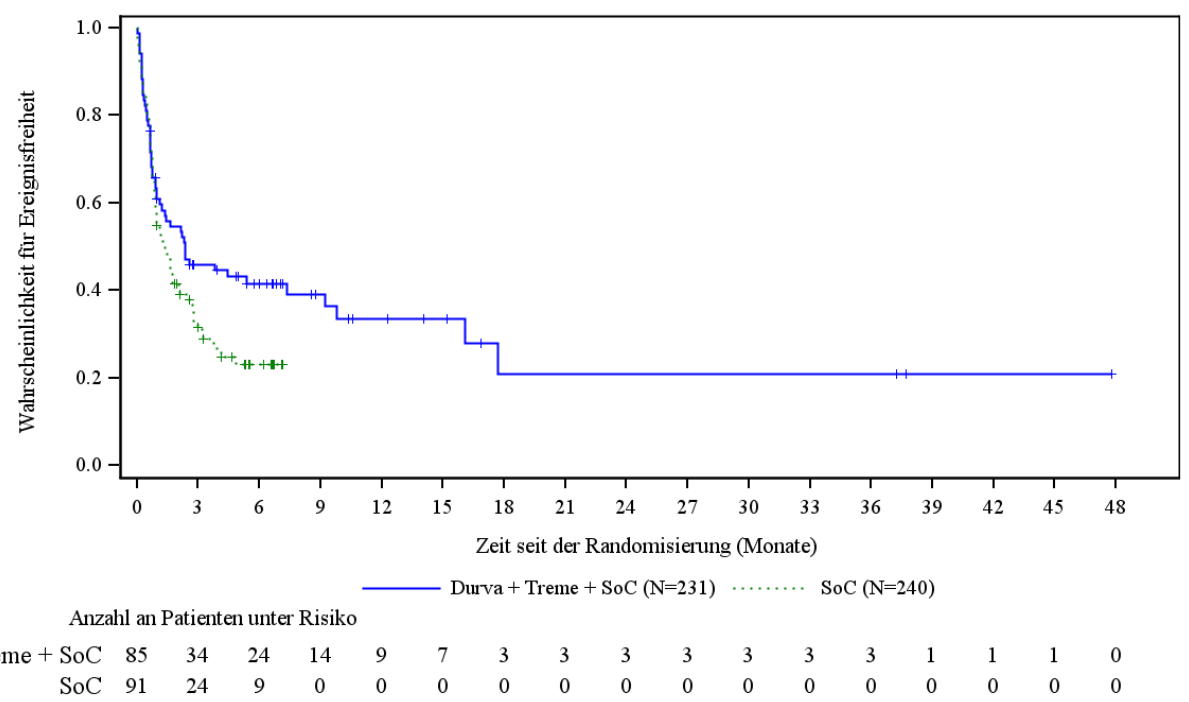
Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021



Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

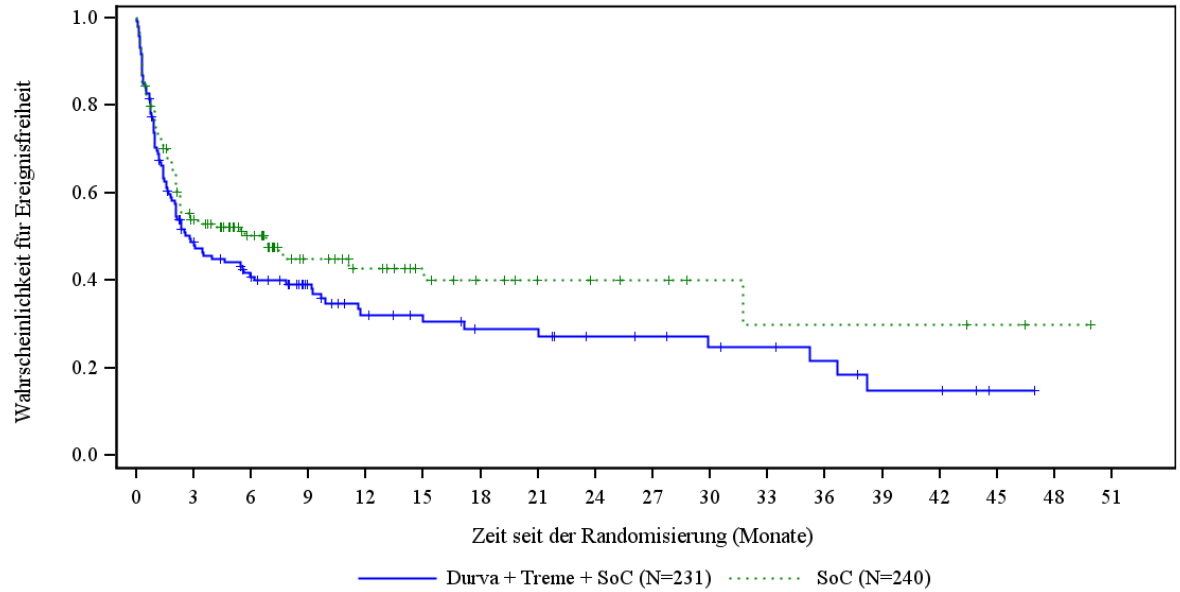


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
UE mit max. CTCAE Grad >/=3



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	146	63	50	36	24	20	17	17	13	12	10	9	7	4	4	1	0	0
SoC	149	70	47	27	21	15	11	8	7	6	4	3	3	3	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Ja
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae313g.sas Executed : 2022-11-21T162135

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Nein
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Anhang 4-G 1.3.4.4: Schwerwiegende unerwünschte Ereignisse

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Schwerwiegende unerwünschte Ereignisse (SUE)	191	80 (41,9)	21,7 [9,7; NE]	181	64 (35,4)	21,2 [15,0; NE]	1,04	[0,75; 1,46]	0,8161
Weiblich	Schwerwiegende unerwünschte Ereignisse (SUE)	40	19 (47,5)	12,9 [5,2; NE]	59	16 (27,1)	NE [17,1; NE]	1,64	[0,84; 3,23]	0,1475
Interaktion p-Wert										0,2332

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Schwerwiegende unerwünschte Ereignisse (SUE)	127	47 (37,0)	26,7 [12,9; NE]	125	34 (27,2)	31,7 [31,7; NE]	1,20	[0,77; 1,89]	0,4205
>/= 65 Jahre	Schwerwiegende unerwünschte Ereignisse (SUE)	104	52 (50,0)	8,5 [4,9; 36,3]	115	46 (40,0)	15,0 [5,7; NE]	1,17	[0,78; 1,75]	0,4463
Interaktion p-Wert										0,9212

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Schwerwiegende unerwünschte Ereignisse (SUE)	65	41 (63,1)	2,3 [1,4; 6,4]	83	34 (41,0)	15,0 [5,5; NE]	1,89	[1,20; 2,99]	0,0054
Nicht-Asiatisch	Schwerwiegende unerwünschte Ereignisse (SUE)	166	58 (34,9)	35,7 [17,7; NE]	157	46 (29,3)	31,7 [17,1; NE]	0,98	[0,66; 1,45]	0,7167
Interaktion p-Wert										0,0316

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Schwerwiegende unerwünschte Ereignisse (SUE)	81	33 (40,7)	17,7 [9,2; NE]	79	27 (34,2)	17,1 [17,1; NE]	1,02	[0,61; 1,71]	0,9864
1	Schwerwiegende unerwünschte Ereignisse (SUE)	150	66 (44,0)	21,0 [7,8; NE]	161	53 (32,9)	31,7 [15,0; NE]	1,25	[0,87; 1,80]	0,2190
Interaktion p-Wert										0,5229

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Schwerwiegende unerwünschte Ereignisse (SUE)	122	48 (39,3)	21,0 [11,6; NE]	119	37 (31,1)	21,2 [15,0; NE]	1,14	[0,74; 1,76]	0,5767
Stadium IVB	Schwerwiegende unerwünschte Ereignisse (SUE)	108	51 (47,2)	12,9 [3,8; 35,7]	121	43 (35,5)	31,7 [6,8; NE]	1,23	[0,82; 1,86]	0,3054
Interaktion p-Wert										0,7848

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Schwerwiegende unerwünschte Ereignisse (SUE)	65	24 (36,9)	36,3 [7,3; NE]	49	18 (36,7)	NE [2,8; NE]	0,74	[0,40; 1,39]	0,2918
Ehemals	Schwerwiegende unerwünschte Ereignisse (SUE)	133	63 (47,4)	9,8 [4,5; NE]	134	50 (37,3)	21,2 [15,0; NE]	1,19	[0,82; 1,73]	0,2924
Nie	Schwerwiegende unerwünschte Ereignisse (SUE)	33	12 (36,4)	35,7 [11,6; 35,7]	57	12 (21,1)	NE [17,1; NE]	1,60	[0,71; 3,61]	0,3160
Interaktion p-Wert										0,2718

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Schwerwiegende unerwünschte Ereignisse (SUE)	136	45 (33,1)	35,7 [17,1; NE]	124	36 (29,0)	31,7 [21,2; 31,7]	0,96	[0,62; 1,50]	0,6110
Rest of the World	Schwerwiegende unerwünschte Ereignisse (SUE)	95	54 (56,8)	5,6 [2,3; 21,7]	116	44 (37,9)	17,1 [10,4; NE]	1,53	[1,03; 2,29]	0,0255
Interaktion p-Wert										0,1238

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Schwerwiegende unerwünschte Ereignisse (SUE)	12	3 (25,0)	NE [3,8; NE]	12	6 (50,0)	5,7 [0,5; NE]	NC	[NC; NC]	NC
Pemetrexed-Doublette	Schwerwiegende unerwünschte Ereignisse (SUE)	139	66 (47,5)	17,1 [7,8; 36,3]	145	44 (30,3)	31,7 [17,1; NE]	1,51	[1,03; 2,22]	0,0367
Gemcitabin-Doublette	Schwerwiegende unerwünschte Ereignisse (SUE)	80	30 (37,5)	17,7 [7,3; NE]	83	30 (36,1)	NE [NE; NE]	0,90	[0,54; 1,50]	0,6521
Interaktion p-Wert										0,1100

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Schwerwiegende unerwünschte Ereignisse (SUE)	85	32 (37,6)	17,7 [7,3; NE]	91	34 (37,4)	NE [3,8; NE]	0,85	[0,52; 1,39]	0,5255
Nicht-Plattenepithelial	Schwerwiegende unerwünschte Ereignisse (SUE)	146	67 (45,9)	21,0 [8,5; 36,3]	149	46 (30,9)	31,7 [17,1; NE]	1,39	[0,95; 2,03]	0,0922
Interaktion p-Wert										0,1213

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Schwerwiegende unerwünschte Ereignisse (SUE)	120	48 (40,0)	17,7 [12,9; NE]	130	45 (34,6)	NE [17,1; NE]	1,01	[0,67; 1,53]	0,9947
PD-L1 >/=1%	Schwerwiegende unerwünschte Ereignisse (SUE)	111	51 (45,9)	26,7 [5,6; NE]	110	35 (31,8)	21,2 [15,0; NE]	1,36	[0,89; 2,12]	0,1287
Interaktion p-Wert										0,3244

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Schwerwiegende unerwünschte Ereignisse (SUE)	22	12 (54,5)	8,5 [2,1; 35,7]	34	13 (38,2)	NE [3,8; NE]	1,34	[0,60; 2,97]	0,6020
Nein	Schwerwiegende unerwünschte Ereignisse (SUE)	209	87 (41,6)	21,7 [9,8; NE]	206	67 (32,5)	31,7 [17,1; NE]	1,16	[0,84; 1,60]	0,3365
Interaktion p-Wert										0,7349

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae233g.sas Executed : 2022-09-13T163346

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Männlich
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Weiblich
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - <65 Jahre
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

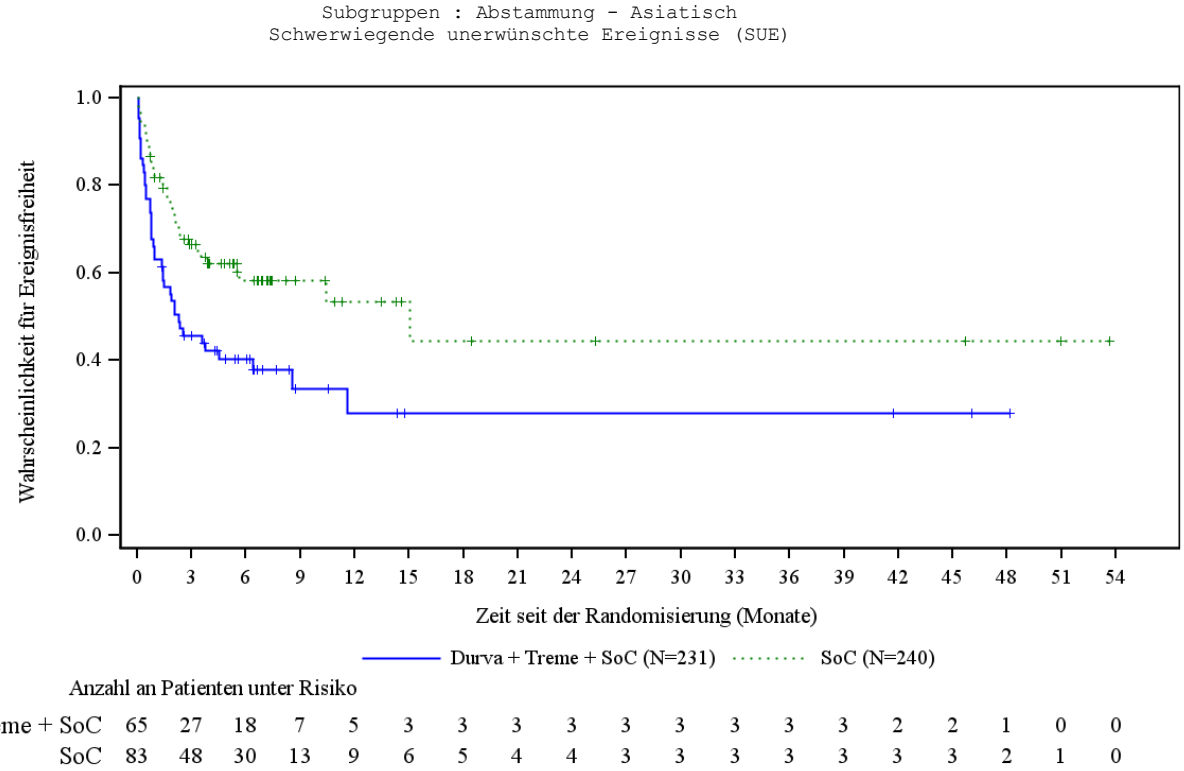
Subgruppen : Alter - >/= 65 Jahre
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

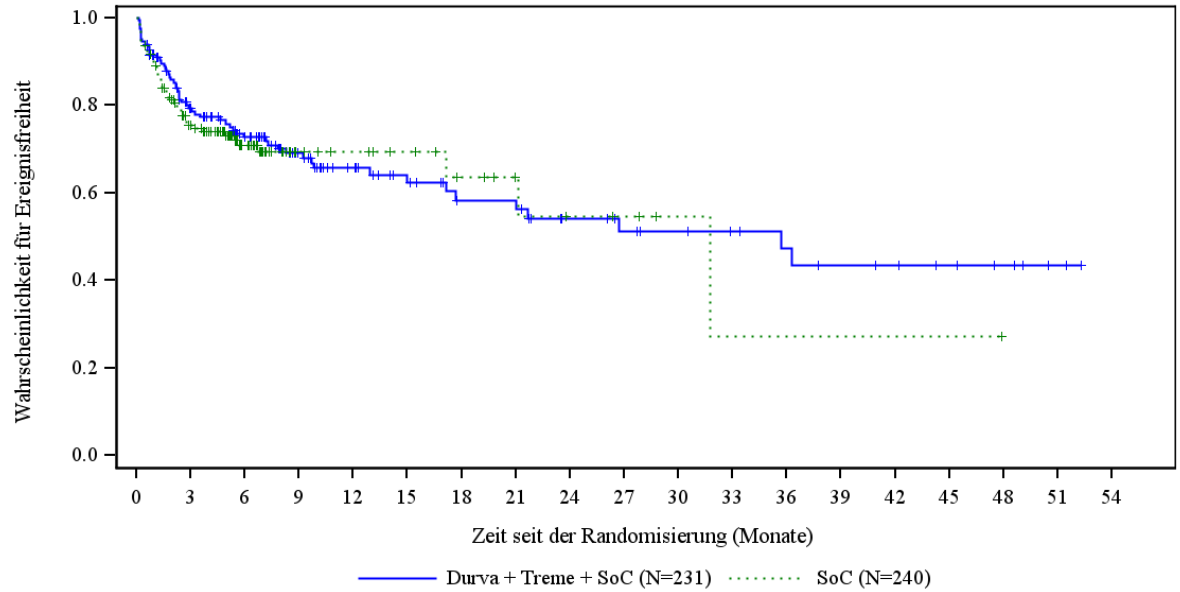


Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Abstammung - Nicht-Asiatisch
Schwerwiegende unerwünschte Ereignisse (SUE)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	166	116	92	64	45	36	28	28	21	18	16	14	12	10	9	7	5	2	0
SoC	157	102	59	20	17	14	10	7	5	4	2	1	1	1	1	1	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Performance status zu baseline - 0
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Performance status zu baseline - 1
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVA
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVB
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Aktiv
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Ehemals
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Nie
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Europa und Nordamerika
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Rest of the World
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Plattenepithelial
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Nicht-Plattenepithelial
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Hirnmetastasen - Ja
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Hirnmetastasen - Nein
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae333g.sas Executed : 2022-11-21T195040

Anhang 4-G 1.3.5: Gesamtraten unerwünschter Ereignisse von speziellem Interesse

Anhang 4-G 1.3.5.1: Unerwünschte Ereignisse von speziellem Interesse

Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse von speziellem Interesse (UESI)	191	103 (53,9)	4,2 [2,1; 6,5]	181	47 (26,0)	NE [14,1; NE]	2,39	[1,70; 3,40]	<0,0001
Weiblich	Unerwünschte Ereignisse von speziellem Interesse (UESI)	40	26 (65,0)	2,3 [0,9; 10,6]	59	20 (33,9)	21,4 [11,5; NE]	2,30	[1,29; 4,17]	0,0057
Interaktion p-Wert										0,9137

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI)	127	68 (53,5)	3,8 [1,9; 13,1]	125	33 (26,4)	21,4 [14,1; NE]	2,34	[1,56; 3,59]	<0,0001
>/= 65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI)	104	61 (58,7)	3,7 [1,8; 10,2]	115	34 (29,6)	24,2 [11,5; NE]	2,32	[1,54; 3,57]	<0,0001
Interaktion p-Wert										0,9821

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Unerwünschte Ereignisse von speziellem Interesse (UESI)	65	39 (60,0)	2,1 [1,0; 5,1]	83	29 (34,9)	12,2 [11,5; NE]	2,19	[1,36; 3,57]	0,0010
Nicht-Asiatisch	Unerwünschte Ereignisse von speziellem Interesse (UESI)	166	90 (54,2)	4,4 [2,4; 10,6]	157	38 (24,2)	NE [14,1; NE]	2,52	[1,74; 3,73]	<0,0001
Interaktion p-Wert										0,6479

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Unerwünschte Ereignisse von speziellem Interesse (UESI)	81	50 (61,7)	1,9 [1,0; 6,2]	79	16 (20,3)	NE [11,1; NE]	3,78	[2,20; 6,86]	<0,0001
1	Unerwünschte Ereignisse von speziellem Interesse (UESI)	150	79 (52,7)	4,5 [2,4; 11,0]	161	51 (31,7)	24,2 [14,1; NE]	1,87	[1,32; 2,67]	0,0004
Interaktion p-Wert										0,0376

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse von speziellem Interesse (UESI)	122	71 (58,2)	3,0 [1,6; 10,6]	119	36 (30,3)	21,4 [11,5; NE]	2,31	[1,56; 3,49]	<0,0001
Stadium IVB	Unerwünschte Ereignisse von speziellem Interesse (UESI)	108	58 (53,7)	3,8 [1,9; 10,2]	121	31 (25,6)	NE [12,2; NE]	2,37	[1,55; 3,72]	<0,0001
Interaktion p-Wert										0,9315

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Unerwünschte Ereignisse von speziellem Interesse (UESI)	65	33 (50,8)	10,6 [1,6; NE]	49	5 (10,2)	NE [NE; NE]	5,63	[2,40; 16,47]	<0,0001
Ehemals	Unerwünschte Ereignisse von speziellem Interesse (UESI)	133	79 (59,4)	2,9 [1,5; 4,5]	134	44 (32,8)	NE [24,2; NE]	2,19	[1,52; 3,19]	<0,0001
Nie	Unerwünschte Ereignisse von speziellem Interesse (UESI)	33	17 (51,5)	11,0 [1,6; NE]	57	18 (31,6)	14,1 [11,1; NE]	1,68	[0,86; 3,27]	0,1576
Interaktion p-Wert										0,1101

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse von speziellem Interesse (UESI)	136	66 (48,5)	6,0 [2,9; NE]	124	25 (20,2)	24,2 [14,1; NE]	2,66	[1,70; 4,29]	<0,0001
Rest of the World	Unerwünschte Ereignisse von speziellem Interesse (UESI)	95	63 (66,3)	1,9 [1,0; 3,0]	116	42 (36,2)	21,4 [11,5; NE]	2,33	[1,58; 3,47]	<0,0001
Interaktion p-Wert										0,6721

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI)	12	11 (91,7)	0,5 [0,0; 3,9]	12	7 (58,3)	3,0 [0,4; NE]	2,38	[0,94; 6,46]	0,0890
Pemetrexed-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI)	139	82 (59,0)	3,0 [1,9; 6,5]	145	46 (31,7)	24,2 [12,2; NE]	2,15	[1,51; 3,11]	<0,0001
Gemcitabin-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI)	80	36 (45,0)	10,6 [2,0; NE]	83	14 (16,9)	NE [NE; NE]	3,03	[1,67; 5,81]	0,0003
Interaktion p-Wert										0,6441

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI)	85	41 (48,2)	5,2 [1,6; NE]	91	19 (20,9)	NE [NE; NE]	2,64	[1,55; 4,65]	0,0003
Nicht-Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI)	146	88 (60,3)	2,8 [1,9; 6,0]	149	48 (32,2)	24,2 [12,2; NE]	2,20	[1,55; 3,15]	<0,0001
Interaktion p-Wert										0,5816

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Unerwünschte Ereignisse von speziellem Interesse (UESI)	120	61 (50,8)	3,9 [2,3; NE]	130	35 (26,9)	21,4 [11,5; NE]	2,09	[1,38; 3,19]	0,0003
PD-L1 >/=1%	Unerwünschte Ereignisse von speziellem Interesse (UESI)	111	68 (61,3)	2,9 [1,5; 5,2]	110	32 (29,1)	24,2 [14,1; NE]	2,59	[1,71; 3,99]	<0,0001
Interaktion p-Wert										0,4749

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Unerwünschte Ereignisse von speziellem Interesse (UESI)	22	13 (59,1)	1,0 [0,4; NE]	34	6 (17,6)	NE [12,2; NE]	4,90	[1,94; 13,97]	0,0009
Nein	Unerwünschte Ereignisse von speziellem Interesse (UESI)	209	116 (55,5)	3,8 [2,1; 8,3]	206	61 (29,6)	24,2 [14,1; NE]	2,12	[1,56; 2,91]	<0,0001
Interaktion p-Wert										0,1062

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Asiatisch
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Nicht-Asiatisch
Unerwünschte Ereignisse von speziellem Interesse (UESI)

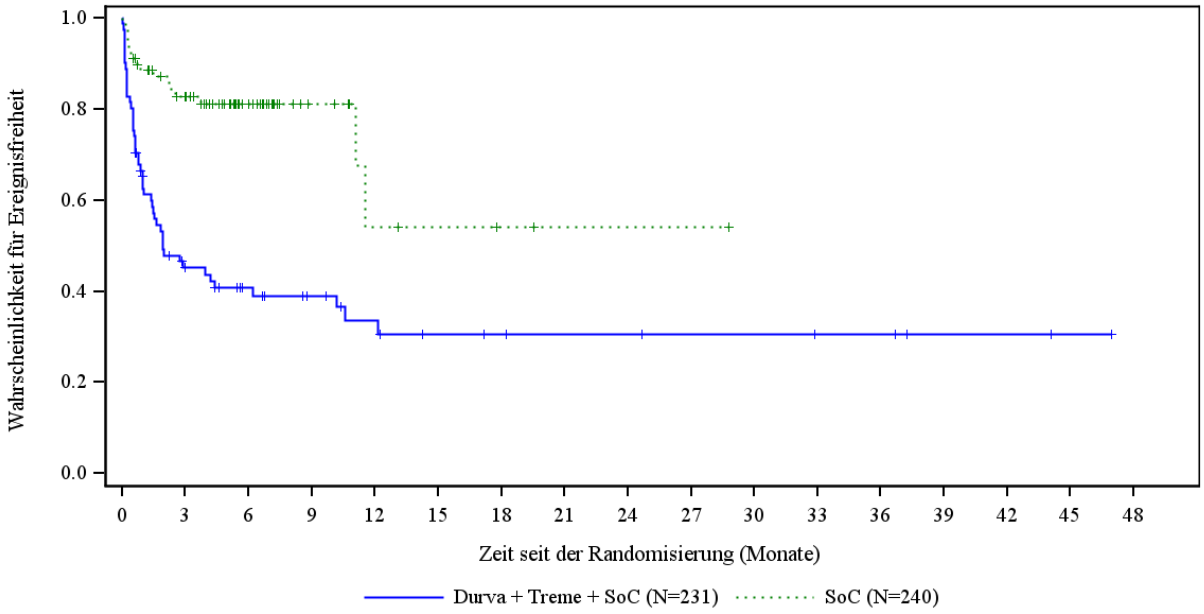
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae343g.sas Executed : 2022-11-21T200659

Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 0
Unerwünschte Ereignisse von speziellem Interesse (UESI)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	81	31	23	17	11	8	7	6	6	5	5	4	4	2	2	1	0
SoC	79	56	31	9	4	3	2	1	1	1	0	0	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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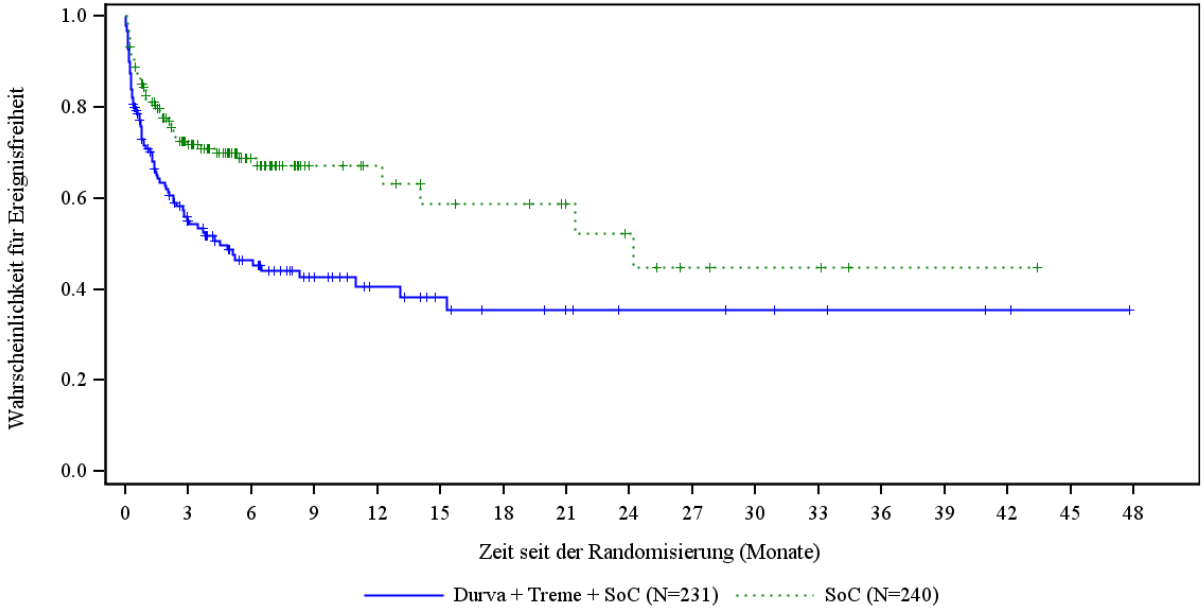
Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 1
Unerwünschte Ereignisse von speziellem Interesse (UESI)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	150	65	41	26	18	13	10	8	6	6	5	4	3	3	2	1	0
SoC	161	85	48	20	17	13	12	9	7	4	3	3	1	1	1	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Aktiv
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Ehemals
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Nie
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae343g.sas Executed : 2022-11-21T200659

Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Ja
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Nein
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Anhang 4-G 1.3.5.2: Schwere unerwünschte Ereignisse von speziellem Interesse (CTCAE-Grad $\geq$ 3)

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 13

Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	191	19 (9,9)	NE [NE; NE]	181	5 (2,8)	NE [NE; NE]	3,32	[1,33; 10,01]	0,0107
Weiblich	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	40	4 (10,0)	NE [NE; NE]	59	1 (1,7)	NE [NE; NE]	5,90	[0,87; 115,31]	0,0845
Interaktion p-Wert										0,6385

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	127	8 (6,3)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	3,69	[0,92; 24,45]	0,0730
>/= 65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	104	15 (14,4)	NE [NE; NE]	115	4 (3,5)	NE [NE; NE]	3,97	[1,44; 13,95]	0,0085
Interaktion p-Wert										0,9395

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	65	16 (24,6)	NE [NE; NE]	83	3 (3,6)	NE [NE; NE]	7,22	[2,41; 31,05]	0,0002
Nicht-Asiatisch	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	166	7 (4,2)	NE [NE; NE]	157	3 (1,9)	NE [NE; NE]	1,97	[0,55; 9,17]	0,3206
Interaktion p-Wert										0,1650

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	81	10 (12,3)	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC; NC]	NC
1	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	150	13 (8,7)	NE [NE; NE]	161	6 (3,7)	NE [NE; NE]	2,22	[0,88; 6,32]	0,0975
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	122	13 (10,7)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	4,12	[1,33; 17,96]	0,0169
Stadium IVB	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	108	10 (9,3)	NE [NE; NE]	121	3 (2,5)	NE [NE; NE]	3,45	[1,05; 15,39]	0,0519
Interaktion p-Wert										0,8475

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	65	4 (6,2)	NE [NE; NE]	49	1 (2,0)	NE [NE; NE]	2,55	[0,38; 49,95]	0,5329
Ehemals	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	133	17 (12,8)	NE [NE; NE]	134	4 (3,0)	NE [NE; NE]	4,16	[1,54; 14,47]	0,0046

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Nie	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	33	2 (6,1)	NE [NE; NE]	57	1 (1,8)	NE [NE; NE]	3,24	[0,31; 69,65]	0,2981
Interaktion p-Wert										0,9202

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	136	3 (2,2)	NE [NE; NE]	124	3 (2,4)	NE [NE; NE]	0,82	[0,15; 4,41]	0,8798
Rest of the World	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	95	20 (21,1)	NE [NE; NE]	116	3 (2,6)	NE [NE; NE]	8,22	[2,82; 34,90]	<0,0001
Interaktion p-Wert										0,0241

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	12	2 (16,7)	NE [3,8; NE]	12	2 (16,7)	NE [1,6; NE]	0,70	[0,08; 5,87]	0,8138
Pemetrexed-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	139	15 (10,8)	NE [NE; NE]	145	2 (1,4)	NE [NE; NE]	7,61	[2,15; 48,31]	0,0014

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Gemcitabin-Doublette	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	80	6 (7,5)	NE [NE; NE]	83	2 (2,4)	NE [NE; NE]	2,91	[0,67; 19,86]	0,2464
Interaktion p-Wert										0,1630

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	85	8 (9,4)	NE [NE; NE]	91	4 (4,4)	NE [NE; NE]	1,96	[0,62; 7,37]	0,3445
Nicht-Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	146	15 (10,3)	NE [NE; NE]	149	2 (1,3)	NE [NE; NE]	7,35	[2,07; 46,67]	0,0018
Interaktion p-Wert										0,1739

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	120	8 (6,7)	NE [NE; NE]	130	2 (1,5)	NE [NE; NE]	3,92	[0,98; 25,96]	0,0642
PD-L1 >/=1%	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	111	15 (13,5)	NE [NE; NE]	110	4 (3,6)	NE [NE; NE]	3,71	[1,34; 13,00]	0,0144
Interaktion p-Wert										0,9545

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	22	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC; NC]	NC
Nein	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	209	23 (11,0)	NE [NE; NE]	206	6 (2,9)	NE [NE; NE]	3,54	[1,53; 9,60]	0,0033
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Asiatisch
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Abstammung - Nicht-Asiatisch
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 0
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Performance status zu baseline - 1
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Aktiv
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Ehemals
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Raucherstatus - Nie
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

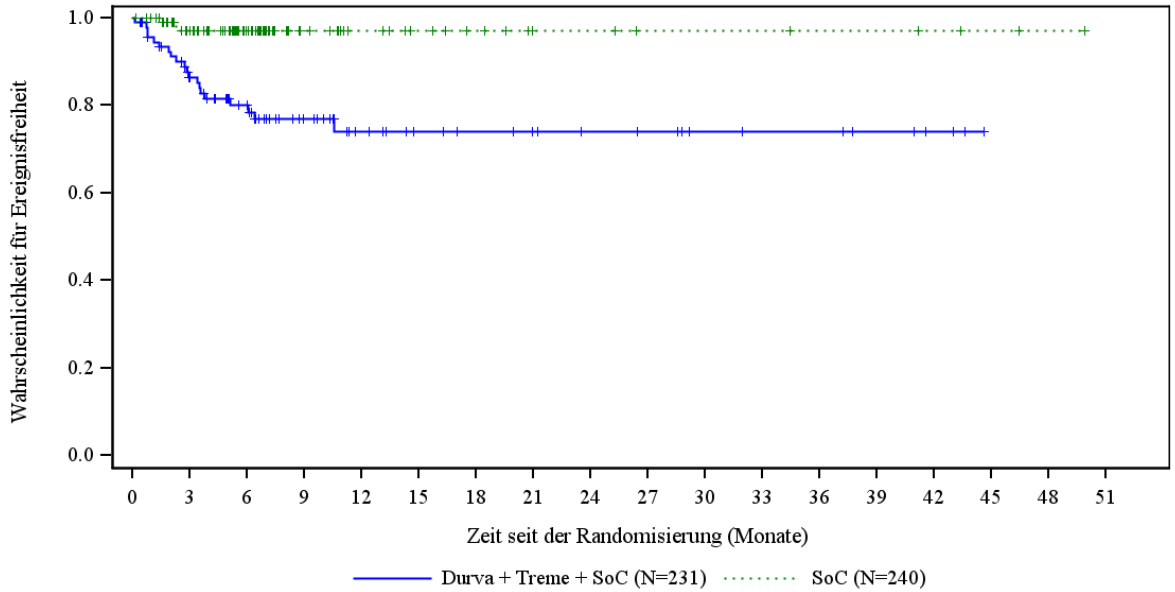
PLOT IS NOT CREATED BECAUSE FEWER THAN 10 EVENTS OCCUR

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	95	71	53	34	24	19	17	15	12	11	8	7	7	5	3	0	0	0
SoC	116	91	57	25	18	14	11	7	7	5	5	5	4	4	3	2	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae363g.sas Executed : 2022-11-21T204110

Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Ja
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 25th October 2021

Subgruppen : Hirnmetastasen - Nein
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest with maximum CTCAE grade >=3.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Anhang 4-G 1.3.5.3: Schwerwiegende unerwünschte Ereignisse von speziellem Interesse

Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	191	20 (10,5)	NE [NE; NE]	181	4 (2,2)	NE [NE; NE]	4,61	[1,74; 15,86]	0,0021
Weiblich	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	40	6 (15,0)	NE [NE; NE]	59	0	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	127	10 (7,9)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	4,67	[1,23; 30,43]	0,0287
>/= 65 Jahre	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	104	16 (15,4)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	8,60	[2,44; 54,43]	0,0005
Interaktion p-Wert										0,5717

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Abstammung										
Asiatisch	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	65	17 (26,2)	NE [13,1; NE]	83	3 (3,6)	NE [NE; NE]	7,84	[2,63; 33,56]	<0,0001
Nicht-Asiatisch	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	166	9 (5,4)	NE [NE; NE]	157	1 (0,6)	NE [NE; NE]	7,71	[1,44; 142,21]	0,0218
Interaktion p-Wert										0,9893

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SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
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At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Performance status zu baseline										
0	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	81	11 (13,6)	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	10,33	[2,01; 188,81]	0,0056
1	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	150	15 (10,0)	NE [NE; NE]	161	3 (1,9)	NE [NE; NE]	5,15	[1,70; 22,26]	0,0038
Interaktion p-Wert										0,5689

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
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At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	122	15 (12,3)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	7,13	[2,01; 45,28]	0,0028
Stadium IVB	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	108	11 (10,2)	NE [NE; NE]	121	2 (1,7)	NE [NE; NE]	5,87	[1,57; 37,96]	0,0089
Interaktion p-Wert										0,8566

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SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
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At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Raucherstatus										
Aktiv	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	65	4 (6,2)	NE [NE; NE]	49	0	NE [NE; NE]	NC	[NC; NC]	NC
Ehemals	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	133	18 (13,5)	NE [NE; NE]	134	4 (3,0)	NE [NE; NE]	4,66	[1,74; 16,13]	0,0022
Nie	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	33	4 (12,1)	NE [NE; NE]	57	0	NE [NE; NE]	NC	[NC; NC]	NC

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SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Interaktion p-Wert									NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
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(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	136	6 (4,4)	NE [NE; NE]	124	1 (0,8)	NE [NE; NE]	5,05	[0,86; 95,44]	0,0783
Rest of the World	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	95	20 (21,1)	NE [NE; NE]	116	3 (2,6)	NE [NE; NE]	8,20	[2,81; 34,82]	<0,0001
Interaktion p-Wert										0,6975

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Chemotherapie										
Paclitaxel-Doublette	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	12	2 (16,7)	NE [3,8; NE]	12	1 (8,3)	NE [NE; NE]	1,52	[0,14; 32,64]	0,6842
Pemetrexed-Doublette	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	139	18 (12,9)	NE [NE; NE]	145	2 (1,4)	NE [NE; NE]	9,29	[2,68; 58,46]	0,0002
Gemcitabin-Doublette	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	80	6 (7,5)	NE [NE; NE]	83	1 (1,2)	NE [NE; NE]	5,88	[1,00; 111,08]	0,0939

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SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Interaktion p-Wert									0,4495

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
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(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	85	8 (9,4)	NE [NE; NE]	91	2 (2,2)	NE [NE; NE]	4,00	[1,00; 26,52]	0,0849
Nicht-Plattenepithelial	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	146	18 (12,3)	NE [NE; NE]	149	2 (1,3)	NE [NE; NE]	8,97	[2,59; 56,46]	0,0003
Interaktion p-Wert										0,4573

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(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PD-L1-Status (1% cut-off)										
PD-L1 <1%	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	120	10 (8,3)	NE [NE; NE]	130	2 (1,5)	NE [NE; NE]	5,02	[1,32; 32,65]	0,0184
PD-L1 >/=1%	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	111	16 (14,4)	NE [NE; NE]	110	2 (1,8)	NE [NE; NE]	7,95	[2,26; 50,31]	0,0014
Interaktion p-Wert										0,6694

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=231)			SoC (N=240)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Hirnmetastasen										
Ja	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	22	1 (4,5)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC; NC]	NC
Nein	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	209	25 (12,0)	NE [NE; NE]	206	4 (1,9)	NE [NE; NE]	5,85	[2,26; 19,89]	0,0002
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated.
SAESI Serious adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Männlich
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Weiblich
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - <65 Jahre
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - >/= 65 Jahre
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Abstammung - Asiatisch
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Abstammung - Nicht-Asiatisch
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Performance status zu baseline - 0
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Performance status zu baseline - 1
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVA
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVB
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Aktiv
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Ehemals
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Raucherstatus - Nie
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Europa und Nordamerika
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Rest of the World
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Paclitaxel-Doublette
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Pemetrexed-Doublette
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Chemotherapie - Gemcitabin-Doublette
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Plattenepithelial
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Nicht-Plattenepithelial
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 <1%
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : PD-L1-Status (1% cut-off) - PD-L1 >/=1%
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Hirnmetastasen - Ja
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special (modified Safety analysis set - Patients with PD-L1<50%)
Data Cut-off: 11th March 2022

Subgruppen : Hirnmetastasen - Nein
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Anhang 4-G 2: Population mit einer PD-L1-Expression $\geq$ 50%

Anhang 4-G 2.1: Subgruppenanalysen

Anhang 4-G 2.1.1: Gesamtüberleben

Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=101)			SoC (N=97)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht									
Männlich	74	48 (64,9)	19,5 [12,7; 28,3]	69	64 (92,8)	10,6 [9,0; 13,2]	0,48	[0,32; 0,69]	<0,0001
Weiblich	27	22 (81,5)	9,9 [6,1; 16,6]	28	20 (71,4)	12,1 [6,7; 21,6]	1,25	[0,68; 2,31]	0,4550
Interaktion p-Wert									0,0079
Alter									
<65 Jahre	61	41 (67,2)	16,1 [10,2; 27,2]	51	42 (82,4)	12,0 [8,6; 19,7]	0,68	[0,44; 1,05]	0,0776
>/= 65 Jahre	40	29 (72,5)	14,7 [9,6; 26,3]	46	42 (91,3)	10,1 [8,2; 13,2]	0,55	[0,34; 0,88]	0,0105
Interaktion p-Wert									0,5095

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=101)			SoC (N=97)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium									
Stadium IVA	48	30 (62,5)	24,4 [14,2; NE]	46	41 (89,1)	10,0 [8,8; 17,5]	0,46	[0,28; 0,74]	0,0005
Stadium IVB	53	40 (75,5)	11,0 [6,1; 16,6]	50	42 (84,0)	11,6 [5,8; 14,9]	0,82	[0,53; 1,27]	0,3776
Interaktion p-Wert									0,0767
Region									
Europa und Nordamerika	56	44 (78,6)	13,1 [10,2; 19,7]	38	32 (84,2)	9,7 [7,2; 21,6]	0,75	[0,48; 1,20]	0,1893
Rest of the World	45	26 (57,8)	19,6 [9,8; NE]	59	52 (88,1)	11,7 [9,0; 14,9]	0,47	[0,29; 0,74]	0,0022
Interaktion p-Wert									0,1504

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 3.2.2.1 Summary of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

	Durva + Treme + SoC (N=101)			SoC (N=97)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate)[a]	Hazard ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie									
Plattenepithelial	36	31 (86,1)	12,6 [9,7; 19,3]	32	30 (93,8)	11,2 [7,2; 19,7]	0,81	[0,49; 1,35]	0,4013
Nicht-Plattenepithelial	65	39 (60,0)	20,1 [11,8; NE]	64	53 (82,8)	10,6 [8,3; 13,5]	0,52	[0,34; 0,78]	0,0032
Interaktion p-Wert									0,1697

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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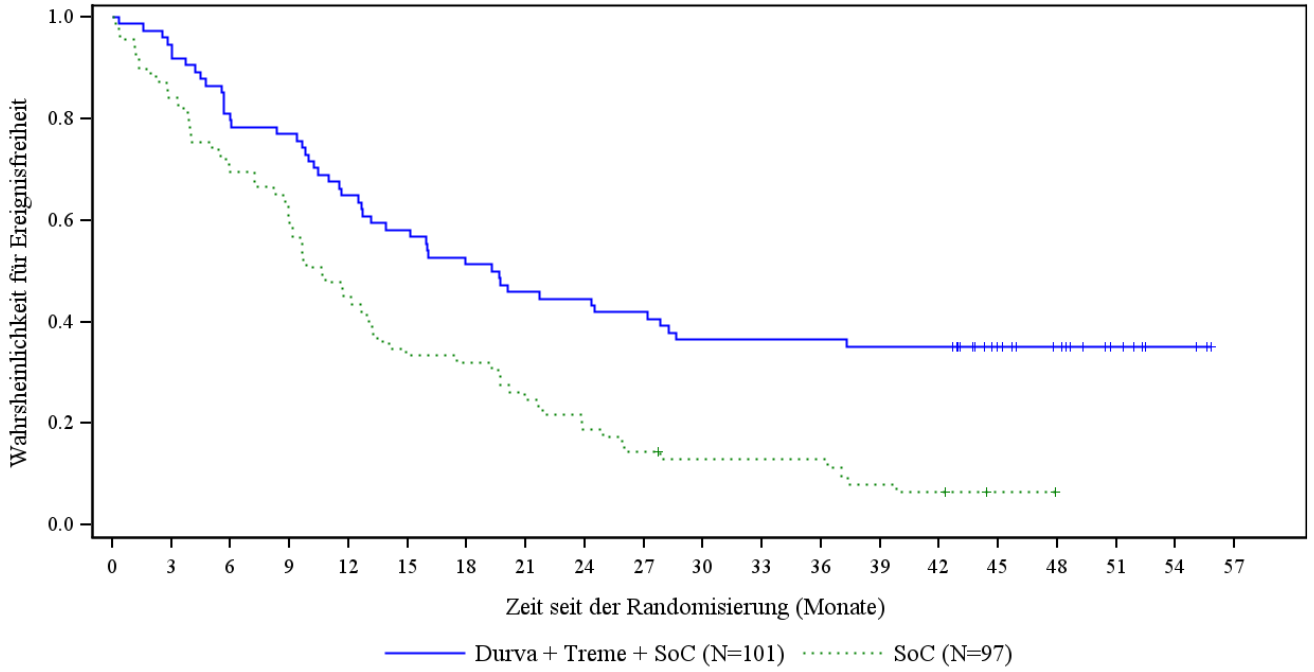
Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 10

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Geschlecht - Männlich



Anzahl an Patienten unter Risiko

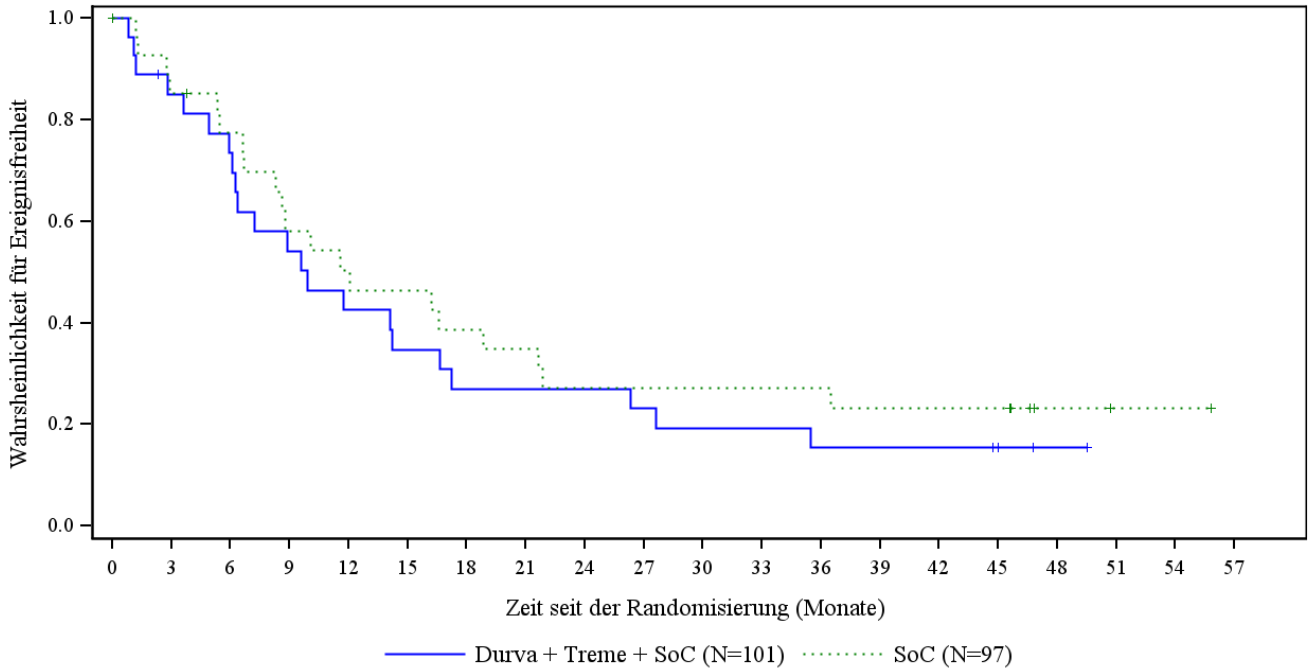
Durva + Treme + SoC	74	70	59	57	48	43	38	34	33	31	27	27	27	26	26	17	13	7	3	0
SoC	69	58	48	42	31	23	22	17	13	10	8	8	8	5	4	1	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Geschlecht - Weiblich



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	27	22	19	14	11	9	7	7	7	6	5	5	4	4	4	2	1	0	0	0
SoC	28	23	20	15	13	12	10	9	7	7	7	7	7	6	6	6	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Alter - <65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Alter - >/= 65 Jahre

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Krankheitsstadium - Stadium IVA

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Krankheitsstadium - Stadium IVB

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Region - Europa und Nordamerika

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Region - Rest of the World

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Histologie - Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ef302g.sas Executed : 2022-11-21T151905

Figure 3.2.2.2 Kaplan-Meier of subgroup analyses of overall survival
(modified Full analysis set - Patients with PD-L1>=50%)

Subgroup: Histologie - Nicht-Plattenepithelial

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
+ indicates a censored observation.

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Anhang 4-G 2.1.2: Gesamtraten unerwünschter Ereignisse

Anhang 4-G 2.1.2.1: Unerwünschte Ereignisse

Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse (UE)	73	72 (98,6)	0,2 [0,1; 0,3]	66	62 (93,9)	0,2 [0,1; 0,3]	1,01	[0,72; 1,42]	0,9799
Weiblich	Unerwünschte Ereignisse (UE)	26	26 (100)	0,1 [0,1; 0,3]	27	26 (96,3)	0,2 [0,1; 0,5]	1,31	[0,75; 2,28]	0,3461
Interaktion p-Wert										0,4310

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse (UE)	60	59 (98,3)	0,1 [0,1; 0,3]	49	45 (91,8)	0,2 [0,1; 0,3]	1,05	[0,71; 1,56]	0,7556
>/= 65 Jahre	Unerwünschte Ereignisse (UE)	39	39 (100)	0,1 [0,1; 0,3]	44	43 (97,7)	0,2 [0,1; 0,3]	1,20	[0,77; 1,86]	0,3101
Interaktion p-Wert										0,6584

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse (UE)	47	46 (97,9)	0,1 [0,1; 0,3]	45	43 (95,6)	0,2 [0,1; 0,3]	1,01	[0,66; 1,54]	0,9518
Stadium IVB	Unerwünschte Ereignisse (UE)	52	52 (100)	0,2 [0,1; 0,3]	48	45 (93,8)	0,2 [0,1; 0,3]	1,18	[0,79; 1,77]	0,2954
Interaktion p-Wert										0,5827

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse (UE)	54	53 (98,1)	0,3 [0,2; 0,4]	35	33 (94,3)	0,2 [0,1; 0,3]	0,78	[0,50; 1,22]	0,2367
Rest of the World	Unerwünschte Ereignisse (UE)	45	45 (100)	0,1 [0,1; 0,1]	58	55 (94,8)	0,2 [0,1; 0,3]	1,94	[1,29; 2,90]	0,0020
Interaktion p-Wert										0,0032

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Table 4.2.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse (UE)	35	34 (97,1)	0,2 [0,1; 0,3]	31	29 (93,5)	0,2 [0,1; 0,3]	0,94	[0,57; 1,55]	0,9038
Nicht-Plattenepithelial	Unerwünschte Ereignisse (UE)	64	64 (100)	0,1 [0,1; 0,3]	62	59 (95,2)	0,2 [0,1; 0,3]	1,19	[0,83; 1,70]	0,3136
Interaktion p-Wert										0,4477

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE Adverse event.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test.
For certain subgroups there are patients who belong to a subgroup with too few patients and so are not analysed. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis. Includes treatment-emergent AEs only.

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Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse (UE)

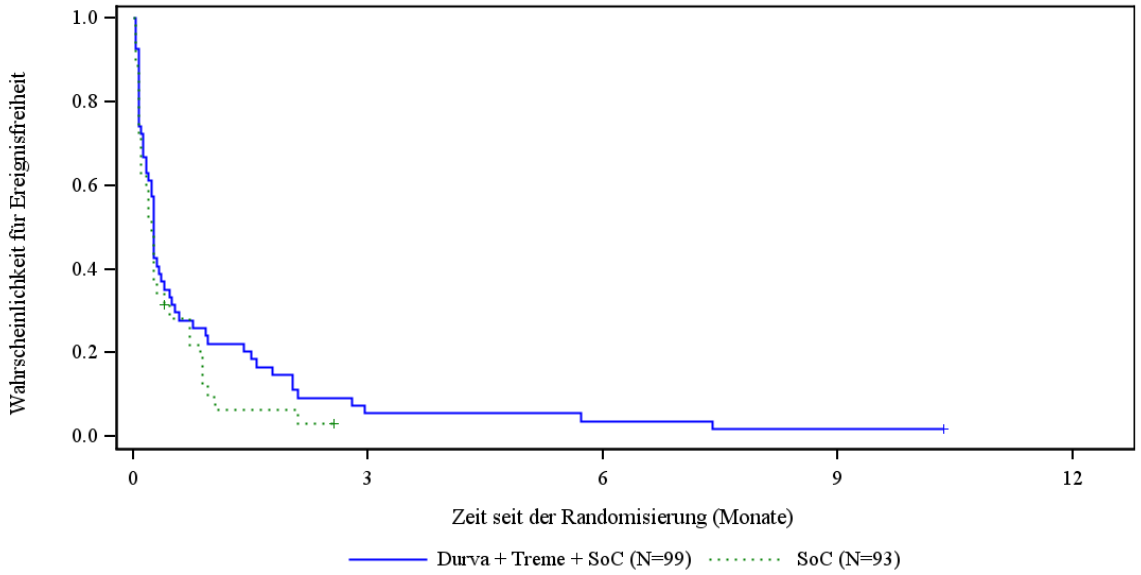
PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse (UE)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	54	3	2	1	0
SoC	35	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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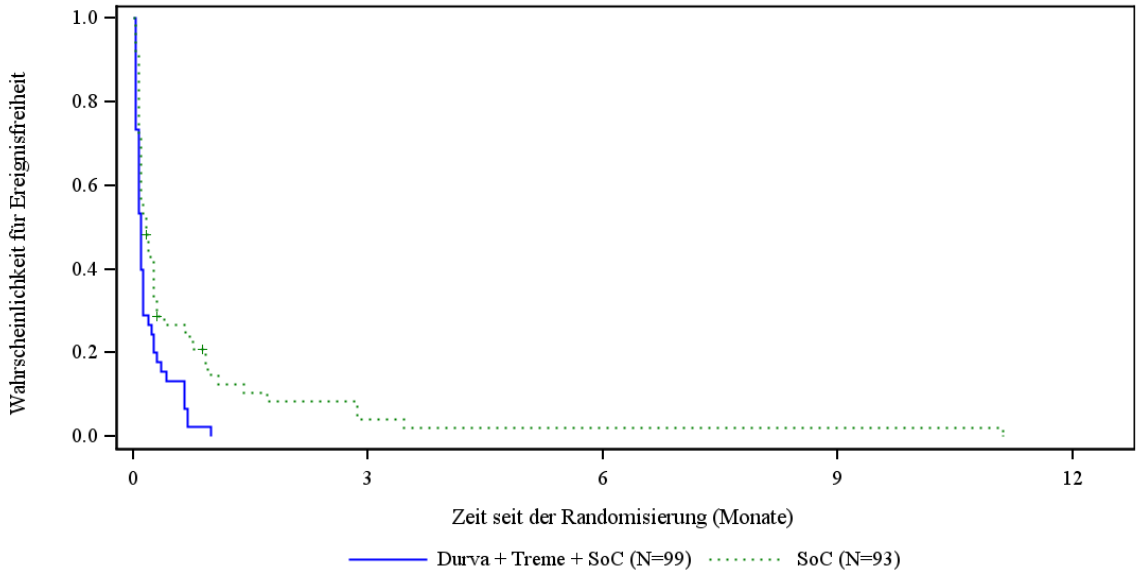
Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse (UE)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	45	0	0	0	0
SoC	58	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

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Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Figure 4.2.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse (UE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. AE Adverse event.
N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few
patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation. Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae302g.sas Executed : 2022-11-21T154447

Anhang 4-G 2.1.2.2: Behandlungsabbruch aufgrund unerwünschter Ereignisse

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Therapieabbrüche aufgrund von UE	73	25 (34,2)	33,1 [14,1; NE]	66	14 (21,2)	NE [NE; NE]	1,01	[0,51; 2,04]	0,9995
Weiblich	Therapieabbrüche aufgrund von UE	26	6 (23,1)	NE [7,3; NE]	27	2 (7,4)	NE [NE; NE]	3,12	[0,72; 21,29]	0,1168
Interaktion p-Wert										0,2023

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Therapieabbrüche aufgrund von UE	60	13 (21,7)	NE [29,8; NE]	49	6 (12,2)	NE [NE; NE]	1,24	[0,49; 3,57]	0,6621
>/= 65 Jahre	Therapieabbrüche aufgrund von UE	39	18 (46,2)	16,4 [5,8; NE]	44	10 (22,7)	NE [7,4; NE]	1,50	[0,69; 3,41]	0,3177
Interaktion p-Wert										0,7712

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae222g.sas Executed : 2022-09-13T154257

Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Therapieabbrüche aufgrund von UE	47	16 (34,0)	NE [14,1; NE]	45	10 (22,2)	NE [7,4; NE]	0,98	[0,44; 2,27]	0,7552
Stadium IVB	Therapieabbrüche aufgrund von UE	52	15 (28,8)	NE [12,9; NE]	48	6 (12,5)	NE [NE; NE]	1,90	[0,77; 5,34]	0,1201
Interaktion p-Wert										0,2936

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Therapieabbrüche aufgrund von UE	54	18 (33,3)	33,1 [11,1; NE]	35	7 (20,0)	NE [7,4; NE]	1,18	[0,51; 3,05]	0,9071
Rest of the World	Therapieabbrüche aufgrund von UE	45	13 (28,9)	NE [16,4; NE]	58	9 (15,5)	NE [NE; NE]	1,31	[0,55; 3,21]	0,4314
Interaktion p-Wert										0,8650

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.4.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Therapieabbrüche aufgrund von UE	35	10 (28,6)	29,8 [11,1; NE]	31	4 (12,9)	NE [NE; NE]	1,45	[0,48; 5,32]	0,9587
Nicht-Plattenepithelial	Therapieabbrüche aufgrund von UE	64	21 (32,8)	NE [14,1; NE]	62	12 (19,4)	NE [NE; NE]	1,29	[0,63; 2,73]	0,3473
Interaktion p-Wert										0,8647

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
DAE Adverse event leading to discontinuation. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Figure 4.4.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events leading to discontinuation of study treatment (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Therapieabbrüche aufgrund von UE

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE leading to discontinuation of study treatment.
For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Anhang 4-G 2.1.2.3: Schwere unerwünschte Ereignisse (CTCAE-Grad $\geq$ 3)

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	UE mit max. CTCAE Grad >/=3	73	49 (67,1)	1,7 [1,3; 2,7]	66	42 (63,6)	1,8 [1,0; 3,5]	0,92	[0,60; 1,40]	0,8523
Weiblich	UE mit max. CTCAE Grad >/=3	26	19 (73,1)	2,1 [0,8; 7,9]	27	15 (55,6)	6,8 [2,3; 11,1]	1,58	[0,80; 3,16]	0,2412
Interaktion p-Wert										0,1817

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE G>=3 Adverse event with maximum CTCAE grade >= 3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

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Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	UE mit max. CTCAE Grad >/=3	60	37 (61,7)	2,0 [1,4; 7,9]	49	27 (55,1)	4,1 [1,7; 11,1]	1,08	[0,66; 1,78]	0,7691
>/= 65 Jahre	UE mit max. CTCAE Grad >/=3	39	31 (79,5)	1,5 [0,8; 2,6]	44	30 (68,2)	2,3 [0,7; 3,5]	1,16	[0,70; 1,93]	0,4900
Interaktion p-Wert										0,8370

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE G>=3 Adverse event with maximum CTCAE grade >= 3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae212g.sas Executed : 2022-09-13T152901

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	UE mit max. CTCAE Grad >/=3	47	33 (70,2)	1,7 [1,0; 5,5]	45	30 (66,7)	2,5 [1,8; 6,8]	0,99	[0,60; 1,63]	0,9381
Stadium IVB	UE mit max. CTCAE Grad >/=3	52	35 (67,3)	1,8 [1,3; 2,6]	48	27 (56,3)	2,8 [1,0; NE]	1,18	[0,72; 1,97]	0,5225
Interaktion p-Wert										0,6232

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE G>=3 Adverse event with maximum CTCAE grade >= 3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae212g.sas Executed : 2022-09-13T152901

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	UE mit max. CTCAE Grad >/=3	54	33 (61,1)	1,8 [1,3; 23,3]	35	20 (57,1)	2,9 [1,4; 7,7]	1,05	[0,61; 1,87]	0,8709
Rest of the World	UE mit max. CTCAE Grad >/=3	45	35 (77,8)	1,6 [0,8; 2,6]	58	37 (63,8)	2,3 [1,0; 6,5]	1,22	[0,76; 1,94]	0,3472
Interaktion p-Wert										0,6892

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE G>=3 Adverse event with maximum CTCAE grade >= 3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae212g.sas Executed : 2022-09-13T152901

Table 4.3.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	UE mit max. CTCAE Grad >/=3	35	24 (68,6)	1,5 [0,8; 2,8]	31	17 (54,8)	1,8 [1,0; NE]	1,20	[0,65; 2,27]	0,4101
Nicht-Plattenepithelial	UE mit max. CTCAE Grad >/=3	64	44 (68,8)	1,8 [1,4; 4,7]	62	40 (64,5)	2,8 [1,7; 6,8]	1,03	[0,67; 1,58]	0,9480
Interaktion p-Wert										0,6853

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. AE G>=3 Adverse event with maximum CTCAE grade >= 3. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group.
Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae212g.sas Executed : 2022-09-13T152901

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Figure 4.3.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events with maximum CTCAE grade >= 3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
UE mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any AE with maximum CTCAE grade >=3. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae312g.sas Executed : 2022-11-21T161536

Anhang 4-G 2.1.2.4: Schwerwiegende unerwünschte Ereignisse

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Schwerwiegende unerwünschte Ereignisse (SUE)	73	34 (46,6)	15,4 [7,2; NE]	66	28 (42,4)	18,3 [3,5; NE]	0,73	[0,44; 1,24]	0,2594
Weiblich	Schwerwiegende unerwünschte Ereignisse (SUE)	26	13 (50,0)	7,9 [1,4; NE]	27	9 (33,3)	24,7 [6,8; NE]	1,59	[0,68; 3,85]	0,3026
Interaktion p-Wert										0,1283

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae232g.sas Executed : 2022-09-13T172327

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Schwerwiegende unerwünschte Ereignisse (SUE)	60	21 (35,0)	NE [11,4; NE]	49	14 (28,6)	NE [18,3; NE]	0,94	[0,48; 1,90]	0,9182
>/= 65 Jahre	Schwerwiegende unerwünschte Ereignisse (SUE)	39	26 (66,7)	5,3 [2,5; 15,4]	44	23 (52,3)	6,8 [2,5; 24,7]	0,99	[0,56; 1,76]	0,9173
Interaktion p-Wert										0,9061

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae232g.sas Executed : 2022-09-13T172327

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Schwerwiegende unerwünschte Ereignisse (SUE)	47	20 (42,6)	29,8 [7,9; NE]	45	20 (44,4)	8,6 [3,5; NE]	0,65	[0,34; 1,22]	0,1727
Stadium IVB	Schwerwiegende unerwünschte Ereignisse (SUE)	52	27 (51,9)	7,2 [4,3; NE]	48	17 (35,4)	18,3 [4,6; NE]	1,27	[0,69; 2,38]	0,3912
Interaktion p-Wert										0,1295

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae232g.sas Executed : 2022-09-13T172327

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Schwerwiegende unerwünschte Ereignisse (SUE)	54	25 (46,3)	15,4 [7,2; NE]	35	13 (37,1)	8,6 [2,9; NE]	0,94	[0,49; 1,91]	0,5914
Rest of the World	Schwerwiegende unerwünschte Ereignisse (SUE)	45	22 (48,9)	27,8 [3,2; NE]	58	24 (41,4)	18,3 [4,6; NE]	0,93	[0,51; 1,68]	0,9637
Interaktion p-Wert										0,9736

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae232g.sas Executed : 2022-09-13T172327

Table 4.5.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Schwerwiegende unerwünschte Ereignisse (SUE)	35	19 (54,3)	11,4 [4,3; 29,8]	31	8 (25,8)	NE [NE; NE]	1,72	[0,78; 4,20]	0,3589
Nicht-Plattenepithelial	Schwerwiegende unerwünschte Ereignisse (SUE)	64	28 (43,8)	NE [7,2; NE]	62	29 (46,8)	8,6 [3,8; NE]	0,69	[0,41; 1,18]	0,2386
Interaktion p-Wert										0,0685

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
SAE Serious adverse event. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. [a] Calculated using the Kaplan-Meier technique.
[b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test using the Breslow approach for handling ties.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae232g.sas Executed : 2022-09-13T172327

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Männlich
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Weiblich
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - <65 Jahre
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - >/= 65 Jahre
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVA
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVB
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Europa und Nordamerika
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Rest of the World
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Plattenepithelial
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae332g.sas Executed : 2022-11-21T194734

Figure 4.5.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Nicht-Plattenepithelial
Schwerwiegende unerwünschte Ereignisse (SUE)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any serious adverse event. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.
Includes treatment-emergent AEs only.

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Anhang 4-G 2.1.3: Gesamtraten unerwünschter Ereignisse von speziellem Interesse

Anhang 4-G 2.1.3.1: Unerwünschte Ereignisse von speziellem Interesse

Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse von speziellem Interesse (UESI)	73	42 (57,5)	4,4 [2,0; 15,6]	66	17 (25,8)	NE [NE; NE]	2,20	[1,27; 3,98]	0,0054
Weiblich	Unerwünschte Ereignisse von speziellem Interesse (UESI)	26	19 (73,1)	2,4 [0,7; 3,9]	27	10 (37,0)	NE [3,8; NE]	2,34	[1,11; 5,25]	0,0188
Interaktion p-Wert										0,8987

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI)	60	33 (55,0)	4,4 [2,1; NE]	49	12 (24,5)	NE [NE; NE]	2,23	[1,18; 4,51]	0,0162
>/= 65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI)	39	28 (71,8)	2,5 [0,7; 4,3]	44	15 (34,1)	NE [7,1; NE]	2,33	[1,26; 4,48]	0,0071
Interaktion p-Wert										0,9241

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse von speziellem Interesse (UESI)	47	30 (63,8)	3,0 [2,0; 33,1]	45	13 (28,9)	NE [7,1; NE]	2,21	[1,17; 4,40]	0,0185
Stadium IVB	Unerwünschte Ereignisse von speziellem Interesse (UESI)	52	31 (59,6)	2,8 [1,4; 15,6]	48	14 (29,2)	NE [NE; NE]	2,18	[1,18; 4,23]	0,0119
Interaktion p-Wert										0,9755

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae242g.sas Executed : 2022-09-13T162506

Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse von speziellem Interesse (UESI)	54	27 (50,0)	9,5 [2,8; NE]	35	12 (34,3)	NE [1,1; NE]	1,22	[0,63; 2,51]	0,6087
Rest of the World	Unerwünschte Ereignisse von speziellem Interesse (UESI)	45	34 (75,6)	2,0 [0,5; 3,0]	58	15 (25,9)	NE [7,1; NE]	3,83	[2,12; 7,24]	<0,0001
Interaktion p-Wert										0,0145

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae242g.sas Executed : 2022-09-13T162506

Table 4.6.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI)	35	21 (60,0)	3,4 [1,4; 33,1]	31	7 (22,6)	NE [NE; NE]	2,48	[1,10; 6,32]	0,0502
Nicht-Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI)	64	40 (62,5)	3,0 [1,6; 4,4]	62	20 (32,3)	NE [7,1; NE]	2,12	[1,25; 3,71]	0,0040
Interaktion p-Wert										0,7610

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval.
AESI Adverse event of special interest. NE Not estimable as median (or 95% CI) not reached.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae342g.sas Executed : 2022-11-21T200308

Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

Program: P:\AZ\Durvalumab\POSEIDON\PRIO2\Prog\Output\ae342g.sas Executed : 2022-11-21T200308

Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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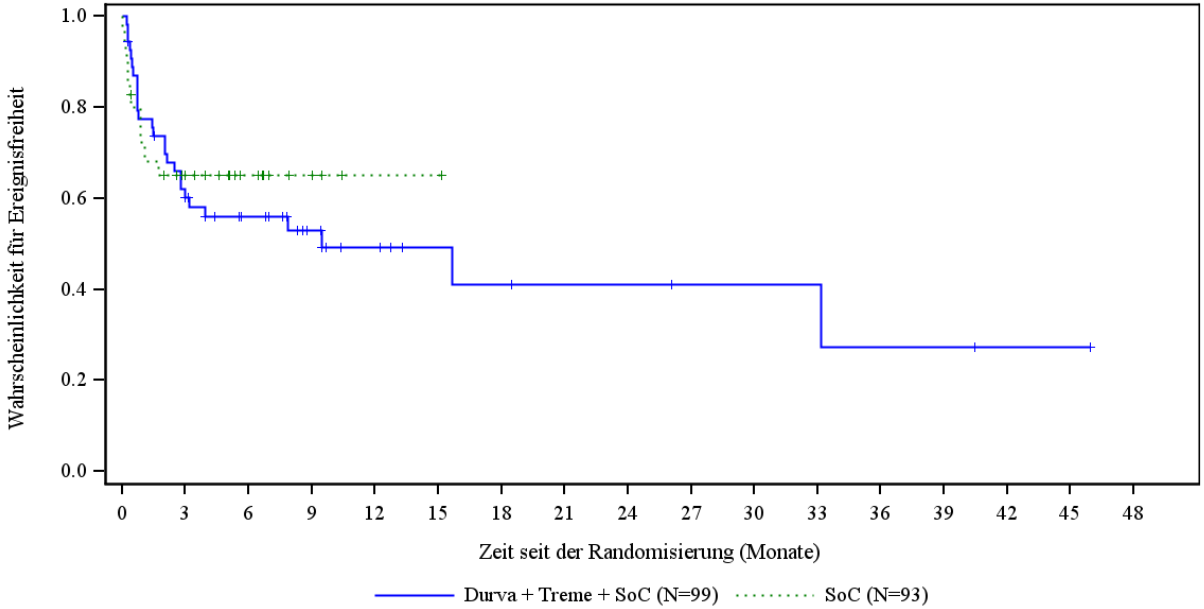
Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse von speziellem Interesse (UESI)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	54	30	23	15	10	6	5	4	4	3	3	3	2	2	1	1	0
SoC	35	18	11	4	1	1	0	0	0	0	0	0	0	0	0	0	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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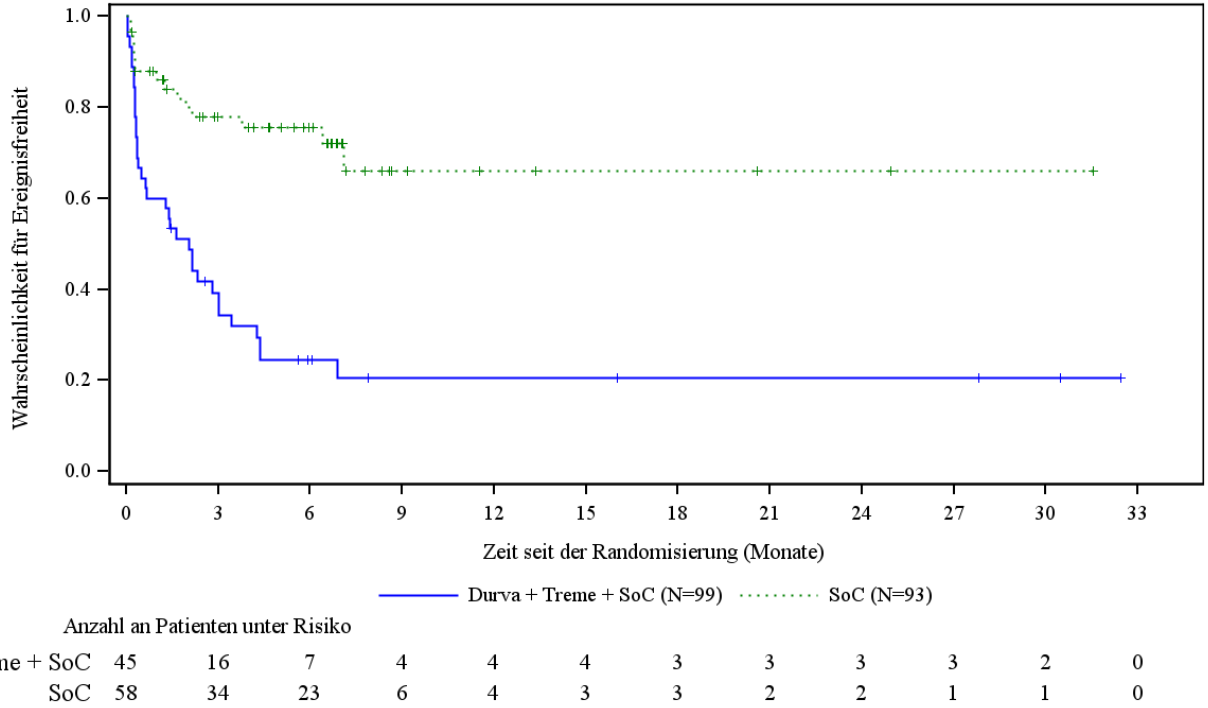
Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse von speziellem Interesse (UESI)



Anzahl an Patienten unter Risiko

Durva + Treme + SoC	45	16	7	4	4	4	3	3	3	3	2	0
SoC	58	34	23	6	4	3	3	2	2	1	1	0

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.6.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of any adverse event of special interest. For certain subgroups there are patients with missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Kaplan-Meier plots are only produced if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Anhang 4-G 2.1.3.2: Schwere unerwünschte Ereignisse von speziellem Interesse (CTCAE-Grad $\geq$ 3)

Durvalumab, POSEIDON (D419MC00004), German benefit assessment Page 1 of 5

Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen	Kategorie/ Sub-Kategorie/ Preferred term	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	73	15 (20,5)	NE [NE; NE]	66	5 (7,6)	NE [NE; NE]	1,86	[0,69; 5,88]	0,2395
Weiblich	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	26	2 (7,7)	NE [NE; NE]	27	0	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. Analysis only performed if significant in main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen	Kategorie/ Sub-Kategorie/ Preferred term	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	60	8 (13,3)	NE [NE; NE]	49	1 (2,0)	NE [NE; NE]	5,05	[0,92; 94,08]	0,1146
>/= 65 Jahre	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	39	9 (23,1)	NE [12,9; NE]	44	4 (9,1)	NE [NE; NE]	2,00	[0,64; 7,48]	0,2021
Interaktion p-Wert										0,4476

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. Analysis only performed if significant in main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen	Kategorie/ Sub-Kategorie/ Preferred term	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	47	10 (21,3)	NE [NE; NE]	45	4 (8,9)	NE [NE; NE]	1,75	[0,57; 6,50]	0,3329
Stadium IVB	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	52	7 (13,5)	NE [NE; NE]	48	1 (2,1)	NE [NE; NE]	5,48	[0,97; 102,59]	0,0799
Interaktion p-Wert										0,3516

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. Analysis only performed if significant in main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen	Kategorie/ Sub-Kategorie/ Preferred term	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	54	6 (11,1)	NE [NE; NE]	35	3 (8,6)	NE [NE; NE]	0,97	[0,25; 4,64]	0,8002
Rest of the World	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	45	11 (24,4)	NE [29,8; NE]	58	2 (3,4)	NE [NE; NE]	5,80	[1,53; 37,74]	0,0077
Interaktion p-Wert										0,0871

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. Analysis only performed if significant in main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.8.2.1 Summary of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen	Kategorie/ Sub-Kategorie/ Preferred term	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	35	6 (17,1)	NE [29,8; NE]	31	0	NE [NE; NE]	NC	[NC; NC]	NC
Nicht-Plattenepithelial	Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3	64	11 (17,2)	NE [NE; NE]	62	5 (8,1)	NE [NE; NE]	1,86	[0,67; 5,95]	0,2477
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. AESI G>=3 Adverse event of special interest with maximum CTCAE grade >=3. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories.
[a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated from an unstratified Cox proportional hazards model using the Efron method to control for ties, with treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated from an unstratified log-rank test. Analysis only performed if significant in main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Männlich
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Geschlecht - Weiblich
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - <65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Alter - >/= 65 Jahre
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVA
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Krankheitsstadium - Stadium IVB
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Europa und Nordamerika
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Region - Rest of the World
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.8.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any adverse events of special interest with maximum CTCAE grade >=3 (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 25th October 2021

Subgruppen : Histologie - Nicht-Plattenepithelial
Unerwünschte Ereignisse von speziellem Interesse (UESI) mit max. CTCAE Grad >/=3

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Anhang 4-G 2.1.3.3: Schwerwiegende unerwünschte Ereignisse von speziellem Interesse

Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Geschlecht										
Männlich	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	73	14 (19,2)	NE [NE; NE]	66	2 (3,0)	NE [NE; NE]	4,56	[1,23; 29,49]	0,0306
Weiblich	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	26	1 (3,8)	NE [NE; NE]	27	0	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. SAESI Serious adverse event of special interest. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE categories. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis is only performed for a particular event if significant in the main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Alter										
<65 Jahre	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	60	8 (13,3)	NE [NE; NE]	49	0	NE [NE; NE]	NC	[NC; NC]	NC
>/= 65 Jahre	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	39	7 (17,9)	NE [NE; NE]	44	2 (4,5)	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. SAESI Serious adverse event of special interest. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE categories. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis is only performed for a particular event if significant in the main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Krankheitsstadium										
Stadium IVA	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	47	8 (17,0)	NE [NE; NE]	45	1 (2,2)	NE [NE; NE]	NC	[NC; NC]	NC
Stadium IVB	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	52	7 (13,5)	NE [NE; NE]	48	1 (2,1)	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. SAESI Serious adverse event of special interest. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE categories. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis is only performed for a particular event if significant in the main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Region										
Europa und Nordamerika	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	54	4 (7,4)	NE [NE; NE]	35	2 (5,7)	NE [NE; NE]	0,83	[0,15; 6,21]	0,8382
Rest of the World	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	45	11 (24,4)	NE [29,8; NE]	58	0	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. SAESI Serious adverse event of special interest. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE categories. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis is only performed for a particular event if significant in the main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Table 4.9.2.1 Summary of subgroup analyses of time to first occurrence of any serious adverse events of special interest
(modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

		Durva + Treme + SoC (N=99)			SoC (N=93)					
Subgruppen		n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Histologie										
Plattenepithelial	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	35	8 (22,9)	NE [29,8; NE]	31	0	NE [NE; NE]	NC	[NC; NC]	NC
Nicht-Plattenepithelial	Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)	64	7 (10,9)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	NC	[NC; NC]	NC
Interaktion p-Wert										NC

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy. CI Confidence interval. NC Not calculated. SAESI Serious adverse event of special interest. PT Preferred term. SOC System organ class. NE Not estimable as median (or 95% CI) not reached. N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE categories. [a] Calculated using the Kaplan-Meier technique. [b] The hazard ratio and CI are estimated using an unstratified Cox proportional hazards model with Efron ties and treatment, subgroup and treatment-by-subgroup interaction as covariates. The CI is calculated using a profile likelihood approach. [c] P-values are generated using an unstratified log-rank test. Analysis is only performed for a particular event if significant in the main analysis. At least 10 patients in each subgroup level and at least 10 events in at least one subgroup level combined for both arms is required for a meaningful analysis.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Männlich
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Geschlecht - Weiblich
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - <65 Jahre
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Alter - >/= 65 Jahre
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVA
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Krankheitsstadium - Stadium IVB
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Europa und Nordamerika
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Region - Rest of the World
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Plattenepithelial
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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Figure 4.9.2.2 Kaplan-Meier of subgroup analyses of time to first occurrence of any serious adverse events of special interest (modified Safety analysis set - Patients with PD-L1>=50%)
Data Cut-off: 11th March 2022

Subgruppen : Histologie - Nicht-Plattenepithelial
Schwerwiegende Unerwünschte Ereignisse von speziellem Interesse (SUESI)

PLOT IS NOT CREATED BECAUSE INTERACTION P-VALUE IS >0.05

Durva Durvalumab. Treme Tremelimumab. SoC Standard of care chemotherapy.
N Number of patients in treatment group. Time to event analysis for AE is defined as the time from the date of first dose until the date of first onset of the respective AE (total, SOC, PT) categories. For certain subgroups there are patients with
missing status or who belong to a subgroup with too few patients and so are not included in the analysis.
Analysis is only performed for a particular event if significant in the main analysis
Kaplan-Meier plots are only produced on SOC and PT levels if the interaction p-value in the corresponding time to event analysis is <0.05.
+ indicates a censored observation.

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