Dokumentvorlage, Version vom 16.12.2021

Durvalumab (IMFINZI®)

AstraZeneca GmbH

Modul 4A – Anhang 4-G

Durvalumab zur Behandlung des kleinzelligen Lungenkarzinoms bei Erwachsenen im nicht fortgeschrittenen Stadium (limited-stage small cell lung cancer, LS-SCLC), deren Erkrankung nach einer platinbasierten Radiochemotherapie nicht progredient ist

Stand: 25.07.2025

Anhang 4-G: Daten zur Studie ADRIATIC

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Anhang 4-G1: Beobachtungszeiten

Anhang 4-G1.1: Wirksamkeit

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Table 1.1 ADRIATIC: Summary of observation period (months) for efficacy endpoints
Full Analysis Set, DCO 15JAN2024

		Durva (N=264)	Placebo (N=266)
Gesamtüberleben	n	264	266
	Mediane	30,75	28,63
	Min	0,1	0,7
	Max	60,2	60,9
Progressionsfreies Überleben	n	264	266
	Mediane	9,07	7,39
	Min	0,0	0,0
	Max	55,4	55,8
Progressionsfreies Überleben 2	n	264	266
	Mediane	28,53	16,16
	Min	0,0	0,0
	Max	60,2	60,9
Zeit bis zur ersten Folgetherapie	n	264	266
	Mediane	21,19	14,42
	Min	0,1	0,7
	Max	60,1	60,9
Zeit bis zum Tod oder einer Fernmetastase	n	264	266
	Mediane	12,35	9,40
	Min	0,0	0,0
	Max	55,4	55,8

Observation period for an efficacy endpoint is defined as the time from randomisation to the date of that event, if occurred or otherwise, to the date of the last evaluable assessment of that efficacy endpoint or randomisation if no assessments.
Second progression-free survival assessed by investigation assessment, Progression-free survival and Time to Death or Distant Metastasis assessed by BICR assessment.
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Anhang 4-G1.2: Sicherheit

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Table 2.1 ADRIATIC: Summary of observation period (months) for all safety outcomes
Safety Analysis Set, DCO 15JAN2024

		Durvalumab (N=262)	Placebo (N=265)
UE	n	262	265
	Mediane	10,32	9,23
	Min	1,3	1,1
	Max	26,9	26,9

Observation period for all safety outcomes is defined as the duration from the date of first dose of study treatment to the earliest of the date of data cut-off, 90 days following discontinuation of study treatment, date of starting subsequent cancer therapy or date of death.
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Anhang 4-G2: Mortalität: Gesamtüberleben

Table 1.2.1 ADRIATIC: Summary of analysis of Overall Survival
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Gesamtüberleben	264	115 (43,6)	55,9 [37,3; NE]	266	146 (54,9)	33,4 [25,5;39,9]	0,72	[0,56; 0,92]	0,0075*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G2.1: Mortalität: Gesamtüberleben - Kaplan-Meier-Plot

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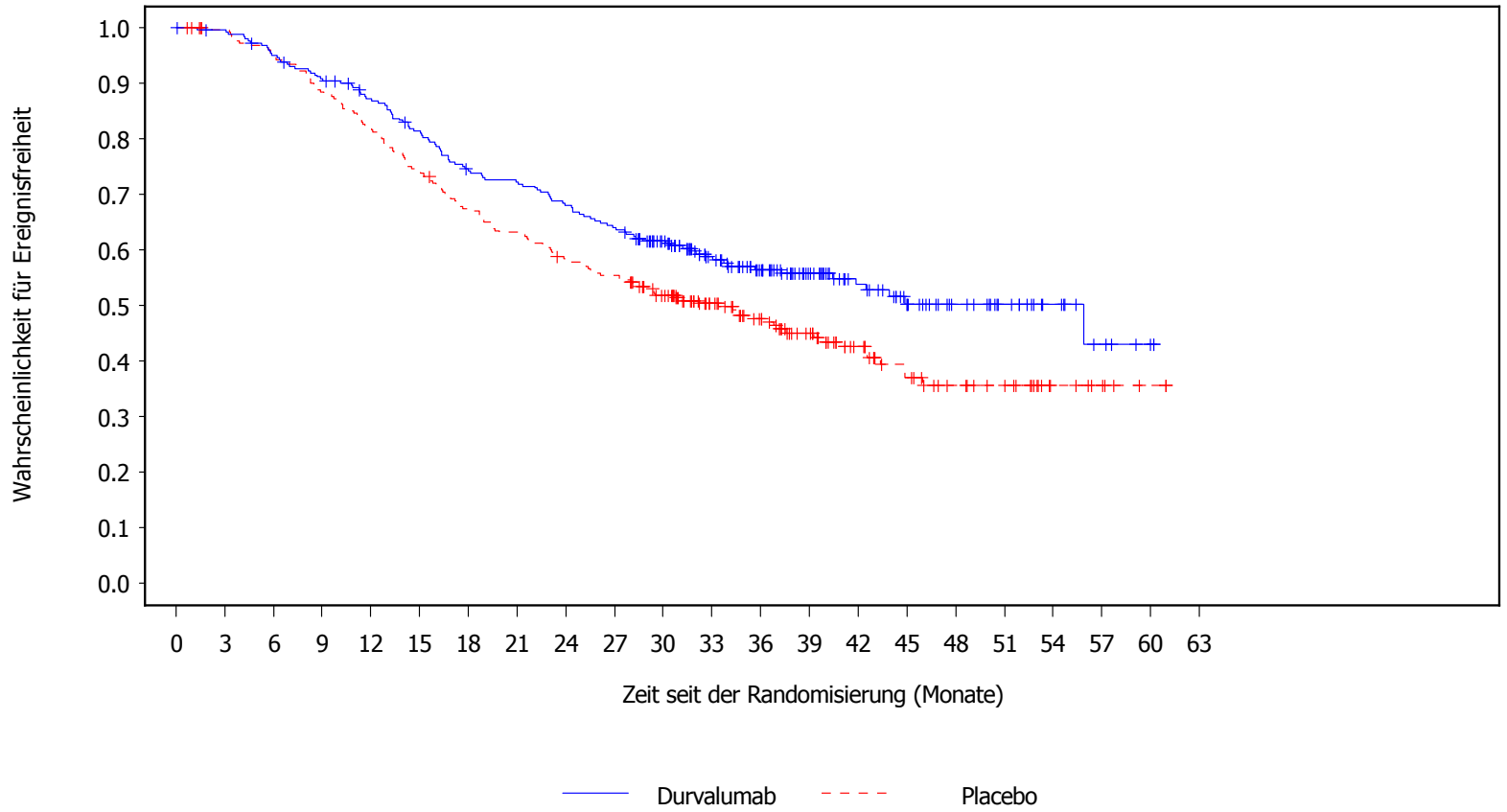
Figure 1.3.1 ADRIATIC: Kaplan-Meier plot of Overall Survival
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0	Durvalumab
266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0	Placebo

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Anhang 4-G2.2: Mortalität: Gesamtüberleben - Subgruppenanalysen

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Table 4.1.1 ADRIATIC: Summary of subgroup analysis of Overall Survival
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	14 (38,9)	NE [NE; NE]	37	14 (37,8)	NE [NE; NE]	1,03	[0,49; 2,18]	0,9367
Stadium III	228	101 (44,3)	44,9 [34,0; NE]	229	132 (57,6)	29,5 [24,1;37,6]	0,69	[0,54; 0,90]	0,0057*
Interaktions p-Wert									0,3261
TNM Status (eCRF) - DEU									
Stadium I/II	33	11 (33,3)	NE [NE; NE]	34	12 (35,3)	NE [NE; NE]	0,93	[0,40; 2,12]	0,8642
Stadium III	231	104 (45,0)	44,9 [33,0; NE]	232	134 (57,8)	29,4 [24,1;37,0]	0,71	[0,55; 0,91]	0,0078*
Interaktions p-Wert									0,5310
Erhalt einer PCI (IVRS) - DEU									
Ja	142	53 (37,3)	NE [NE; NE]	144	68 (47,2)	42,5 [33,4; NE]	0,74	[0,52; 1,06]	0,1013
Nein	122	62 (50,8)	37,3 [24,3; NE]	122	78 (63,9)	23,9 [18,7;31,1]	0,71	[0,51; 0,99]	0,0425*
Interaktions p-Wert									0,8576
Erhalt einer PCI (eCRF) - DEU									
Ja	142	53 (37,3)	NE [NE; NE]	143	67 (46,9)	42,5 [33,4; NE]	0,75	[0,52; 1,07]	0,1113
Nein	122	62 (50,8)	37,3 [24,3; NE]	123	79 (64,2)	24,1 [18,8;31,1]	0,71	[0,51; 0,98]	0,0403*
Interaktions p-Wert									0,8264
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	14 (43,8)	NE [NE; NE]	32	24 (75,0)	16,0 [11,9;23,5]	0,46	[0,23; 0,87]	0,0170*
>=14 bis <28 Tage	79	37 (46,8)	42,5 [28,7; NE]	80	51 (63,8)	25,5 [18,8;30,8]	0,60	[0,39; 0,92]	0,0187*
>=28 Tage	153	64 (41,8)	NE [NE; NE]	154	71 (46,1)	42,5 [34,6; NE]	0,90	[0,64; 1,26]	0,5482
Interaktions p-Wert									0,1193
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	5 (31,3)	NE [NE; NE]	24	18 (75,0)	14,4 [8,1;24,2]	0,28	[0,09; 0,70]	0,0052*
>=28 bis <56 Tage	104	54 (51,9)	34,0 [25,5; NE]	104	59 (56,7)	27,3 [19,9;44,8]	0,83	[0,58; 1,21]	0,3370
>=56 bis <84 Tage	98	35 (35,7)	NE [NE; NE]	76	37 (48,7)	36,8 [23,2; NE]	0,62	[0,39; 0,99]	0,0463*
>=84 Tage	46	21 (45,7)	NE [NE; NE]	62	32 (51,6)	42,5 [29,4; NE]	1,02	[0,58; 1,75]	0,9548
Interaktions p-Wert									0,0869

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG Seite 2 von 3

Table 4.1.1 ADRIATIC: Summary of subgroup analysis of Overall Survival
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	31 (34,1)	NE [NE; NE]	88	46 (52,3)	33,4 [21,7; NE]	0,56	[0,35; 0,88]	0,0119*
Cisplatin	173	84 (48,6)	41,9 [27,7; NE]	178	100 (56,2)	34,3 [25,4;40,7]	0,82	[0,61; 1,10]	0,1810
Interaktions p-Wert									0,1656
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	92 (47,2)	41,9 [32,0; NE]	187	107 (57,2)	26,1 [21,7;36,8]	0,72	[0,55; 0,95]	0,0219*
Zweimal täglich	69	23 (33,3)	NE [NE; NE]	79	39 (49,4)	44,8 [29,4; NE]	0,68	[0,40; 1,13]	0,1367
Interaktions p-Wert									0,8399
Bestes Ansprechen auf cCRT - DEU									
CR	31	12 (38,7)	NE [NE; NE]	34	15 (44,1)	NE [NE; NE]	0,85	[0,39; 1,82]	0,6769
PR	191	88 (46,1)	42,5 [30,2; NE]	200	116 (58,0)	30,8 [24,1;39,3]	0,76	[0,57; 0,997]	0,0477*
SD	42	15 (35,7)	55,9 [43,9; NE]	32	15 (46,9)	NE [NE; NE]	0,55	[0,27; 1,14]	0,1088
Interaktions p-Wert									0,6773
Geschlecht - DEU									
Männer	178	79 (44,4)	55,9 [33,0; NE]	188	108 (57,4)	28,2 [22,8;39,9]	0,69	[0,52; 0,93]	0,0134*
Frauen	86	36 (41,9)	NE [NE; NE]	78	38 (48,7)	39,3 [29,2; NE]	0,83	[0,53; 1,31]	0,4305
Interaktions p-Wert									0,5128
Altersgruppe - DEU									
<65 Jahre	160	69 (43,1)	55,9 [35,6; NE]	162	83 (51,2)	35,3 [25,0;46,0]	0,76	[0,55; 1,04]	0,0886
>=65 Jahre	104	46 (44,2)	44,9 [28,7; NE]	104	63 (60,6)	29,2 [21,4;40,7]	0,69	[0,47; 1,01]	0,0581
Interaktions p-Wert									0,7272
PD-L1-Status - DEU									
TC and IC <1%	78	40 (51,3)	34,0 [26,2; NE]	73	42 (57,5)	31,1 [21,6;42,5]	0,84	[0,54; 1,30]	0,4302
TC or IC >=1%	84	31 (36,9)	NE [NE; NE]	98	53 (54,1)	33,4 [23,5; NE]	0,59	[0,38; 0,92]	0,0191*
Interaktions p-Wert									0,2709
Raucherstatus - DEU									
Raucher	241	108 (44,8)	44,9 [33,7; NE]	240	138 (57,5)	29,4 [23,9;37,6]	0,72	[0,56; 0,92]	0,0092*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 4.1.1 ADRIATIC: Summary of subgroup analysis of Overall Survival
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nichtraucher	23	7 (30,4)	NE [NE; NE]	26	8 (30,8)	NE [NE; NE]	0,89	[0,31; 2,48]	0,8211
Interaktions p-Wert									0,6862
Abstammung - DEU									
Weiß	130	60 (46,2)	40,4 [32,0; NE]	137	77 (56,2)	29,4 [22,8;43,4]	0,75	[0,53; 1,05]	0,0913
Schwarz/Afroamerikanisch	1	1 (100)	26,6 [NE; NE]	3	2 (66,7)	25,7 [2,2; NE]	NC	[NC]	NC
Asiatisch	131	53 (40,5)	55,9 [41,9; NE]	121	64 (52,9)	36,5 [28,1;44,9]	0,72	[0,50; 1,04]	0,0788
Andere	2	1 (50,0)	NE [NE; NE]	5	3 (60,0)	19,9 [11,1; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8871
Geographische Region - DEU									
Asien	129	51 (39,5)	55,9 [41,9; NE]	120	62 (51,7)	37,0 [28,1; NE]	0,72	[0,49; 1,04]	0,0785
Europa	94	41 (43,6)	NE [NE; NE]	112	64 (57,1)	25,7 [21,4;43,4]	0,66	[0,44; 0,98]	0,0373*
Nordamerika	41	23 (56,1)	34,0 [17,8;43,9]	34	20 (58,8)	34,6 [16,6; NE]	0,98	[0,54; 1,79]	0,9384
Interaktions p-Wert									0,5618
ECOG-Status zu Baseline - DEU									
0	133	48 (36,1)	NE [NE; NE]	131	74 (56,5)	29,4 [22,6;42,5]	0,55	[0,38; 0,79]	0,0011*
1	131	67 (51,1)	40,4 [26,6; NE]	135	72 (53,3)	34,6 [25,7;44,8]	0,94	[0,67; 1,31]	0,7235
Interaktions p-Wert									0,0320*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G2.3: Mortalität: Gesamtüberleben - Subgruppenanalysen Kaplan-Meier-Plot

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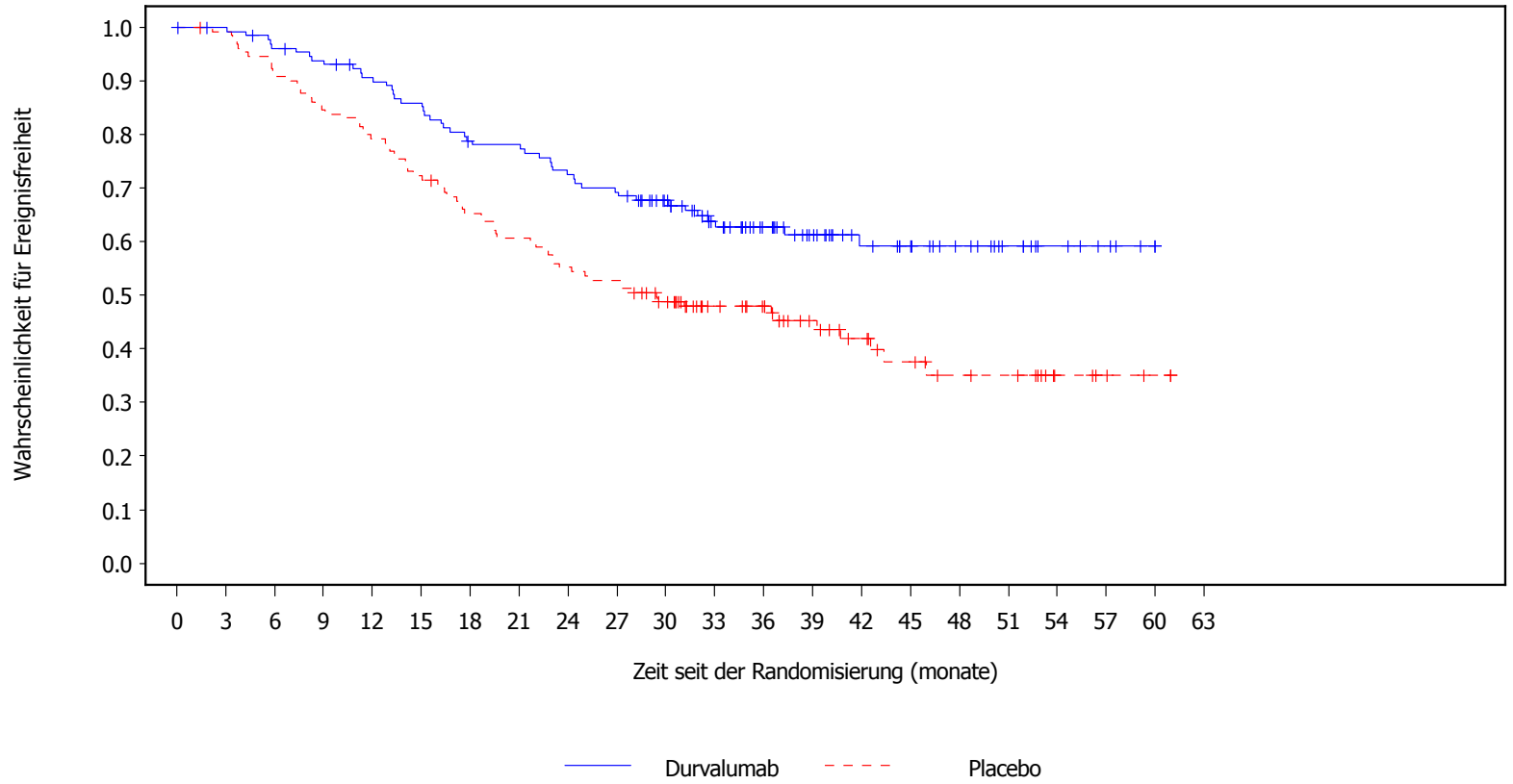
Figure 4.1.3 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Gesamtüberleben for ECOG-Status zu Baseline - DEU = 0
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

133	131	125	121	115	109	99	98	91	87	76	60	48	38	28	24	18	12	7	4	0	0	Durvalumab
131	129	118	110	103	94	84	78	71	68	58	44	39	28	22	17	13	12	5	3	1	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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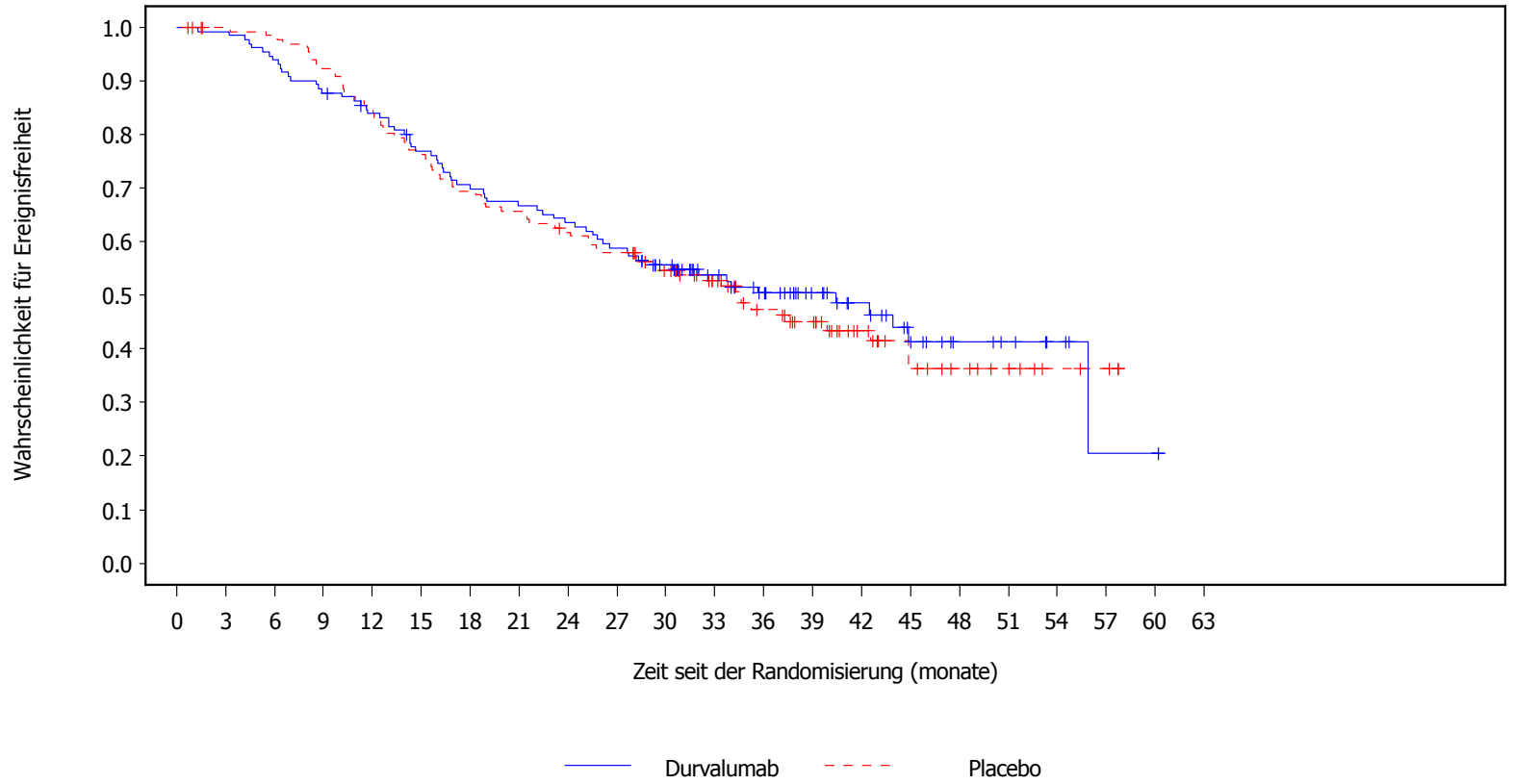
Figure 4.1.4 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Gesamtüberleben for ECOG-Status zu Baseline - DEU = 1
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

131	130	123	115	108	98	90	85	81	75	65	50	42	30	23	15	9	7	4	1	1	0	Durvalumab
135	131	129	121	111	101	91	86	80	75	65	53	41	34	22	14	10	7	3	2	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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Anhang 4-G3: Mortalität: Gesamtüberleben - ergänzende Analysen

Anhang 4-G3.1: Mortalität: Gesamtüberleben nach 24 Monaten und 36 Monaten

D933QC00001
PFS_IA_OS_IA1 (Unblinded output) - DB export=12FEB2024
Table 14.2.2.1.A
Overall survival (Full analysis set)

	Durva (N=264)	Placebo (N=266)
Death, n (%)	115 (43.6)	146 (54.9)
Censored subjects, n (%)	149 (56.4)	120 (45.1)
Still in survival follow-up [a]	140 (53.0)	111 (41.7)
Terminated prior to death [b]	9 (3.4)	9 (3.4)
Lost to follow-up	0	0
Withdrawn consent	9 (3.4)	9 (3.4)
Other	0	0
Median overall survival (months) [c]	55.9	33.4
95% CI for median overall survival [c]	37.3, NR	25.5, 39.9
Survival rate at 24 months (OS24) [c]	68.0	58.5
95% CI for OS24 [c]	61.9, 73.3	52.3, 64.3
Survival rate at 36 months (OS36) [c]	56.5	47.6
95% CI for OS36 [c]	50.0, 62.5	41.3, 53.7

Page 1 of 2

Durva Durvalumab.
CI Confidence interval; NR Not reached; One month is calculated as 30.4375 days.
[a] Includes subjects known to be alive at data cut-off.
[b] Includes subjects with unknown survival status or subjects who were lost to follow-up.
[c] Calculated using the Kaplan-Meier technique. CI for median overall survival is derived based on Brookmeyer-Crowley method with log-log transformation. CI for OS24 and OS36 are derived based on a log(-log(.)) transformation.
[d] The hazard ratio and CI were calculated using a stratified Cox proportional hazards model, adjusting for receipt of PCI (yes versus no), with treatment as only covariate and ties handled by Efron approach. CIs were calculated using the profile likelihood approach.
[e] Based on a Lan-DeMets alpha spending function with O'Brien Fleming type boundary with the actual number of events observed, the boundaries for declaring statistical significance are 1.679% for a 4.5% overall alpha for OS. The Lan DeMets spending function that approximates the O'Brien Fleming approach was used to derive the adjusted alpha level.
[f] The analysis was performed using the stratified log-rank test, adjusting for receipt of PCI (yes versus no).
[g] A hazard ratio < 1 favors Durva to be associated with a longer survival than Placebo.
Stratification factor is based on the values entered into the IVRS.

Data cut-off: 15JAN2024
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Anhang 4-G4: Morbidität: Progressionsfreies Überleben

Nutzenbewertung nach AMNOG

Table 1.2.2 ADRIATIC: Summary of analysis of Progression-free Survival by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Progressionsfreies Überleben	264	139 (52,7)	16,6 [10,2;28,2]	266	169 (63,5)	9,2 [7,4;12,9]	0,76	[0,61; 0,95]	0,0161*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G4.1: Morbidität: Progressionsfreies Überleben - Kaplan-Meier-Plot

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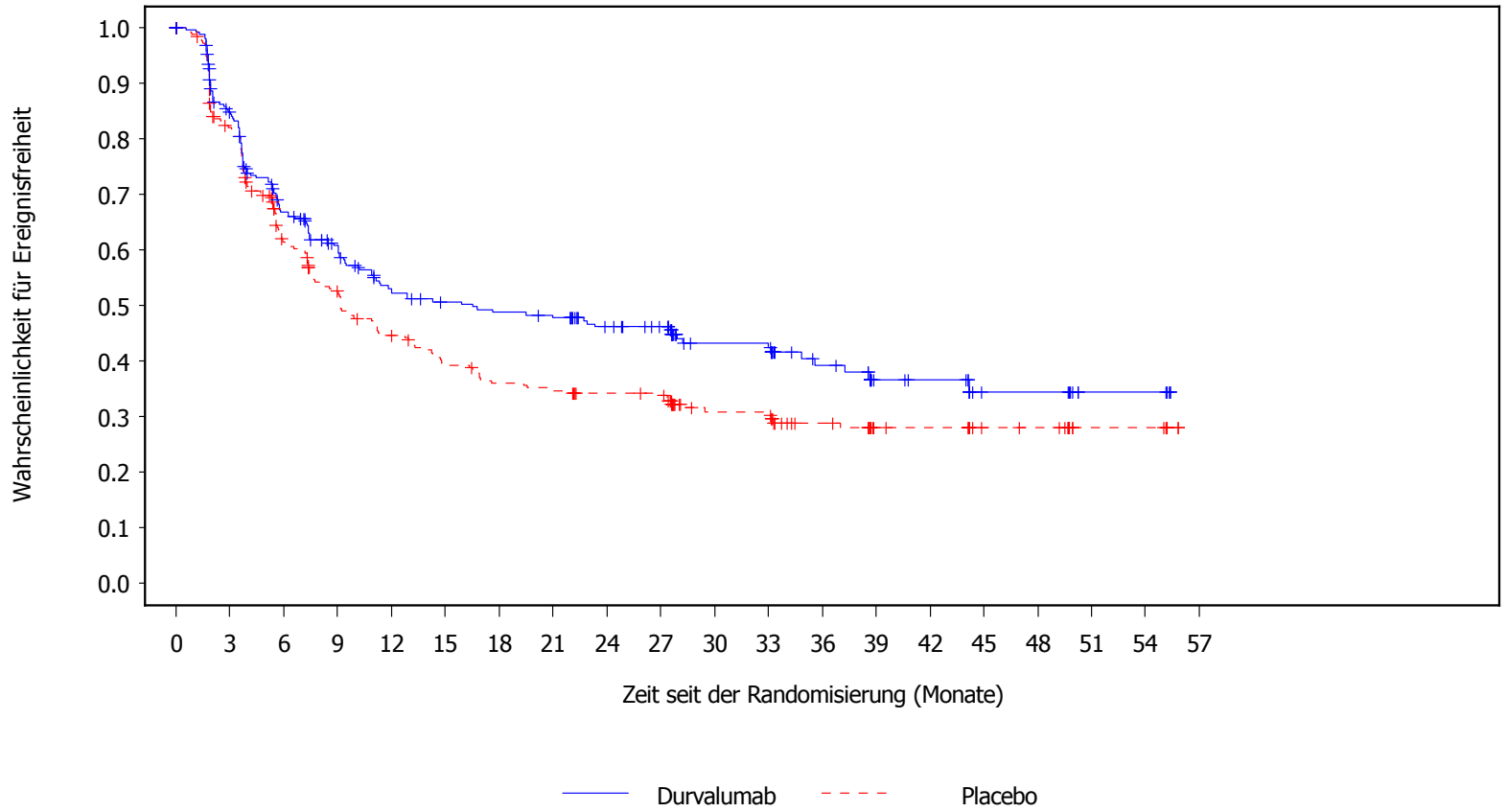
Figure 1.3.2 ADRIATIC: Kaplan-Meier plot of Progression-free Survival by BICR assessment
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	Durvalumab
266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	Placebo

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Anhang 4-G4.2: Morbidität: Progressionsfreies Überleben - Subgruppenanalysen

Nutzenbewertung nach AMNOG Seite 1 von 3

Table 4.1.2 ADRIATIC: Summary of subgroup analysis of Progression Free Survival by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	17 (47,2)	34,9 [10,2; NE]	37	21 (56,8)	19,4 [7,2; NE]	0,82	[0,43; 1,55]	0,5410
Stadium III	228	122 (53,5)	12,0 [9,1;27,6]	229	148 (64,6)	9,1 [7,4;11,2]	0,76	[0,60; 0,97]	0,0254*
Interaktions p-Wert									0,8324
TNM Status (eCRF) - DEU									
Stadium I/II	33	14 (42,4)	34,9 [17,6; NE]	34	19 (55,9)	19,4 [8,6; NE]	0,74	[0,36; 1,47]	0,3876
Stadium III	231	125 (54,1)	12,0 [9,1;23,4]	232	150 (64,7)	9,0 [7,3;11,2]	0,77	[0,61; 0,98]	0,0317*
Interaktions p-Wert									0,9078
Erhalt einer PCI (IVRS) - DEU									
Ja	142	65 (45,8)	28,2 [16,8;44,2]	144	85 (59,0)	13,2 [9,2;19,4]	0,73	[0,53; 1,01]	0,0571
Nein	122	74 (60,7)	9,1 [7,3;14,3]	122	84 (68,9)	7,4 [5,7; 9,2]	0,80	[0,59; 1,10]	0,1680
Interaktions p-Wert									0,6870
Erhalt einer PCI (eCRF) - DEU									
Ja	142	65 (45,8)	28,2 [16,8;44,2]	143	84 (58,7)	13,0 [9,2;17,0]	0,73	[0,53; 1,01]	0,0582
Nein	122	74 (60,7)	9,1 [7,3;14,3]	123	85 (69,1)	7,4 [5,7; 9,2]	0,81	[0,59; 1,10]	0,1738
Interaktions p-Wert									0,6768
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	18 (56,3)	11,0 [3,7; NE]	32	27 (84,4)	5,7 [3,2; 8,1]	0,46	[0,25; 0,84]	0,0108*
>=14 bis <28 Tage	79	43 (54,4)	9,4 [5,7;21,0]	80	50 (62,5)	7,7 [5,6;16,6]	0,91	[0,61; 1,37]	0,6685
>=28 Tage	153	78 (51,0)	27,9 [12,0;37,3]	154	92 (59,7)	13,0 [9,2;19,4]	0,79	[0,58; 1,07]	0,1278
Interaktions p-Wert									0,1722
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	8 (50,0)	9,4 [3,5; NE]	24	20 (83,3)	4,7 [2,8; 8,1]	0,37	[0,15; 0,82]	0,0128*
>=28 bis <56 Tage	104	57 (54,8)	10,9 [7,5;35,6]	104	69 (66,3)	7,3 [5,6; 9,2]	0,71	[0,50; 1,01]	0,0567
>=56 bis <84 Tage	98	49 (50,0)	27,5 [11,3;38,7]	76	45 (59,2)	13,3 [7,4;19,4]	0,76	[0,51; 1,15]	0,1907
>=84 Tage	46	25 (54,3)	12,9 [7,5;44,2]	62	35 (56,5)	17,0 [9,2;37,0]	1,16	[0,69; 1,93]	0,5720
Interaktions p-Wert									0,1208

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.

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Nutzenbewertung nach AMNOG Seite 2 von 3

Table 4.1.2 ADRIATIC: Summary of subgroup analysis of Progression Free Survival by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	27,9 [11,1;38,7]	88	57 (64,8)	9,2 [5,8;14,6]	0,62	[0,42; 0,92]	0,0162*
Cisplatin	173	95 (54,9)	11,4 [9,0;23,4]	178	112 (62,9)	9,7 [7,4;13,3]	0,86	[0,66; 1,13]	0,2918
Interaktions p-Wert									0,1719
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	108 (55,4)	11,4 [9,0;19,5]	187	122 (65,2)	7,8 [6,4;11,5]	0,77	[0,60; 1,001]	0,0508
Zweimal täglich	69	31 (44,9)	38,7 [22,7; NE]	79	47 (59,5)	14,3 [9,1;28,1]	0,72	[0,45; 1,12]	0,1449
Interaktions p-Wert									0,7740
Bestes Ansprechen auf cCRT - DEU									
CR	31	15 (48,4)	21,0 [8,8; NE]	34	18 (52,9)	19,4 [9,0; NE]	1,02	[0,51; 2,02]	0,9624
PR	191	106 (55,5)	12,0 [7,5;28,2]	200	130 (65,0)	9,2 [7,4;11,5]	0,81	[0,62; 1,04]	0,0968
SD	42	18 (42,9)	NE [NE; NE]	32	21 (65,6)	7,3 [3,7;21,9]	0,49	[0,26; 0,92]	0,0260*
Interaktions p-Wert									0,2531
Geschlecht - DEU									
Männer	178	96 (53,9)	11,9 [9,4;27,5]	188	120 (63,8)	9,2 [7,4;13,8]	0,80	[0,61; 1,04]	0,1010
Frauen	86	43 (50,0)	27,9 [9,1;38,7]	78	49 (62,8)	9,2 [7,1;16,9]	0,72	[0,48; 1,08]	0,1137
Interaktions p-Wert									0,6700
Altersgruppe - DEU									
<65 Jahre	160	83 (51,9)	14,3 [9,4;35,6]	162	98 (60,5)	9,2 [7,2;12,8]	0,77	[0,58; 1,03]	0,0826
>=65 Jahre	104	56 (53,8)	16,8 [8,8;34,9]	104	71 (68,3)	9,2 [7,3;16,7]	0,77	[0,54; 1,09]	0,1454
Interaktions p-Wert									0,9976
PD-L1-Status - DEU									
TC and IC <1%	78	45 (57,7)	12,0 [9,0;34,9]	73	46 (63,0)	9,2 [5,6;16,9]	0,81	[0,53; 1,22]	0,3084
TC or IC >=1%	84	44 (52,4)	27,9 [9,4;38,7]	98	61 (62,2)	11,3 [7,5;16,6]	0,79	[0,53; 1,16]	0,2236
Interaktions p-Wert									0,9286
Raucherstatus - DEU									
Raucher	241	129 (53,5)	12,9 [9,5;27,9]	240	154 (64,2)	9,2 [7,4;12,8]	0,78	[0,62; 0,99]	0,0407*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.

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Nutzenbewertung nach AMNOG

Table 4.1.2 ADRIATIC: Summary of subgroup analysis of Progression Free Survival by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nichtraucher	23	10 (43,5)	38,7 [3,8; NE]	26	15 (57,7)	12,9 [5,7;27,4]	0,64	[0,28; 1,41]	0,2673
Interaktions p-Wert									0,6294
Abstammung - DEU									
Weiß	130	65 (50,0)	22,7 [10,9;35,6]	137	90 (65,7)	7,5 [5,6;11,0]	0,67	[0,49; 0,92]	0,0143*
Schwarz/Afroamerikanisch	1	1 (100)	5,4 [NE; NE]	3	3 (100)	2,0 [1,8; NE]	NC	[NC]	NC
Asiatisch	131	72 (55,0)	12,9 [8,5;33,1]	121	75 (62,0)	14,2 [9,1;19,6]	0,91	[0,66; 1,26]	0,5732
Andere	2	1 (50,0)	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,1904
Geographische Region - DEU									
Asien	129	70 (54,3)	12,9 [9,0;38,7]	120	73 (60,8)	14,2 [9,1;20,7]	0,91	[0,65; 1,26]	0,5555
Europa	94	46 (48,9)	27,6 [10,9; NE]	112	75 (67,0)	7,4 [5,6; 9,2]	0,60	[0,41; 0,86]	0,0051*
Nordamerika	41	23 (56,1)	9,5 [5,2;37,3]	34	21 (61,8)	11,0 [3,1;17,6]	0,89	[0,49; 1,62]	0,7054
Interaktions p-Wert									0,2144
ECOG-Status zu Baseline - DEU									
0	133	60 (45,1)	33,1 [12,9; NE]	131	82 (62,6)	9,2 [7,1;13,0]	0,64	[0,46; 0,90]	0,0088*
1	131	79 (60,3)	10,2 [7,4;21,0]	135	87 (64,4)	9,9 [7,3;14,6]	0,91	[0,67; 1,24]	0,5495
Interaktions p-Wert									0,1296

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction.
Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G5: Morbidität: Progressionsfreies Überleben - ergänzende Analysen

Anhang 4-G5.1: Morbidität: Progressionsfreies Überleben 2

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Table 1.2.3 ADRIATIC: Summary of analysis of Second Progression-free Survival by investigator assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Progressionsfreies Überleben 2	264	82 (31,1)	NE [NE; NE]	266	108 (40,6)	37,6 [25,3; NE]	0,66	[0,49; 0,88]	0,0045*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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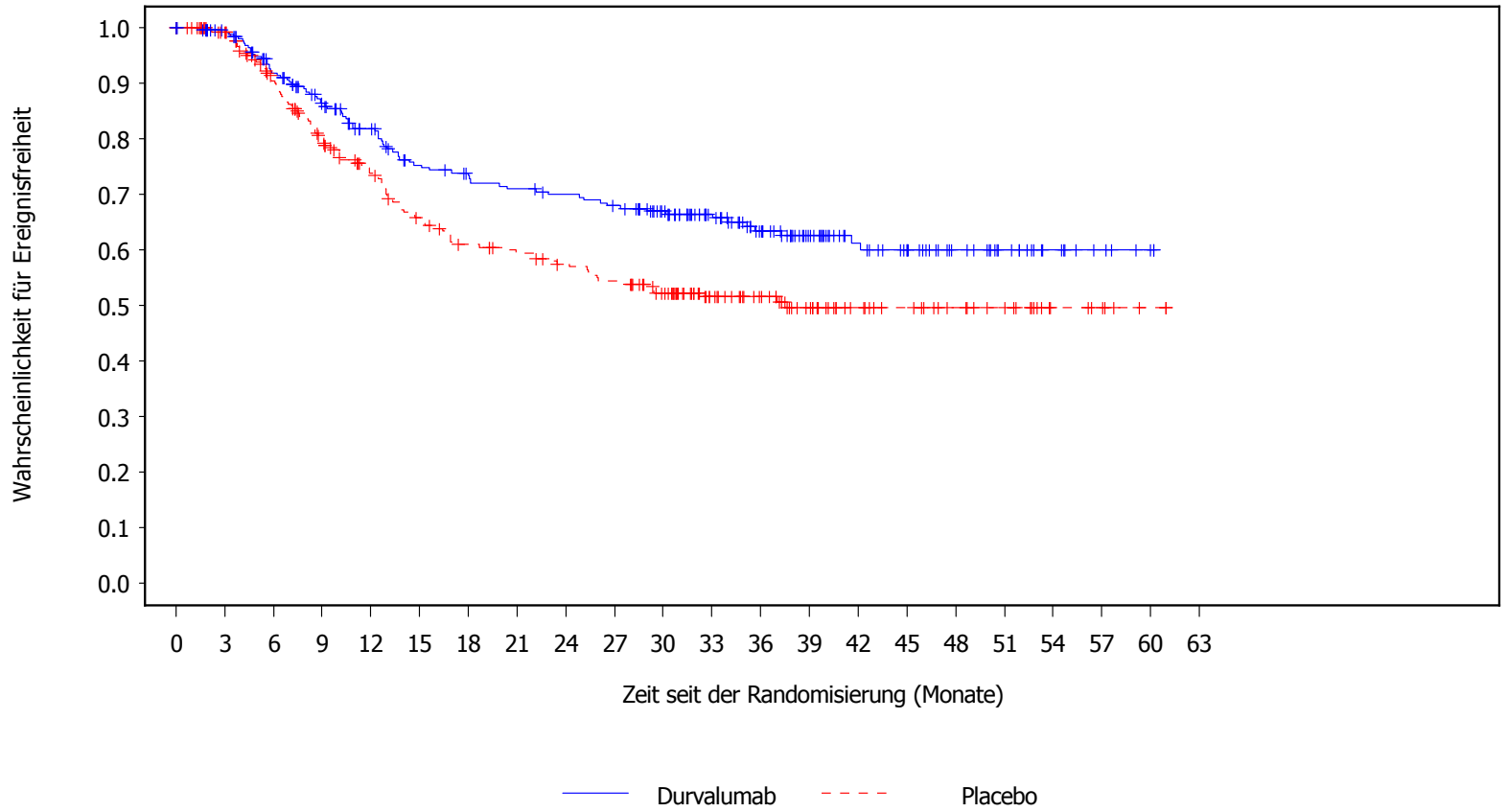
Anhang 4-G5.1.1: Morbidität: Progressionsfreies Überleben 2 - Kaplan-Meier-Plot

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 1.3.3 ADRIATIC: Kaplan-Meier plot of Second Progression-free Survival by investigator assessment
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	251	223	199	178	158	152	146	142	137	122	98	79	60	45	38	26	18	10	5	1	0	Durvalumab
266	248	214	182	158	138	125	119	112	106	92	69	58	44	32	27	21	17	7	5	1	0	Placebo

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Anhang 4-G5.2: Morbidität: Zeit bis zum Tod oder einer Fernmetastase

Nutzenbewertung nach AMNOG

Table 1.2.6 ADRIATIC: Summary of analysis of Time to Death or Distant Metastasis by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zum Tod oder einer Fernmetastase	264	86 (32,6)	NE [NE; NE]	266	104 (39,1)	37,0 [16,9; NE]	0,76	[0,57; 1,01]	0,0580

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G5.2.1: Morbidität: Zeit bis zum Tod oder einer Fernmetastase - Kaplan-Meier-Plot

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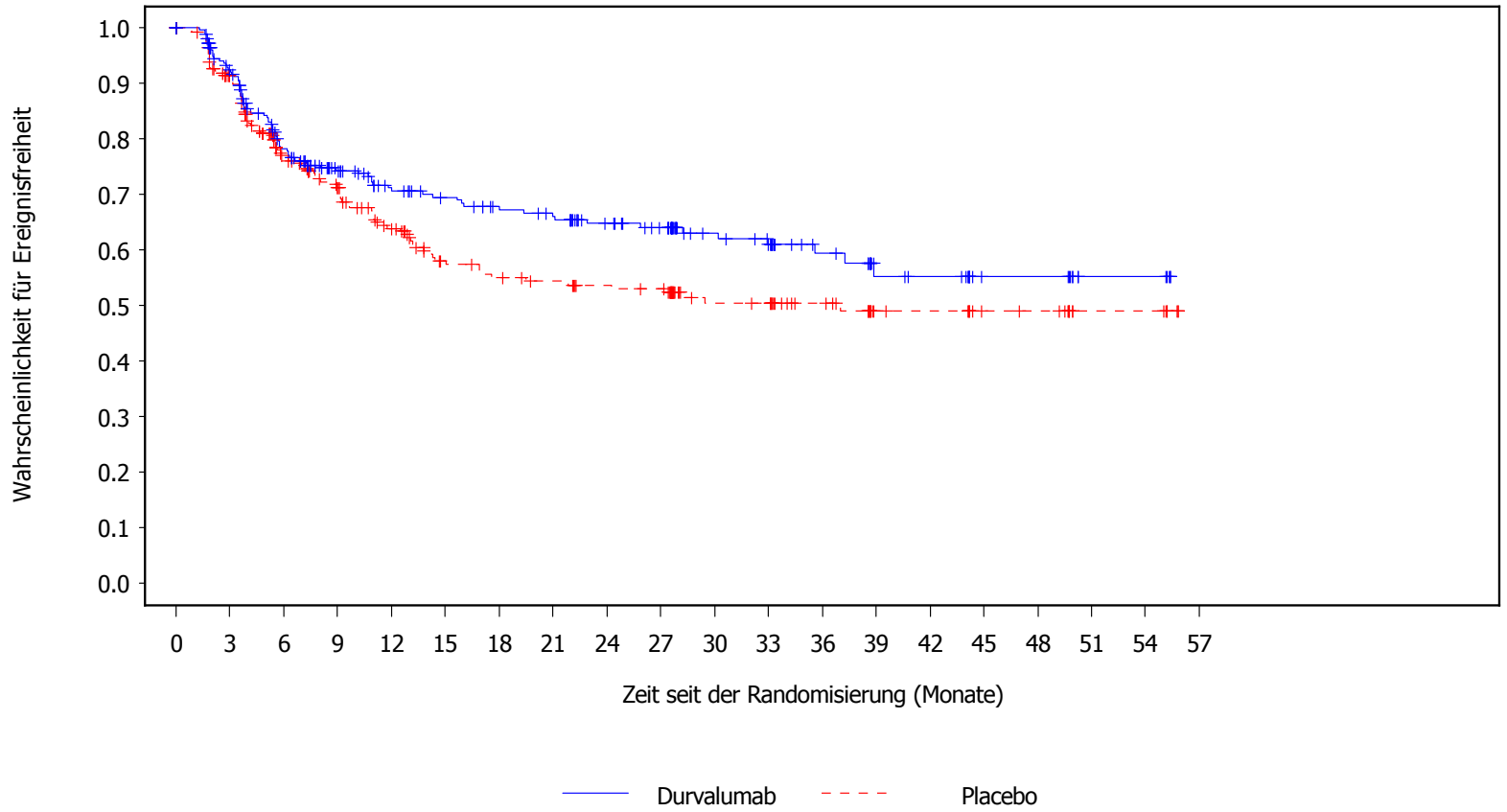
Figure 1.3.6 ADRIATIC: Kaplan-Meier plot of Time to Death or Distant Metastasis by BICR assessment
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	229	182	151	133	124	116	111	96	88	61	57	37	23	21	11	11	4	4	0	Durvalumab
266	224	166	143	116	95	89	85	80	78	51	50	39	24	23	16	15	6	6	0	Placebo

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Anhang 4-G5.3: Morbidität: Zeit bis zur ersten Folgetherapie

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Table 1.2.5 ADRIATIC: Summary of analysis of Time to First Subsequent Cancer Therapy or Death
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur ersten Folgetherapie	264	143 (54,2)	25,4 [18,1;37,3]	266	176 (66,2)	15,1 [12,0;18,1]	0,72	[0,58; 0,90]	0,0032*

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G5.3.1: Morbidität: Zeit bis zur ersten Folgetherapie - Kaplan-Meier-Plot

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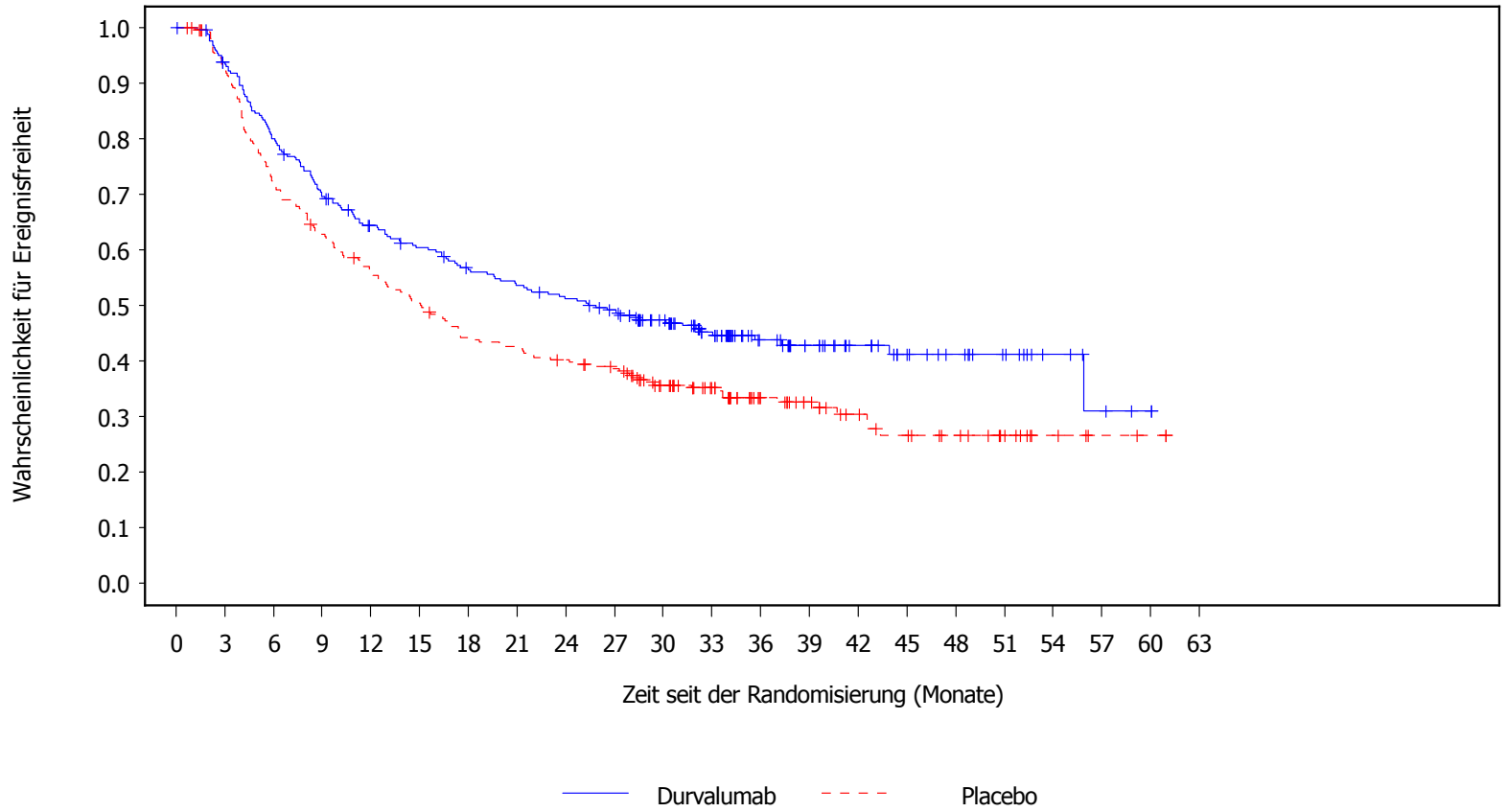
Figure 1.3.5 ADRIATIC: Kaplan-Meier plot of Time to First Subsequent Cancer Therapy or Death
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	244	208	182	162	151	140	132	125	117	97	75	51	39	30	22	17	12	6	3	1	0	Durvalumab
266	241	188	163	145	130	113	108	102	95	76	62	41	33	25	20	16	11	5	2	1	0	Placebo

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Anhang 4-G5.4: Morbidität: Allgemeine Ansprechrate

Table 1.4 ADRIATIC: Summary of analysis of overall response rate by BICR assessment
(odds ratio, relative risk and risk difference)
Full Analysis Set, DCO 15JAN2024

	Durva (N=264)		Placebo (N=266)		Behandlungseffekt					
					Odds Ratio		Relatives Risiko		Risikodifferenz	
	n	Anzahl (%) der Patienten mit Ereignis	n	Anzahl (%) der Patienten mit Ereignis	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert
Allgemeine Ansprechrate [a][d][h]	264	45(17,0)	266	46(17,3)	0,98[0,62; 1,54]	0,9397	0,99[0,68; 1,43]	0,9397	-0,00[-0,07; 0,06]	0,9397

NC=Not calculable. CI=Confidence interval. PL=Profile likelihood. LR=Likelihood ratio test.
All models include the response and a term for treatment as a factor and are stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No).
[a] Odds ratio (OR), 95% PL CI, LR p-value via logistic regression. [b] As [a] but with Firth method.
[c] OR NC via [a] or [b]. [d] Relative risk (RR), 95% PL CI, LR p-value via log-binomial regression.
[e] RR, 95% CI, p-value via modified Poisson regression. [f] RR, 95% CI, p-value via modified Wald method.
[g] RR NC via [d], [e] or [f]. [h] Risk difference (RD), 95% PL CI, LR p-value via binomial regression.
[i] RD, 95% CI, p-value via Agresti-Caffo method. [j] RD NC via [h] or [i]. OR and RR >1, and RD >0 favours Durva. *p<0.05.
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Anhang 4-G5.5: Morbidität: Dauer des Ansprechens

Nutzenbewertung nach AMNOG

Table 1.2.4 ADRIATIC: Summary of analysis of Duration of Response by BICR assessment
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Dauer des Ansprechens	45	16 (35,6)	38,8 [25,9; NE]	46	20 (43,5)	27,8 [9,9; NE]	0,65	[0,33; 1,28]	0,2156

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] p-value estimated using log-rank test with stratification by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No)
Hazard ratio and 95% confidence interval derived from stratified Cox proportional hazards model.
Hazard ratio <1 favours Durva. * p<0.05.
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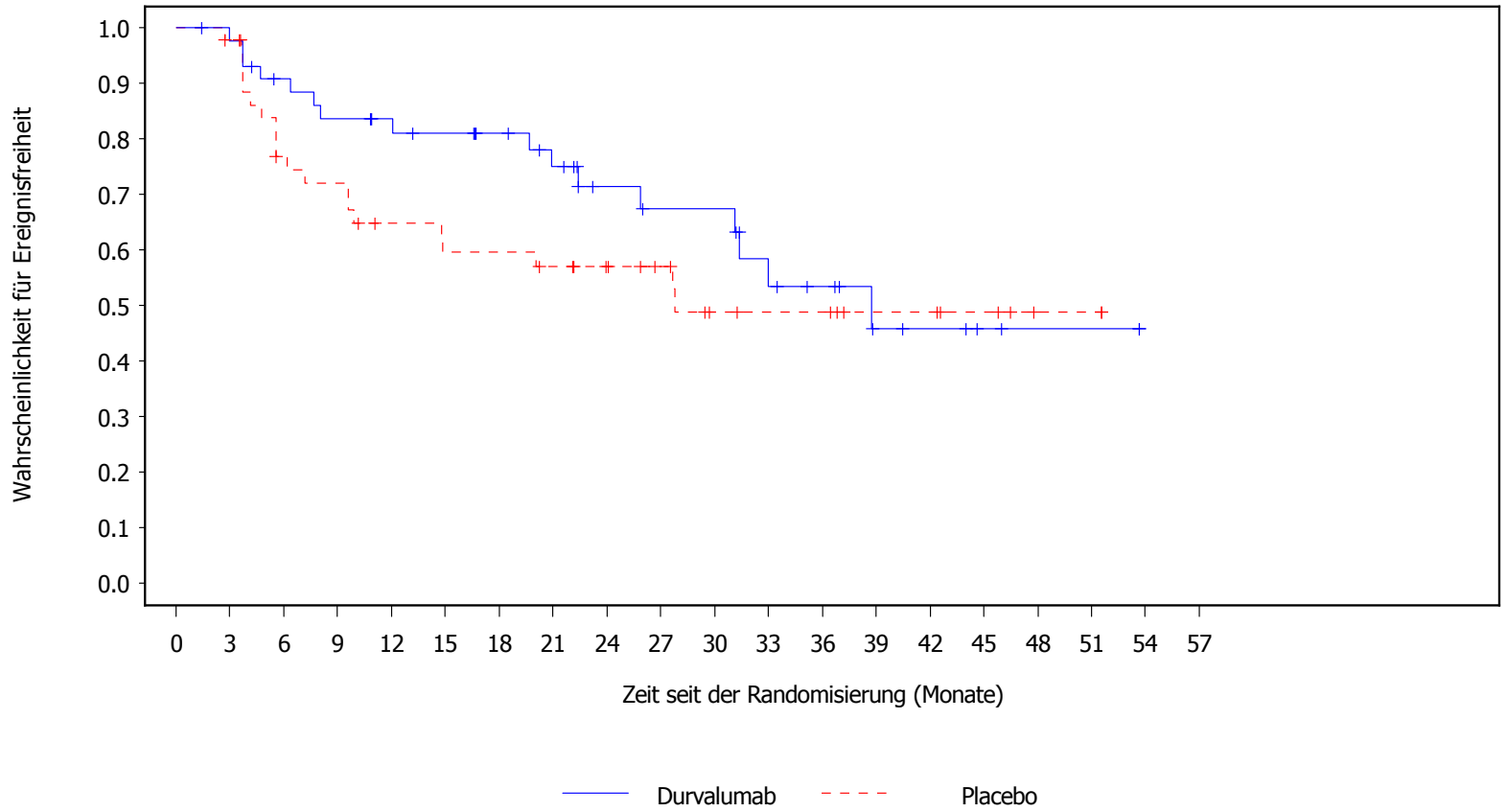
Anhang 4-G5.5.1: Morbidität: Dauer des Ansprechens - Kaplan-Meier-Plot

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 1.3.4 ADRIATIC: Kaplan-Meier plot of Duration of Response by BICR assessment
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

45	43	38	35	33	31	28	24	18	16	16	11	9	5	4	2	1	1	0	0	Durvalumab
46	44	32	30	25	23	23	21	18	15	10	9	9	6	6	4	1	1	0	0	Placebo

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Anhang 4-G6: Patientenberichtete Morbidität und gesundheitsbezogene Lebensqualität

Anhang 4-G6.1: Rücklaufqouten

Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Baseline	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	216	212
	auswertbare Anzahl Fragebögen [c]	216	212
	Rücklaufquote (%) [d]	81,8	79,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 4	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	236	230
	auswertbare Anzahl Fragebögen [c]	236	230
	Rücklaufquote (%) [d]	89,4	86,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 8	erwartete Anzahl Fragebögen [a]	262	264
	erhaltene Anzahl Fragebögen [b]	221	209
	auswertbare Anzahl Fragebögen [c]	221	209
	Rücklaufquote (%) [d]	84,4	79,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 12	erwartete Anzahl Fragebögen [a]	261	259
	erhaltene Anzahl Fragebögen [b]	202	198
	auswertbare Anzahl Fragebögen [c]	202	198
	Rücklaufquote (%) [d]	77,4	76,4
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 16	erwartete Anzahl Fragebögen [a]	259	259
	erhaltene Anzahl Fragebögen [b]	189	197
	auswertbare Anzahl Fragebögen [c]	189	197
	Rücklaufquote (%) [d]	73,0	76,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 20	erwartete Anzahl Fragebögen [a]	256	250
	erhaltene Anzahl Fragebögen [b]	179	180
	auswertbare Anzahl Fragebögen [c]	179	180
	Rücklaufquote (%) [d]	69,9	72,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 24	erwartete Anzahl Fragebögen [a]	248	244
	erhaltene Anzahl Fragebögen [b]	169	172
	auswertbare Anzahl Fragebögen [c]	169	172
	Rücklaufquote (%) [d]	68,1	70,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 28	erwartete Anzahl Fragebögen [a]	241	237
	erhaltene Anzahl Fragebögen [b]	163	158
	auswertbare Anzahl Fragebögen [c]	163	158
	Rücklaufquote (%) [d]	67,6	66,7
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 32	erwartete Anzahl Fragebögen [a]	236	227
	erhaltene Anzahl Fragebögen [b]	159	150
	auswertbare Anzahl Fragebögen [c]	159	150
	Rücklaufquote (%) [d]	67,4	66,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 36	erwartete Anzahl Fragebögen [a]	232	220
	erhaltene Anzahl Fragebögen [b]	149	141
	auswertbare Anzahl Fragebögen [c]	149	141
	Rücklaufquote (%) [d]	64,2	64,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 40	erwartete Anzahl Fragebögen [a]	226	210
	erhaltene Anzahl Fragebögen [b]	135	122
	auswertbare Anzahl Fragebögen [c]	135	122
	Rücklaufquote (%) [d]	59,7	58,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 44	erwartete Anzahl Fragebögen [a]	220	203
	erhaltene Anzahl Fragebögen [b]	131	124
	auswertbare Anzahl Fragebögen [c]	131	124
	Rücklaufquote (%) [d]	59,5	61,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 48	erwartete Anzahl Fragebögen [a]	215	195
	erhaltene Anzahl Fragebögen [b]	123	121
	auswertbare Anzahl Fragebögen [c]	123	121
	Rücklaufquote (%) [d]	57,2	62,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 52	erwartete Anzahl Fragebögen [a]	209	191
	erhaltene Anzahl Fragebögen [b]	124	118
	auswertbare Anzahl Fragebögen [c]	124	118
	Rücklaufquote (%) [d]	59,3	61,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 56	erwartete Anzahl Fragebögen [a]	208	185
	erhaltene Anzahl Fragebögen [b]	121	104
	auswertbare Anzahl Fragebögen [c]	121	104
	Rücklaufquote (%) [d]	58,2	56,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 60	erwartete Anzahl Fragebögen [a]	198	172
	erhaltene Anzahl Fragebögen [b]	118	98
	auswertbare Anzahl Fragebögen [c]	118	98
	Rücklaufquote (%) [d]	59,6	57,0
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 64	erwartete Anzahl Fragebögen [a]	191	166
	erhaltene Anzahl Fragebögen [b]	113	94
	auswertbare Anzahl Fragebögen [c]	113	94
	Rücklaufquote (%) [d]	59,2	56,6
	Auswertbarkeitsquote (%) [e]	100	100
Week 68	erwartete Anzahl Fragebögen [a]	184	162
	erhaltene Anzahl Fragebögen [b]	103	91
	auswertbare Anzahl Fragebögen [c]	103	91
	Rücklaufquote (%) [d]	56,0	56,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 72	erwartete Anzahl Fragebögen [a]	180	157
	erhaltene Anzahl Fragebögen [b]	100	86
	auswertbare Anzahl Fragebögen [c]	100	86
	Rücklaufquote (%) [d]	55,6	54,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 76	erwartete Anzahl Fragebögen [a]	175	150
	erhaltene Anzahl Fragebögen [b]	98	77
	auswertbare Anzahl Fragebögen [c]	98	77
	Rücklaufquote (%) [d]	56,0	51,3
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 80	erwartete Anzahl Fragebögen [a]	173	146
	erhaltene Anzahl Fragebögen [b]	97	75
	auswertbare Anzahl Fragebögen [c]	97	75
	Rücklaufquote (%) [d]	56,1	51,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 84	erwartete Anzahl Fragebögen [a]	168	144
	erhaltene Anzahl Fragebögen [b]	97	75
	auswertbare Anzahl Fragebögen [c]	97	75
	Rücklaufquote (%) [d]	57,7	52,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 88	erwartete Anzahl Fragebögen [a]	167	143
	erhaltene Anzahl Fragebögen [b]	91	70
	auswertbare Anzahl Fragebögen [c]	91	70
	Rücklaufquote (%) [d]	54,5	49,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 92	erwartete Anzahl Fragebögen [a]	165	139
	erhaltene Anzahl Fragebögen [b]	92	69
	auswertbare Anzahl Fragebögen [c]	92	69
	Rücklaufquote (%) [d]	55,8	49,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 96	erwartete Anzahl Fragebögen [a]	163	137
	erhaltene Anzahl Fragebögen [b]	87	64
	auswertbare Anzahl Fragebögen [c]	87	64
	Rücklaufquote (%) [d]	53,4	46,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 100	erwartete Anzahl Fragebögen [a]	160	133
	erhaltene Anzahl Fragebögen [b]	94	66
	auswertbare Anzahl Fragebögen [c]	94	66
	Rücklaufquote (%) [d]	58,8	49,6
	Auswertbarkeitsquote (%) [e]	100	100
Week 104	erwartete Anzahl Fragebögen [a]	157	130
	erhaltene Anzahl Fragebögen [b]	80	62
	auswertbare Anzahl Fragebögen [c]	80	62
	Rücklaufquote (%) [d]	51,0	47,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 108	erwartete Anzahl Fragebögen [a]	154	127
	erhaltene Anzahl Fragebögen [b]	77	59
	auswertbare Anzahl Fragebögen [c]	77	59
	Rücklaufquote (%) [d]	50,0	46,5
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 112	erwartete Anzahl Fragebögen [a]	151	125
	erhaltene Anzahl Fragebögen [b]	73	54
	auswertbare Anzahl Fragebögen [c]	73	54
	Rücklaufquote (%) [d]	48,3	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 116	erwartete Anzahl Fragebögen [a]	150	118
	erhaltene Anzahl Fragebögen [b]	68	56
	auswertbare Anzahl Fragebögen [c]	68	56
	Rücklaufquote (%) [d]	45,3	47,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 120	erwartete Anzahl Fragebögen [a]	147	118
	erhaltene Anzahl Fragebögen [b]	63	51
	auswertbare Anzahl Fragebögen [c]	63	51
	Rücklaufquote (%) [d]	42,9	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 124	erwartete Anzahl Fragebögen [a]	145	113
	erhaltene Anzahl Fragebögen [b]	58	50
	auswertbare Anzahl Fragebögen [c]	58	50
	Rücklaufquote (%) [d]	40,0	44,2
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 128	erwartete Anzahl Fragebögen [a]	138	108
	erhaltene Anzahl Fragebögen [b]	59	45
	auswertbare Anzahl Fragebögen [c]	59	45
	Rücklaufquote (%) [d]	42,8	41,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 132	erwartete Anzahl Fragebögen [a]	132	102
	erhaltene Anzahl Fragebögen [b]	53	44
	auswertbare Anzahl Fragebögen [c]	53	44
	Rücklaufquote (%) [d]	40,2	43,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 136	erwartete Anzahl Fragebögen [a]	124	94
	erhaltene Anzahl Fragebögen [b]	52	39
	auswertbare Anzahl Fragebögen [c]	52	39
	Rücklaufquote (%) [d]	41,9	41,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 140	erwartete Anzahl Fragebögen [a]	114	89
	erhaltene Anzahl Fragebögen [b]	48	39
	auswertbare Anzahl Fragebögen [c]	48	39
	Rücklaufquote (%) [d]	42,1	43,8
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 144	erwartete Anzahl Fragebögen [a]	106	81
	erhaltene Anzahl Fragebögen [b]	39	35
	auswertbare Anzahl Fragebögen [c]	39	35
	Rücklaufquote (%) [d]	36,8	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 148	erwartete Anzahl Fragebögen [a]	100	75
	erhaltene Anzahl Fragebögen [b]	43	32
	auswertbare Anzahl Fragebögen [c]	43	32
	Rücklaufquote (%) [d]	43,0	42,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 152	erwartete Anzahl Fragebögen [a]	96	72
	erhaltene Anzahl Fragebögen [b]	41	33
	auswertbare Anzahl Fragebögen [c]	41	33
	Rücklaufquote (%) [d]	42,7	45,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 156	erwartete Anzahl Fragebögen [a]	88	66
	erhaltene Anzahl Fragebögen [b]	37	32
	auswertbare Anzahl Fragebögen [c]	37	32
	Rücklaufquote (%) [d]	42,0	48,5
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 160	erwartete Anzahl Fragebögen [a]	83	63
	erhaltene Anzahl Fragebögen [b]	33	31
	auswertbare Anzahl Fragebögen [c]	33	31
	Rücklaufquote (%) [d]	39,8	49,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 164	erwartete Anzahl Fragebögen [a]	79	57
	erhaltene Anzahl Fragebögen [b]	33	24
	auswertbare Anzahl Fragebögen [c]	33	24
	Rücklaufquote (%) [d]	41,8	42,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 168	erwartete Anzahl Fragebögen [a]	71	52
	erhaltene Anzahl Fragebögen [b]	29	28
	auswertbare Anzahl Fragebögen [c]	29	28
	Rücklaufquote (%) [d]	40,8	53,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 172	erwartete Anzahl Fragebögen [a]	65	49
	erhaltene Anzahl Fragebögen [b]	32	23
	auswertbare Anzahl Fragebögen [c]	32	23
	Rücklaufquote (%) [d]	49,2	46,9
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 176	erwartete Anzahl Fragebögen [a]	59	43
	erhaltene Anzahl Fragebögen [b]	23	21
	auswertbare Anzahl Fragebögen [c]	23	21
	Rücklaufquote (%) [d]	39,0	48,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 180	erwartete Anzahl Fragebögen [a]	54	37
	erhaltene Anzahl Fragebögen [b]	21	19
	auswertbare Anzahl Fragebögen [c]	21	19
	Rücklaufquote (%) [d]	38,9	51,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 184	erwartete Anzahl Fragebögen [a]	50	35
	erhaltene Anzahl Fragebögen [b]	19	20
	auswertbare Anzahl Fragebögen [c]	19	20
	Rücklaufquote (%) [d]	38,0	57,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 188	erwartete Anzahl Fragebögen [a]	46	30
	erhaltene Anzahl Fragebögen [b]	17	18
	auswertbare Anzahl Fragebögen [c]	17	18
	Rücklaufquote (%) [d]	37,0	60,0
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
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Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 192	erwartete Anzahl Fragebögen [a]	44	27
	erhaltene Anzahl Fragebögen [b]	17	16
	auswertbare Anzahl Fragebögen [c]	17	16
	Rücklaufquote (%) [d]	38,6	59,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 196	erwartete Anzahl Fragebögen [a]	42	27
	erhaltene Anzahl Fragebögen [b]	14	18
	auswertbare Anzahl Fragebögen [c]	14	18
	Rücklaufquote (%) [d]	33,3	66,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 200	erwartete Anzahl Fragebögen [a]	37	26
	erhaltene Anzahl Fragebögen [b]	11	19
	auswertbare Anzahl Fragebögen [c]	11	19
	Rücklaufquote (%) [d]	29,7	73,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 204	erwartete Anzahl Fragebögen [a]	33	24
	erhaltene Anzahl Fragebögen [b]	7	13
	auswertbare Anzahl Fragebögen [c]	7	13
	Rücklaufquote (%) [d]	21,2	54,2
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 208	erwartete Anzahl Fragebögen [a]	31	22
	erhaltene Anzahl Fragebögen [b]	8	12
	auswertbare Anzahl Fragebögen [c]	8	12
	Rücklaufquote (%) [d]	25,8	54,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 212	erwartete Anzahl Fragebögen [a]	28	22
	erhaltene Anzahl Fragebögen [b]	7	15
	auswertbare Anzahl Fragebögen [c]	7	15
	Rücklaufquote (%) [d]	25,0	68,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 216	erwartete Anzahl Fragebögen [a]	26	18
	erhaltene Anzahl Fragebögen [b]	9	12
	auswertbare Anzahl Fragebögen [c]	9	12
	Rücklaufquote (%) [d]	34,6	66,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 220	erwartete Anzahl Fragebögen [a]	24	17
	erhaltene Anzahl Fragebögen [b]	7	9
	auswertbare Anzahl Fragebögen [c]	7	9
	Rücklaufquote (%) [d]	29,2	52,9
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
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[d] Compliance Rate = Evaluable/Expected * 100.
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Timepoints are reported by visit for each treatment arm.
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 224	erwartete Anzahl Fragebögen [a]	20	16
	erhaltene Anzahl Fragebögen [b]	6	11
	auswertbare Anzahl Fragebögen [c]	6	11
	Rücklaufquote (%) [d]	30,0	68,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 228	erwartete Anzahl Fragebögen [a]	18	14
	erhaltene Anzahl Fragebögen [b]	6	9
	auswertbare Anzahl Fragebögen [c]	6	9
	Rücklaufquote (%) [d]	33,3	64,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 232	erwartete Anzahl Fragebögen [a]	15	11
	erhaltene Anzahl Fragebögen [b]	6	5
	auswertbare Anzahl Fragebögen [c]	6	5
	Rücklaufquote (%) [d]	40,0	45,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 236	erwartete Anzahl Fragebögen [a]	12	7
	erhaltene Anzahl Fragebögen [b]	4	5
	auswertbare Anzahl Fragebögen [c]	4	5
	Rücklaufquote (%) [d]	33,3	71,4
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 240	erwartete Anzahl Fragebögen [a]	9	7
	erhaltene Anzahl Fragebögen [b]	3	5
	auswertbare Anzahl Fragebögen [c]	3	5
	Rücklaufquote (%) [d]	33,3	71,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 244	erwartete Anzahl Fragebögen [a]	8	7
	erhaltene Anzahl Fragebögen [b]	2	4
	auswertbare Anzahl Fragebögen [c]	2	4
	Rücklaufquote (%) [d]	25,0	57,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 248	erwartete Anzahl Fragebögen [a]	5	5
	erhaltene Anzahl Fragebögen [b]	1	2
	auswertbare Anzahl Fragebögen [c]	1	2
	Rücklaufquote (%) [d]	20,0	40,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 252	erwartete Anzahl Fragebögen [a]	4	3
	erhaltene Anzahl Fragebögen [b]	2	1
	auswertbare Anzahl Fragebögen [c]	2	1
	Rücklaufquote (%) [d]	50,0	33,3
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.1 ADRIATIC: Summary of compliance with EORTC QLQ-C30 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 256	erwartete Anzahl Fragebögen [a]	3	2
	erhaltene Anzahl Fragebögen [b]	0	1
	auswertbare Anzahl Fragebögen [c]	0	1
	Rücklaufquote (%) [d]	0,0	50,0
	Auswertbarkeitsquote (%) [e]	NC	100
Week 260	erwartete Anzahl Fragebögen [a]	2	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	0,0	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC
Week 264	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC
Week 268	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Baseline	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	217	215
	auswertbare Anzahl Fragebögen [c]	217	215
	Rücklaufquote (%) [d]	82,2	80,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 1	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	208	209
	auswertbare Anzahl Fragebögen [c]	208	209
	Rücklaufquote (%) [d]	78,8	78,6
	Auswertbarkeitsquote (%) [e]	100	100
Week 2	erwartete Anzahl Fragebögen [a]	263	266
	erhaltene Anzahl Fragebögen [b]	203	212
	auswertbare Anzahl Fragebögen [c]	203	212
	Rücklaufquote (%) [d]	77,2	79,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 3	erwartete Anzahl Fragebögen [a]	263	266
	erhaltene Anzahl Fragebögen [b]	205	204
	auswertbare Anzahl Fragebögen [c]	205	204
	Rücklaufquote (%) [d]	77,9	76,7
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 4	erwartete Anzahl Fragebögen [a]	263	265
	erhaltene Anzahl Fragebögen [b]	235	231
	auswertbare Anzahl Fragebögen [c]	235	231
	Rücklaufquote (%) [d]	89,4	87,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 5	erwartete Anzahl Fragebögen [a]	263	264
	erhaltene Anzahl Fragebögen [b]	213	216
	auswertbare Anzahl Fragebögen [c]	213	216
	Rücklaufquote (%) [d]	81,0	81,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 6	erwartete Anzahl Fragebögen [a]	262	264
	erhaltene Anzahl Fragebögen [b]	209	207
	auswertbare Anzahl Fragebögen [c]	209	207
	Rücklaufquote (%) [d]	79,8	78,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 7	erwartete Anzahl Fragebögen [a]	262	263
	erhaltene Anzahl Fragebögen [b]	209	203
	auswertbare Anzahl Fragebögen [c]	209	203
	Rücklaufquote (%) [d]	79,8	77,2
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 8	erwartete Anzahl Fragebögen [a]	262	261
	erhaltene Anzahl Fragebögen [b]	220	211
	auswertbare Anzahl Fragebögen [c]	220	211
	Rücklaufquote (%) [d]	84,0	80,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 12	erwartete Anzahl Fragebögen [a]	261	259
	erhaltene Anzahl Fragebögen [b]	204	202
	auswertbare Anzahl Fragebögen [c]	204	202
	Rücklaufquote (%) [d]	78,2	78,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 16	erwartete Anzahl Fragebögen [a]	259	259
	erhaltene Anzahl Fragebögen [b]	189	198
	auswertbare Anzahl Fragebögen [c]	189	198
	Rücklaufquote (%) [d]	73,0	76,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 20	erwartete Anzahl Fragebögen [a]	256	250
	erhaltene Anzahl Fragebögen [b]	179	180
	auswertbare Anzahl Fragebögen [c]	179	180
	Rücklaufquote (%) [d]	69,9	72,0
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 24	erwartete Anzahl Fragebögen [a]	248	244
	erhaltene Anzahl Fragebögen [b]	169	172
	auswertbare Anzahl Fragebögen [c]	169	172
	Rücklaufquote (%) [d]	68,1	70,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 28	erwartete Anzahl Fragebögen [a]	241	237
	erhaltene Anzahl Fragebögen [b]	166	158
	auswertbare Anzahl Fragebögen [c]	166	158
	Rücklaufquote (%) [d]	68,9	66,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 32	erwartete Anzahl Fragebögen [a]	236	227
	erhaltene Anzahl Fragebögen [b]	159	150
	auswertbare Anzahl Fragebögen [c]	159	150
	Rücklaufquote (%) [d]	67,4	66,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 36	erwartete Anzahl Fragebögen [a]	232	220
	erhaltene Anzahl Fragebögen [b]	153	141
	auswertbare Anzahl Fragebögen [c]	153	141
	Rücklaufquote (%) [d]	65,9	64,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 40	erwartete Anzahl Fragebögen [a]	226	210
	erhaltene Anzahl Fragebögen [b]	137	122
	auswertbare Anzahl Fragebögen [c]	137	122
	Rücklaufquote (%) [d]	60,6	58,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 44	erwartete Anzahl Fragebögen [a]	220	203
	erhaltene Anzahl Fragebögen [b]	131	125
	auswertbare Anzahl Fragebögen [c]	131	125
	Rücklaufquote (%) [d]	59,5	61,6
	Auswertbarkeitsquote (%) [e]	100	100
Week 48	erwartete Anzahl Fragebögen [a]	215	195
	erhaltene Anzahl Fragebögen [b]	124	121
	auswertbare Anzahl Fragebögen [c]	124	121
	Rücklaufquote (%) [d]	57,7	62,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 52	erwartete Anzahl Fragebögen [a]	209	191
	erhaltene Anzahl Fragebögen [b]	124	118
	auswertbare Anzahl Fragebögen [c]	124	118
	Rücklaufquote (%) [d]	59,3	61,8
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
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Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 56	erwartete Anzahl Fragebögen [a]	208	185
	erhaltene Anzahl Fragebögen [b]	122	106
	auswertbare Anzahl Fragebögen [c]	122	106
	Rücklaufquote (%) [d]	58,7	57,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 60	erwartete Anzahl Fragebögen [a]	198	172
	erhaltene Anzahl Fragebögen [b]	118	98
	auswertbare Anzahl Fragebögen [c]	118	98
	Rücklaufquote (%) [d]	59,6	57,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 64	erwartete Anzahl Fragebögen [a]	191	166
	erhaltene Anzahl Fragebögen [b]	113	95
	auswertbare Anzahl Fragebögen [c]	113	95
	Rücklaufquote (%) [d]	59,2	57,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 68	erwartete Anzahl Fragebögen [a]	184	162
	erhaltene Anzahl Fragebögen [b]	103	92
	auswertbare Anzahl Fragebögen [c]	103	92
	Rücklaufquote (%) [d]	56,0	56,8
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 72	erwartete Anzahl Fragebögen [a]	180	157
	erhaltene Anzahl Fragebögen [b]	101	87
	auswertbare Anzahl Fragebögen [c]	101	87
	Rücklaufquote (%) [d]	56,1	55,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 76	erwartete Anzahl Fragebögen [a]	175	150
	erhaltene Anzahl Fragebögen [b]	98	77
	auswertbare Anzahl Fragebögen [c]	98	77
	Rücklaufquote (%) [d]	56,0	51,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 80	erwartete Anzahl Fragebögen [a]	173	146
	erhaltene Anzahl Fragebögen [b]	97	75
	auswertbare Anzahl Fragebögen [c]	97	75
	Rücklaufquote (%) [d]	56,1	51,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 84	erwartete Anzahl Fragebögen [a]	168	144
	erhaltene Anzahl Fragebögen [b]	97	75
	auswertbare Anzahl Fragebögen [c]	97	75
	Rücklaufquote (%) [d]	57,7	52,1
	Auswertbarkeitsquote (%) [e]	100	100

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[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Timepoints are reported by visit for each treatment arm.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 88	erwartete Anzahl Fragebögen [a]	167	143
	erhaltene Anzahl Fragebögen [b]	92	70
	auswertbare Anzahl Fragebögen [c]	92	70
	Rücklaufquote (%) [d]	55,1	49,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 92	erwartete Anzahl Fragebögen [a]	165	139
	erhaltene Anzahl Fragebögen [b]	92	69
	auswertbare Anzahl Fragebögen [c]	92	69
	Rücklaufquote (%) [d]	55,8	49,6
	Auswertbarkeitsquote (%) [e]	100	100
Week 96	erwartete Anzahl Fragebögen [a]	163	137
	erhaltene Anzahl Fragebögen [b]	87	64
	auswertbare Anzahl Fragebögen [c]	87	64
	Rücklaufquote (%) [d]	53,4	46,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 100	erwartete Anzahl Fragebögen [a]	160	133
	erhaltene Anzahl Fragebögen [b]	95	67
	auswertbare Anzahl Fragebögen [c]	95	67
	Rücklaufquote (%) [d]	59,4	50,4
	Auswertbarkeitsquote (%) [e]	100	100

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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 104	erwartete Anzahl Fragebögen [a]	157	130
	erhaltene Anzahl Fragebögen [b]	80	63
	auswertbare Anzahl Fragebögen [c]	80	63
	Rücklaufquote (%) [d]	51,0	48,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 108	erwartete Anzahl Fragebögen [a]	154	127
	erhaltene Anzahl Fragebögen [b]	77	59
	auswertbare Anzahl Fragebögen [c]	77	59
	Rücklaufquote (%) [d]	50,0	46,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 112	erwartete Anzahl Fragebögen [a]	151	125
	erhaltene Anzahl Fragebögen [b]	73	54
	auswertbare Anzahl Fragebögen [c]	73	54
	Rücklaufquote (%) [d]	48,3	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 116	erwartete Anzahl Fragebögen [a]	150	118
	erhaltene Anzahl Fragebögen [b]	68	56
	auswertbare Anzahl Fragebögen [c]	68	56
	Rücklaufquote (%) [d]	45,3	47,5
	Auswertbarkeitsquote (%) [e]	100	100

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[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 120	erwartete Anzahl Fragebögen [a]	147	118
	erhaltene Anzahl Fragebögen [b]	63	51
	auswertbare Anzahl Fragebögen [c]	63	51
	Rücklaufquote (%) [d]	42,9	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 124	erwartete Anzahl Fragebögen [a]	145	113
	erhaltene Anzahl Fragebögen [b]	59	51
	auswertbare Anzahl Fragebögen [c]	59	51
	Rücklaufquote (%) [d]	40,7	45,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 128	erwartete Anzahl Fragebögen [a]	138	108
	erhaltene Anzahl Fragebögen [b]	59	45
	auswertbare Anzahl Fragebögen [c]	59	45
	Rücklaufquote (%) [d]	42,8	41,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 132	erwartete Anzahl Fragebögen [a]	132	102
	erhaltene Anzahl Fragebögen [b]	54	44
	auswertbare Anzahl Fragebögen [c]	54	44
	Rücklaufquote (%) [d]	40,9	43,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 136	erwartete Anzahl Fragebögen [a]	124	94
	erhaltene Anzahl Fragebögen [b]	52	39
	auswertbare Anzahl Fragebögen [c]	52	39
	Rücklaufquote (%) [d]	41,9	41,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 140	erwartete Anzahl Fragebögen [a]	114	89
	erhaltene Anzahl Fragebögen [b]	48	39
	auswertbare Anzahl Fragebögen [c]	48	39
	Rücklaufquote (%) [d]	42,1	43,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 144	erwartete Anzahl Fragebögen [a]	106	81
	erhaltene Anzahl Fragebögen [b]	39	35
	auswertbare Anzahl Fragebögen [c]	39	35
	Rücklaufquote (%) [d]	36,8	43,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 148	erwartete Anzahl Fragebögen [a]	100	75
	erhaltene Anzahl Fragebögen [b]	43	32
	auswertbare Anzahl Fragebögen [c]	43	32
	Rücklaufquote (%) [d]	43,0	42,7
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
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[d] Compliance Rate = Evaluable/Expected * 100.
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Timepoints are reported by visit for each treatment arm.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 152	erwartete Anzahl Fragebögen [a]	96	72
	erhaltene Anzahl Fragebögen [b]	41	33
	auswertbare Anzahl Fragebögen [c]	41	33
	Rücklaufquote (%) [d]	42,7	45,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 156	erwartete Anzahl Fragebögen [a]	88	66
	erhaltene Anzahl Fragebögen [b]	38	32
	auswertbare Anzahl Fragebögen [c]	38	32
	Rücklaufquote (%) [d]	43,2	48,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 160	erwartete Anzahl Fragebögen [a]	83	63
	erhaltene Anzahl Fragebögen [b]	33	31
	auswertbare Anzahl Fragebögen [c]	33	31
	Rücklaufquote (%) [d]	39,8	49,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 164	erwartete Anzahl Fragebögen [a]	79	57
	erhaltene Anzahl Fragebögen [b]	33	24
	auswertbare Anzahl Fragebögen [c]	33	24
	Rücklaufquote (%) [d]	41,8	42,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Timepoints are reported by visit for each treatment arm.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 168	erwartete Anzahl Fragebögen [a]	71	52
	erhaltene Anzahl Fragebögen [b]	29	28
	auswertbare Anzahl Fragebögen [c]	29	28
	Rücklaufquote (%) [d]	40,8	53,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 172	erwartete Anzahl Fragebögen [a]	65	49
	erhaltene Anzahl Fragebögen [b]	32	23
	auswertbare Anzahl Fragebögen [c]	32	23
	Rücklaufquote (%) [d]	49,2	46,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 176	erwartete Anzahl Fragebögen [a]	59	43
	erhaltene Anzahl Fragebögen [b]	23	21
	auswertbare Anzahl Fragebögen [c]	23	21
	Rücklaufquote (%) [d]	39,0	48,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 180	erwartete Anzahl Fragebögen [a]	54	37
	erhaltene Anzahl Fragebögen [b]	21	19
	auswertbare Anzahl Fragebögen [c]	21	19
	Rücklaufquote (%) [d]	38,9	51,4
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 184	erwartete Anzahl Fragebögen [a]	50	35
	erhaltene Anzahl Fragebögen [b]	19	20
	auswertbare Anzahl Fragebögen [c]	19	20
	Rücklaufquote (%) [d]	38,0	57,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 188	erwartete Anzahl Fragebögen [a]	46	30
	erhaltene Anzahl Fragebögen [b]	17	18
	auswertbare Anzahl Fragebögen [c]	17	18
	Rücklaufquote (%) [d]	37,0	60,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 192	erwartete Anzahl Fragebögen [a]	44	27
	erhaltene Anzahl Fragebögen [b]	17	16
	auswertbare Anzahl Fragebögen [c]	17	16
	Rücklaufquote (%) [d]	38,6	59,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 196	erwartete Anzahl Fragebögen [a]	42	27
	erhaltene Anzahl Fragebögen [b]	14	18
	auswertbare Anzahl Fragebögen [c]	14	18
	Rücklaufquote (%) [d]	33,3	66,7
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 200	erwartete Anzahl Fragebögen [a]	37	26
	erhaltene Anzahl Fragebögen [b]	11	19
	auswertbare Anzahl Fragebögen [c]	11	19
	Rücklaufquote (%) [d]	29,7	73,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 204	erwartete Anzahl Fragebögen [a]	33	24
	erhaltene Anzahl Fragebögen [b]	7	13
	auswertbare Anzahl Fragebögen [c]	7	13
	Rücklaufquote (%) [d]	21,2	54,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 208	erwartete Anzahl Fragebögen [a]	31	22
	erhaltene Anzahl Fragebögen [b]	8	12
	auswertbare Anzahl Fragebögen [c]	8	12
	Rücklaufquote (%) [d]	25,8	54,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 212	erwartete Anzahl Fragebögen [a]	28	22
	erhaltene Anzahl Fragebögen [b]	7	15
	auswertbare Anzahl Fragebögen [c]	7	15
	Rücklaufquote (%) [d]	25,0	68,2
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 216	erwartete Anzahl Fragebögen [a]	26	18
	erhaltene Anzahl Fragebögen [b]	9	12
	auswertbare Anzahl Fragebögen [c]	9	12
	Rücklaufquote (%) [d]	34,6	66,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 220	erwartete Anzahl Fragebögen [a]	24	17
	erhaltene Anzahl Fragebögen [b]	7	9
	auswertbare Anzahl Fragebögen [c]	7	9
	Rücklaufquote (%) [d]	29,2	52,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 224	erwartete Anzahl Fragebögen [a]	20	16
	erhaltene Anzahl Fragebögen [b]	6	11
	auswertbare Anzahl Fragebögen [c]	6	11
	Rücklaufquote (%) [d]	30,0	68,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 228	erwartete Anzahl Fragebögen [a]	18	14
	erhaltene Anzahl Fragebögen [b]	6	9
	auswertbare Anzahl Fragebögen [c]	6	9
	Rücklaufquote (%) [d]	33,3	64,3
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 232	erwartete Anzahl Fragebögen [a]	15	11
	erhaltene Anzahl Fragebögen [b]	6	5
	auswertbare Anzahl Fragebögen [c]	6	5
	Rücklaufquote (%) [d]	40,0	45,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 236	erwartete Anzahl Fragebögen [a]	12	7
	erhaltene Anzahl Fragebögen [b]	4	5
	auswertbare Anzahl Fragebögen [c]	4	5
	Rücklaufquote (%) [d]	33,3	71,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 240	erwartete Anzahl Fragebögen [a]	9	7
	erhaltene Anzahl Fragebögen [b]	3	5
	auswertbare Anzahl Fragebögen [c]	3	5
	Rücklaufquote (%) [d]	33,3	71,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 244	erwartete Anzahl Fragebögen [a]	8	7
	erhaltene Anzahl Fragebögen [b]	2	4
	auswertbare Anzahl Fragebögen [c]	2	4
	Rücklaufquote (%) [d]	25,0	57,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 248	erwartete Anzahl Fragebögen [a]	5	5
	erhaltene Anzahl Fragebögen [b]	1	2
	auswertbare Anzahl Fragebögen [c]	1	2
	Rücklaufquote (%) [d]	20,0	40,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 252	erwartete Anzahl Fragebögen [a]	4	3
	erhaltene Anzahl Fragebögen [b]	2	1
	auswertbare Anzahl Fragebögen [c]	2	1
	Rücklaufquote (%) [d]	50,0	33,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 256	erwartete Anzahl Fragebögen [a]	3	2
	erhaltene Anzahl Fragebögen [b]	0	1
	auswertbare Anzahl Fragebögen [c]	0	1
	Rücklaufquote (%) [d]	0,0	50,0
	Auswertbarkeitsquote (%) [e]	NC	100
Week 260	erwartete Anzahl Fragebögen [a]	2	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	0,0	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.2 ADRIATIC: Summary of compliance with EORTC QLQ-LC13 by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 264	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC
Week 268	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Baseline	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	215	211
	auswertbare Anzahl Fragebögen [c]	215	211
	Rücklaufquote (%) [d]	81,4	79,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 8	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	221	204
	auswertbare Anzahl Fragebögen [c]	221	204
	Rücklaufquote (%) [d]	83,7	76,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 16	erwartete Anzahl Fragebögen [a]	261	259
	erhaltene Anzahl Fragebögen [b]	188	191
	auswertbare Anzahl Fragebögen [c]	188	191
	Rücklaufquote (%) [d]	72,0	73,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 24	erwartete Anzahl Fragebögen [a]	251	248
	erhaltene Anzahl Fragebögen [b]	166	170
	auswertbare Anzahl Fragebögen [c]	166	170
	Rücklaufquote (%) [d]	66,1	68,5
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
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Timepoints are reported by visit for each treatment arm.
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 32	erwartete Anzahl Fragebögen [a]	238	232
	erhaltene Anzahl Fragebögen [b]	159	149
	auswertbare Anzahl Fragebögen [c]	159	149
	Rücklaufquote (%) [d]	66,8	64,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 40	erwartete Anzahl Fragebögen [a]	228	214
	erhaltene Anzahl Fragebögen [b]	135	121
	auswertbare Anzahl Fragebögen [c]	135	121
	Rücklaufquote (%) [d]	59,2	56,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 48	erwartete Anzahl Fragebögen [a]	220	197
	erhaltene Anzahl Fragebögen [b]	122	118
	auswertbare Anzahl Fragebögen [c]	122	118
	Rücklaufquote (%) [d]	55,5	59,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 56	erwartete Anzahl Fragebögen [a]	209	187
	erhaltene Anzahl Fragebögen [b]	120	102
	auswertbare Anzahl Fragebögen [c]	120	102
	Rücklaufquote (%) [d]	57,4	54,5
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 64	erwartete Anzahl Fragebögen [a]	193	170
	erhaltene Anzahl Fragebögen [b]	113	94
	auswertbare Anzahl Fragebögen [c]	113	94
	Rücklaufquote (%) [d]	58,5	55,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 72	erwartete Anzahl Fragebögen [a]	182	158
	erhaltene Anzahl Fragebögen [b]	99	86
	auswertbare Anzahl Fragebögen [c]	99	86
	Rücklaufquote (%) [d]	54,4	54,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 80	erwartete Anzahl Fragebögen [a]	174	147
	erhaltene Anzahl Fragebögen [b]	96	74
	auswertbare Anzahl Fragebögen [c]	96	74
	Rücklaufquote (%) [d]	55,2	50,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 88	erwartete Anzahl Fragebögen [a]	167	143
	erhaltene Anzahl Fragebögen [b]	91	68
	auswertbare Anzahl Fragebögen [c]	91	68
	Rücklaufquote (%) [d]	54,5	47,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 96	erwartete Anzahl Fragebögen [a]	163	138
	erhaltene Anzahl Fragebögen [b]	87	63
	auswertbare Anzahl Fragebögen [c]	87	63
	Rücklaufquote (%) [d]	53,4	45,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 104	erwartete Anzahl Fragebögen [a]	159	132
	erhaltene Anzahl Fragebögen [b]	79	60
	auswertbare Anzahl Fragebögen [c]	79	60
	Rücklaufquote (%) [d]	49,7	45,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 112	erwartete Anzahl Fragebögen [a]	153	126
	erhaltene Anzahl Fragebögen [b]	72	54
	auswertbare Anzahl Fragebögen [c]	72	54
	Rücklaufquote (%) [d]	47,1	42,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 120	erwartete Anzahl Fragebögen [a]	149	118
	erhaltene Anzahl Fragebögen [b]	63	50
	auswertbare Anzahl Fragebögen [c]	63	50
	Rücklaufquote (%) [d]	42,3	42,4
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 128	erwartete Anzahl Fragebögen [a]	141	112
	erhaltene Anzahl Fragebögen [b]	59	45
	auswertbare Anzahl Fragebögen [c]	59	45
	Rücklaufquote (%) [d]	41,8	40,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 136	erwartete Anzahl Fragebögen [a]	126	100
	erhaltene Anzahl Fragebögen [b]	52	39
	auswertbare Anzahl Fragebögen [c]	52	39
	Rücklaufquote (%) [d]	41,3	39,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 144	erwartete Anzahl Fragebögen [a]	111	85
	erhaltene Anzahl Fragebögen [b]	39	35
	auswertbare Anzahl Fragebögen [c]	39	35
	Rücklaufquote (%) [d]	35,1	41,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 152	erwartete Anzahl Fragebögen [a]	97	74
	erhaltene Anzahl Fragebögen [b]	41	33
	auswertbare Anzahl Fragebögen [c]	41	33
	Rücklaufquote (%) [d]	42,3	44,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 160	erwartete Anzahl Fragebögen [a]	86	65
	erhaltene Anzahl Fragebögen [b]	33	31
	auswertbare Anzahl Fragebögen [c]	33	31
	Rücklaufquote (%) [d]	38,4	47,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 168	erwartete Anzahl Fragebögen [a]	76	54
	erhaltene Anzahl Fragebögen [b]	29	27
	auswertbare Anzahl Fragebögen [c]	29	27
	Rücklaufquote (%) [d]	38,2	50,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 176	erwartete Anzahl Fragebögen [a]	64	44
	erhaltene Anzahl Fragebögen [b]	23	21
	auswertbare Anzahl Fragebögen [c]	23	21
	Rücklaufquote (%) [d]	35,9	47,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 184	erwartete Anzahl Fragebögen [a]	52	36
	erhaltene Anzahl Fragebögen [b]	19	20
	auswertbare Anzahl Fragebögen [c]	19	20
	Rücklaufquote (%) [d]	36,5	55,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 192	erwartete Anzahl Fragebögen [a]	46	29
	erhaltene Anzahl Fragebögen [b]	17	15
	auswertbare Anzahl Fragebögen [c]	17	15
	Rücklaufquote (%) [d]	37,0	51,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 200	erwartete Anzahl Fragebögen [a]	38	27
	erhaltene Anzahl Fragebögen [b]	11	19
	auswertbare Anzahl Fragebögen [c]	11	19
	Rücklaufquote (%) [d]	28,9	70,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 208	erwartete Anzahl Fragebögen [a]	32	22
	erhaltene Anzahl Fragebögen [b]	8	11
	auswertbare Anzahl Fragebögen [c]	8	11
	Rücklaufquote (%) [d]	25,0	50,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 216	erwartete Anzahl Fragebögen [a]	27	20
	erhaltene Anzahl Fragebögen [b]	9	12
	auswertbare Anzahl Fragebögen [c]	9	12
	Rücklaufquote (%) [d]	33,3	60,0
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 224	erwartete Anzahl Fragebögen [a]	21	17
	erhaltene Anzahl Fragebögen [b]	6	10
	auswertbare Anzahl Fragebögen [c]	6	10
	Rücklaufquote (%) [d]	28,6	58,8
	Auswertbarkeitsquote (%) [e]	100	100
Week 232	erwartete Anzahl Fragebögen [a]	17	14
	erhaltene Anzahl Fragebögen [b]	6	5
	auswertbare Anzahl Fragebögen [c]	6	5
	Rücklaufquote (%) [d]	35,3	35,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 240	erwartete Anzahl Fragebögen [a]	12	7
	erhaltene Anzahl Fragebögen [b]	3	5
	auswertbare Anzahl Fragebögen [c]	3	5
	Rücklaufquote (%) [d]	25,0	71,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 248	erwartete Anzahl Fragebögen [a]	7	7
	erhaltene Anzahl Fragebögen [b]	1	2
	auswertbare Anzahl Fragebögen [c]	1	2
	Rücklaufquote (%) [d]	14,3	28,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.3 ADRIATIC: Summary of compliance with EQ-5D by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 256	erwartete Anzahl Fragebögen [a]	3	2
	erhaltene Anzahl Fragebögen [b]	0	1
	auswertbare Anzahl Fragebögen [c]	0	1
	Rücklaufquote (%) [d]	0,0	50,0
	Auswertbarkeitsquote (%) [e]	NC	100
Week 264	erwartete Anzahl Fragebögen [a]	2	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	0,0	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC
Week 272	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Baseline	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	219	214
	auswertbare Anzahl Fragebögen [c]	219	214
	Rücklaufquote (%) [d]	83,0	80,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 8	erwartete Anzahl Fragebögen [a]	264	266
	erhaltene Anzahl Fragebögen [b]	227	216
	auswertbare Anzahl Fragebögen [c]	227	216
	Rücklaufquote (%) [d]	86,0	81,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 16	erwartete Anzahl Fragebögen [a]	261	259
	erhaltene Anzahl Fragebögen [b]	190	197
	auswertbare Anzahl Fragebögen [c]	190	197
	Rücklaufquote (%) [d]	72,8	76,1
	Auswertbarkeitsquote (%) [e]	100	100
Week 24	erwartete Anzahl Fragebögen [a]	251	248
	erhaltene Anzahl Fragebögen [b]	169	172
	auswertbare Anzahl Fragebögen [c]	169	172
	Rücklaufquote (%) [d]	67,3	69,4
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 32	erwartete Anzahl Fragebögen [a]	238	232
	erhaltene Anzahl Fragebögen [b]	160	150
	auswertbare Anzahl Fragebögen [c]	160	150
	Rücklaufquote (%) [d]	67,2	64,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 40	erwartete Anzahl Fragebögen [a]	228	214
	erhaltene Anzahl Fragebögen [b]	138	121
	auswertbare Anzahl Fragebögen [c]	138	121
	Rücklaufquote (%) [d]	60,5	56,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 48	erwartete Anzahl Fragebögen [a]	220	197
	erhaltene Anzahl Fragebögen [b]	122	119
	auswertbare Anzahl Fragebögen [c]	122	119
	Rücklaufquote (%) [d]	55,5	60,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 56	erwartete Anzahl Fragebögen [a]	209	187
	erhaltene Anzahl Fragebögen [b]	122	105
	auswertbare Anzahl Fragebögen [c]	122	105
	Rücklaufquote (%) [d]	58,4	56,1
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 64	erwartete Anzahl Fragebögen [a]	193	170
	erhaltene Anzahl Fragebögen [b]	113	95
	auswertbare Anzahl Fragebögen [c]	113	95
	Rücklaufquote (%) [d]	58,5	55,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 72	erwartete Anzahl Fragebögen [a]	182	158
	erhaltene Anzahl Fragebögen [b]	101	88
	auswertbare Anzahl Fragebögen [c]	101	88
	Rücklaufquote (%) [d]	55,5	55,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 80	erwartete Anzahl Fragebögen [a]	174	147
	erhaltene Anzahl Fragebögen [b]	97	74
	auswertbare Anzahl Fragebögen [c]	97	74
	Rücklaufquote (%) [d]	55,7	50,3
	Auswertbarkeitsquote (%) [e]	100	100
Week 88	erwartete Anzahl Fragebögen [a]	167	143
	erhaltene Anzahl Fragebögen [b]	92	69
	auswertbare Anzahl Fragebögen [c]	92	69
	Rücklaufquote (%) [d]	55,1	48,3
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 96	erwartete Anzahl Fragebögen [a]	163	138
	erhaltene Anzahl Fragebögen [b]	87	63
	auswertbare Anzahl Fragebögen [c]	87	63
	Rücklaufquote (%) [d]	53,4	45,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 104	erwartete Anzahl Fragebögen [a]	159	132
	erhaltene Anzahl Fragebögen [b]	80	62
	auswertbare Anzahl Fragebögen [c]	80	62
	Rücklaufquote (%) [d]	50,3	47,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 112	erwartete Anzahl Fragebögen [a]	153	126
	erhaltene Anzahl Fragebögen [b]	73	54
	auswertbare Anzahl Fragebögen [c]	73	54
	Rücklaufquote (%) [d]	47,7	42,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 120	erwartete Anzahl Fragebögen [a]	149	118
	erhaltene Anzahl Fragebögen [b]	64	51
	auswertbare Anzahl Fragebögen [c]	64	51
	Rücklaufquote (%) [d]	43,0	43,2
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 128	erwartete Anzahl Fragebögen [a]	141	112
	erhaltene Anzahl Fragebögen [b]	59	45
	auswertbare Anzahl Fragebögen [c]	59	45
	Rücklaufquote (%) [d]	41,8	40,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 136	erwartete Anzahl Fragebögen [a]	126	100
	erhaltene Anzahl Fragebögen [b]	52	39
	auswertbare Anzahl Fragebögen [c]	52	39
	Rücklaufquote (%) [d]	41,3	39,0
	Auswertbarkeitsquote (%) [e]	100	100
Week 144	erwartete Anzahl Fragebögen [a]	111	85
	erhaltene Anzahl Fragebögen [b]	40	36
	auswertbare Anzahl Fragebögen [c]	40	36
	Rücklaufquote (%) [d]	36,0	42,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 152	erwartete Anzahl Fragebögen [a]	97	74
	erhaltene Anzahl Fragebögen [b]	41	33
	auswertbare Anzahl Fragebögen [c]	41	33
	Rücklaufquote (%) [d]	42,3	44,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 160	erwartete Anzahl Fragebögen [a]	86	65
	erhaltene Anzahl Fragebögen [b]	34	31
	auswertbare Anzahl Fragebögen [c]	34	31
	Rücklaufquote (%) [d]	39,5	47,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 168	erwartete Anzahl Fragebögen [a]	76	54
	erhaltene Anzahl Fragebögen [b]	30	28
	auswertbare Anzahl Fragebögen [c]	30	28
	Rücklaufquote (%) [d]	39,5	51,9
	Auswertbarkeitsquote (%) [e]	100	100
Week 176	erwartete Anzahl Fragebögen [a]	64	44
	erhaltene Anzahl Fragebögen [b]	23	21
	auswertbare Anzahl Fragebögen [c]	23	21
	Rücklaufquote (%) [d]	35,9	47,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 184	erwartete Anzahl Fragebögen [a]	52	36
	erhaltene Anzahl Fragebögen [b]	19	20
	auswertbare Anzahl Fragebögen [c]	19	20
	Rücklaufquote (%) [d]	36,5	55,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Nutzenbewertung nach AMNOG

Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 192	erwartete Anzahl Fragebögen [a]	46	29
	erhaltene Anzahl Fragebögen [b]	17	16
	auswertbare Anzahl Fragebögen [c]	17	16
	Rücklaufquote (%) [d]	37,0	55,2
	Auswertbarkeitsquote (%) [e]	100	100
Week 200	erwartete Anzahl Fragebögen [a]	38	27
	erhaltene Anzahl Fragebögen [b]	11	19
	auswertbare Anzahl Fragebögen [c]	11	19
	Rücklaufquote (%) [d]	28,9	70,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 208	erwartete Anzahl Fragebögen [a]	32	22
	erhaltene Anzahl Fragebögen [b]	8	12
	auswertbare Anzahl Fragebögen [c]	8	12
	Rücklaufquote (%) [d]	25,0	54,5
	Auswertbarkeitsquote (%) [e]	100	100
Week 216	erwartete Anzahl Fragebögen [a]	27	20
	erhaltene Anzahl Fragebögen [b]	9	12
	auswertbare Anzahl Fragebögen [c]	9	12
	Rücklaufquote (%) [d]	33,3	60,0
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Nutzenbewertung nach AMNOG

Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 224	erwartete Anzahl Fragebögen [a]	21	17
	erhaltene Anzahl Fragebögen [b]	6	11
	auswertbare Anzahl Fragebögen [c]	6	11
	Rücklaufquote (%) [d]	28,6	64,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 232	erwartete Anzahl Fragebögen [a]	17	14
	erhaltene Anzahl Fragebögen [b]	6	5
	auswertbare Anzahl Fragebögen [c]	6	5
	Rücklaufquote (%) [d]	35,3	35,7
	Auswertbarkeitsquote (%) [e]	100	100
Week 240	erwartete Anzahl Fragebögen [a]	12	7
	erhaltene Anzahl Fragebögen [b]	3	5
	auswertbare Anzahl Fragebögen [c]	3	5
	Rücklaufquote (%) [d]	25,0	71,4
	Auswertbarkeitsquote (%) [e]	100	100
Week 248	erwartete Anzahl Fragebögen [a]	7	7
	erhaltene Anzahl Fragebögen [b]	1	2
	auswertbare Anzahl Fragebögen [c]	1	2
	Rücklaufquote (%) [d]	14,3	28,6
	Auswertbarkeitsquote (%) [e]	100	100

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Table 3.1.4 ADRIATIC: Summary of compliance with PGIS by visit
Full Analysis Set, DCO 15JAN2024

Zeitpunkt	Compliance	Durvalumab (N=264)	Placebo (N=266)
Week 256	erwartete Anzahl Fragebögen [a]	3	2
	erhaltene Anzahl Fragebögen [b]	0	1
	auswertbare Anzahl Fragebögen [c]	0	1
	Rücklaufquote (%) [d]	0,0	50,0
	Auswertbarkeitsquote (%) [e]	NC	100
Week 264	erwartete Anzahl Fragebögen [a]	2	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	0,0	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC
Week 272	erwartete Anzahl Fragebögen [a]	0	1
	erhaltene Anzahl Fragebögen [b]	0	0
	auswertbare Anzahl Fragebögen [c]	0	0
	Rücklaufquote (%) [d]	NC	0,0
	Auswertbarkeitsquote (%) [e]	NC	NC

Baseline is defined as last evaluable assessment on or prior to start of treatment start time.
[a] Expected forms = number of subjects still under QoL follow-up (still on treatment) at given timepoint.
[b] Received forms = number of subjects who completed the form at a given timepoint.
[c] Evaluable forms = forms where at least one subscale can be determined.
[d] Compliance Rate = Evaluable/Expected * 100.
[e] Evaluability Rate = Evaluable/Received * 100.
Timepoints are reported by visit for each treatment arm.
NC = Not Calculable
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Anhang 4-G6.2: EORTC QLQ-C30

Nutzenbewertung nach AMNOG

Table 3.5.1.1 ADRIATIC: Summary of analysis of time to deterioration in EORTC QLQ-C30 global QoL/health status, functional, symptom and single item scales
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus	264	143 (54,2)	3,6 [2,7; 4,5]	266	130 (48,9)	4,5 [2,7; 8,2]	1,08	[0,85; 1,38]	0,4975
Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion	264	125 (47,3)	8,2 [5,5;11,9]	266	124 (46,6)	7,3 [3,6;10,2]	0,91	[0,70; 1,16]	0,4513
Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion	264	140 (53,0)	4,7 [3,6; 6,4]	266	136 (51,1)	5,5 [3,7; 8,2]	0,98	[0,77; 1,24]	0,8798
Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion	264	134 (50,8)	5,5 [3,6; 7,4]	266	123 (46,2)	8,3 [5,5;11,0]	1,17	[0,91; 1,49]	0,2281
Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion	264	138 (52,3)	4,7 [2,8; 7,4]	266	139 (52,3)	3,8 [2,7; 6,4]	0,83	[0,66; 1,06]	0,1424
Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion	264	140 (53,0)	4,6 [3,6; 7,3]	266	132 (49,6)	5,6 [3,7; 8,3]	1,03	[0,81; 1,31]	0,7920

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.5.1.1 ADRIATIC: Summary of analysis of time to deterioration in EORTC QLQ-C30 global QoL/health status, functional, symptom and single item scales
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue	264	159 (60,2)	1,9 [1,8; 3,6]	266	153 (57,5)	2,7 [1,9; 3,6]	1,08	[0,86; 1,35]	0,5301
Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen	264	155 (58,7)	3,7 [2,9; 4,7]	266	154 (57,9)	2,8 [1,8; 5,5]	0,87	[0,70; 1,09]	0,2613
Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen	264	109 (41,3)	14,7 [8,3;23,9]	266	96 (36,1)	16,6 [11,0;28,6]	1,09	[0,83; 1,45]	0,5237
Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust	264	131 (49,6)	5,6 [3,7; 9,2]	266	115 (43,2)	7,4 [4,6;11,9]	1,11	[0,86; 1,43]	0,4108
Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö	264	87 (33,0)	26,6 [14,7;44,2]	266	82 (30,8)	22,0 [13,8;32,2]	0,95	[0,70; 1,29]	0,7378
Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe	264	142 (53,8)	4,5 [2,8; 5,6]	266	125 (47,0)	7,3 [3,7; 9,1]	1,16	[0,91; 1,47]	0,2417
Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten	264	87 (33,0)	22,1 [13,7; NE]	266	84 (31,6)	34,1 [13,8; NE]	0,92	[0,68; 1,24]	0,5812

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Table 3.5.1.1 ADRIATIC: Summary of analysis of time to deterioration in EORTC QLQ-C30 global QoL/health status, functional, symptom and single item scales
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit	264	134 (50,8)	5,6 [4,5; 7,3]	266	114 (42,9)	8,3 [6,4;12,9]	1,24	[0,97; 1,60]	0,0890
Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung	264	113 (42,8)	11,9 [5,6;17,6]	266	105 (39,5)	9,3 [6,5;16,5]	0,97	[0,75; 1,28]	0,8575

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Anhang 4-G6.2.1: EORTC QLQ-C30 - Kaplan-Meier-Plot

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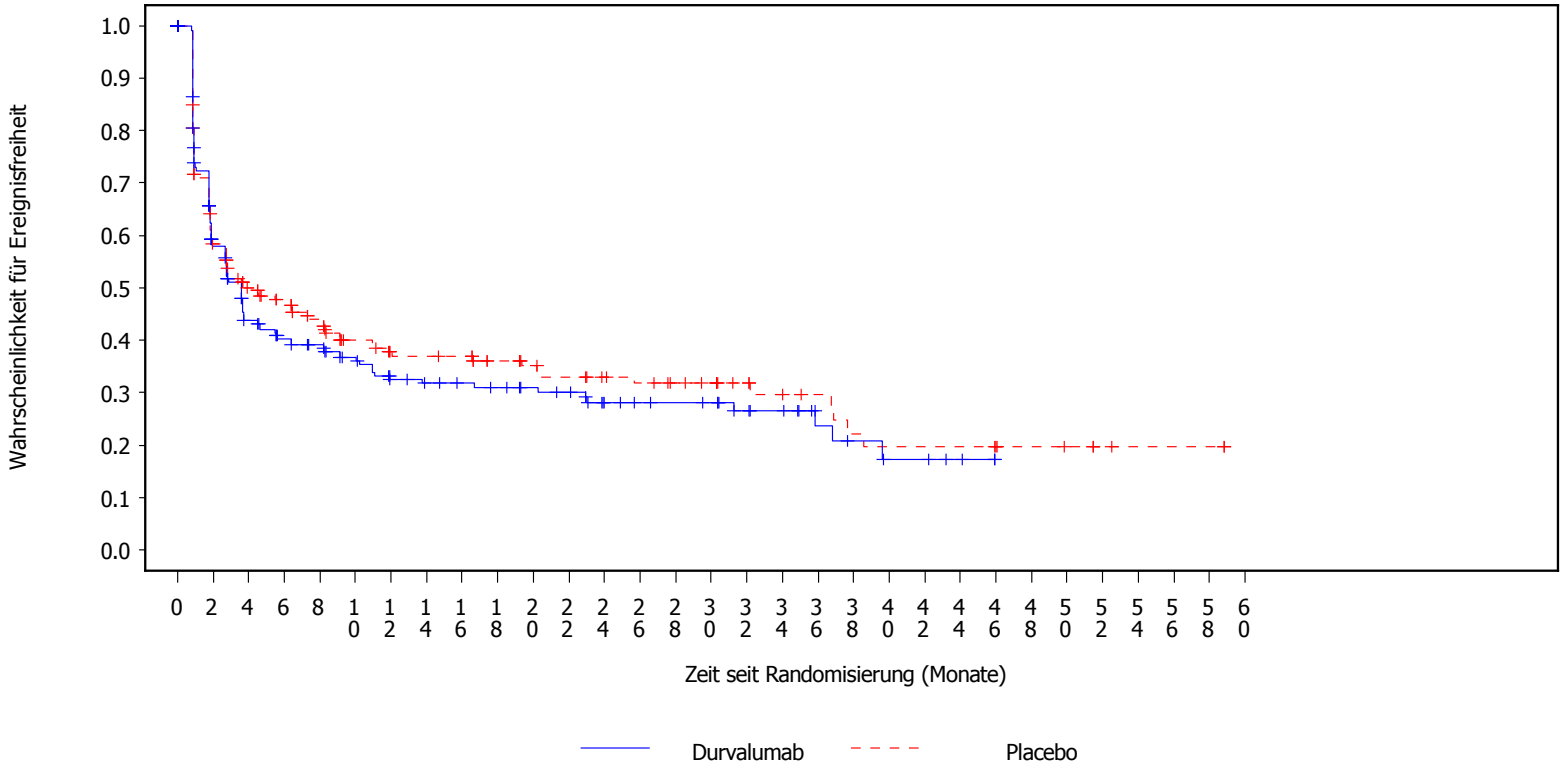
Figure 3.5.1.2 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	114	80	69	64	55	45	42	40	38	35	33	25	23	22	21	16	14	8	6	4	4	2	0	0	0	0	0	0	0	Durvalumab
266	114	90	80	68	54	47	46	45	38	34	31	28	26	23	21	17	14	12	9	8	8	8	6	5	4	2	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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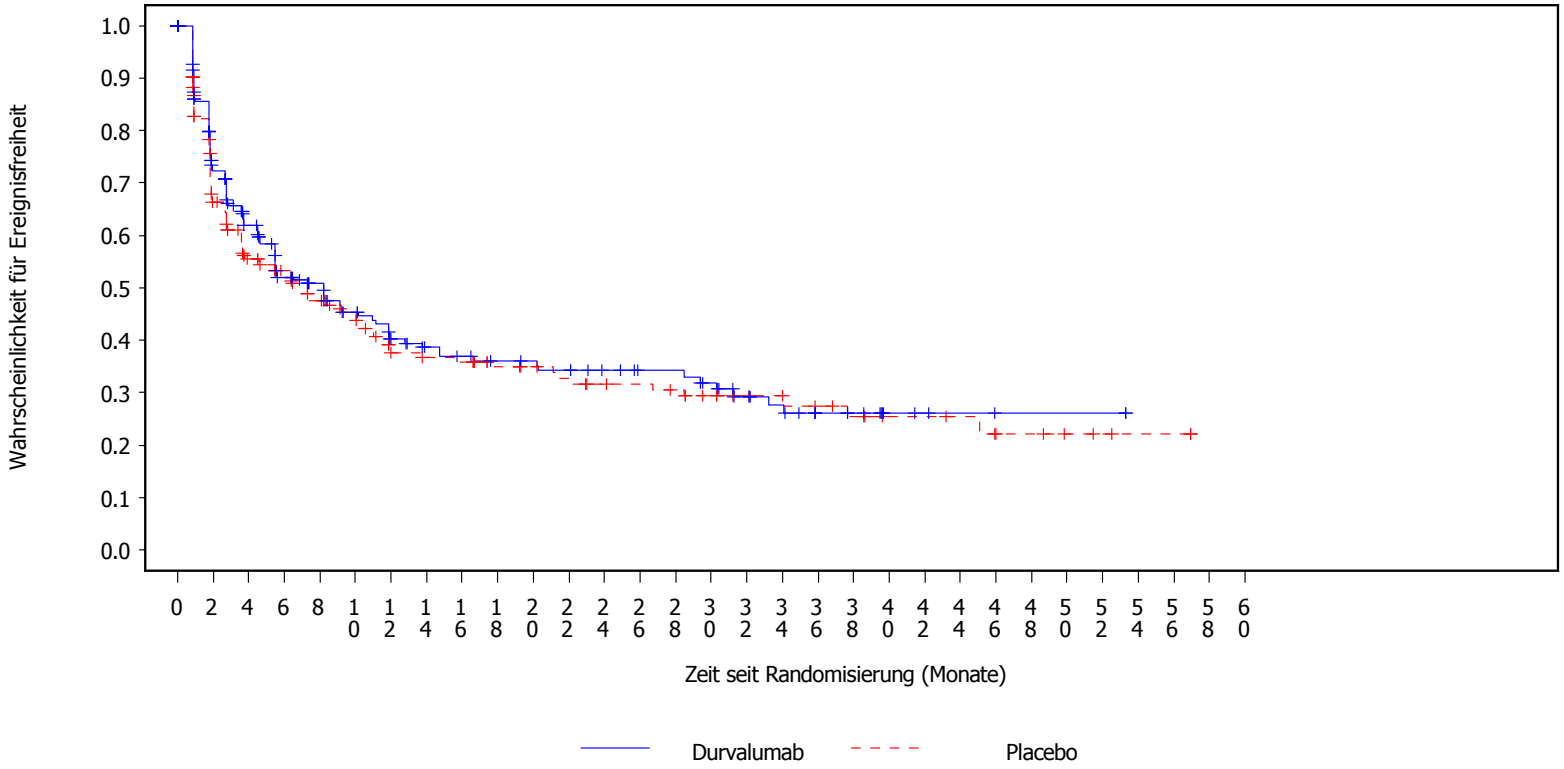
Figure 3.5.1.3 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	144	112	87	76	64	52	46	43	40	39	37	33	30	30	26	20	17	11	9	4	3	2	1	1	1	1	0	0	0	0	Durvalumab
266	127	98	86	71	61	46	43	42	36	34	31	28	27	25	21	18	17	14	12	9	9	8	5	5	3	2	1	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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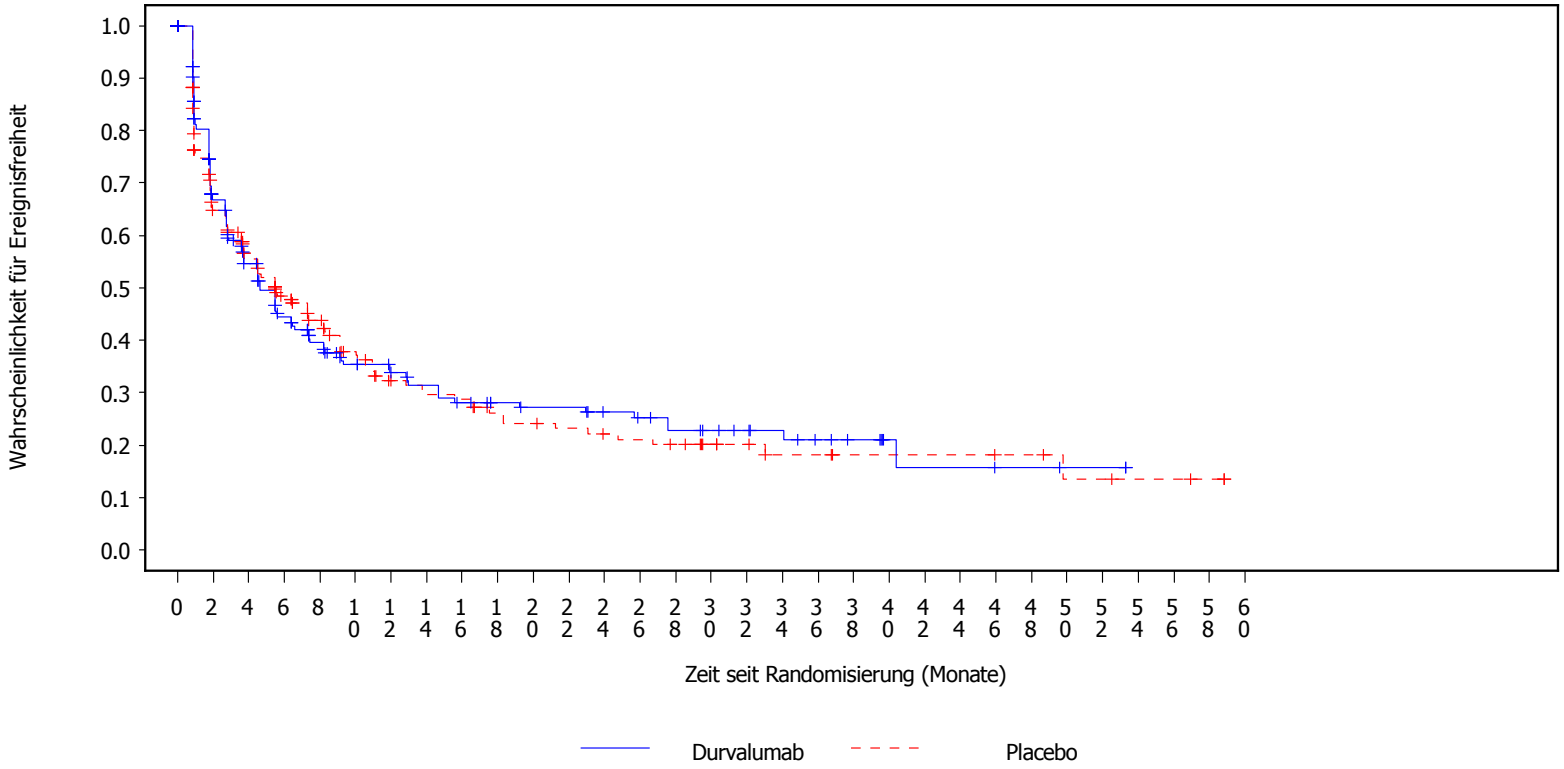
Figure 3.5.1.4 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	129	99	76	60	49	43	39	34	30	28	28	24	22	19	17	15	13	10	8	4	3	3	2	2	1	1	0	0	0	0	Durvalumab
266	122	96	77	63	49	38	34	33	27	25	23	21	20	18	14	11	8	8	6	6	6	6	5	5	3	3	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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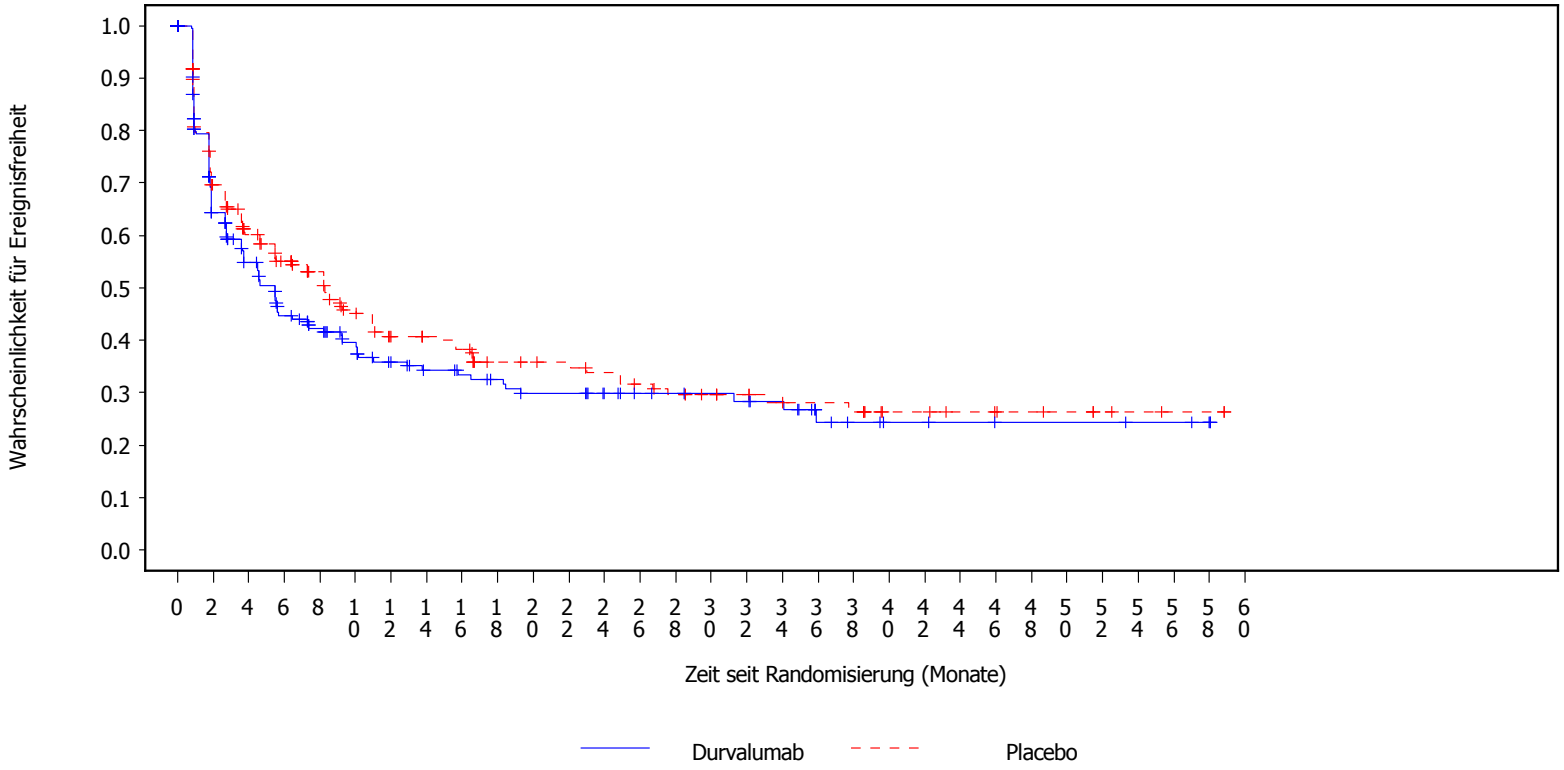
Figure 3.5.1.5 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	128	100	77	66	56	46	41	38	35	31	31	26	23	22	21	20	18	10	8	6	6	5	4	4	4	4	3	3	1	0	Durvalumab
266	135	109	94	81	65	54	50	47	38	37	36	33	30	27	24	21	18	17	16	10	10	8	7	6	5	3	2	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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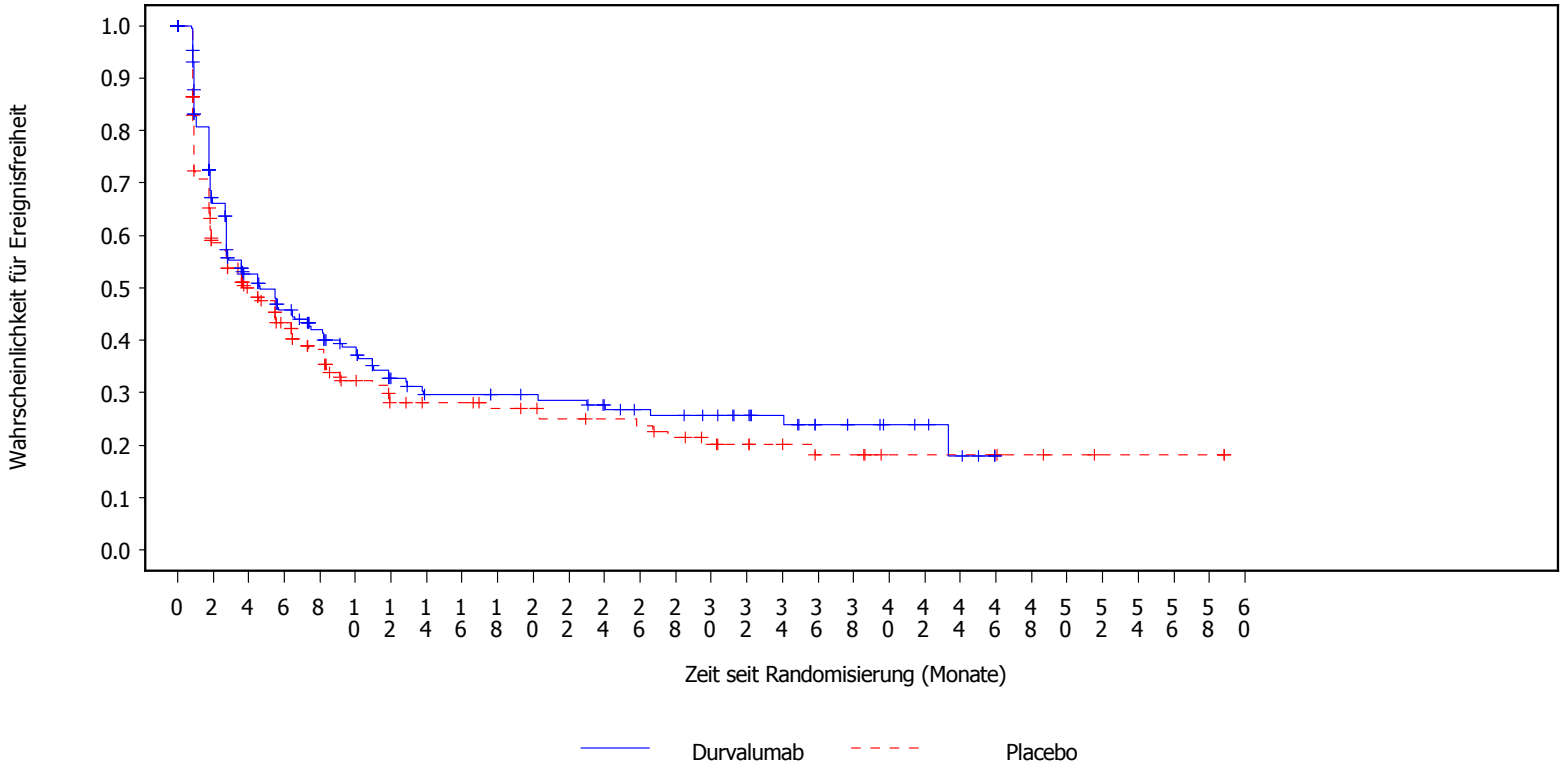
Figure 3.5.1.6 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	130	94	78	64	55	41	35	35	33	32	31	27	24	23	21	18	15	10	8	6	5	3	0	0	0	0	0	0	0	Durvalumab
266	111	87	69	54	40	32	30	30	27	26	23	22	21	18	15	13	11	8	8	5	5	5	4	3	2	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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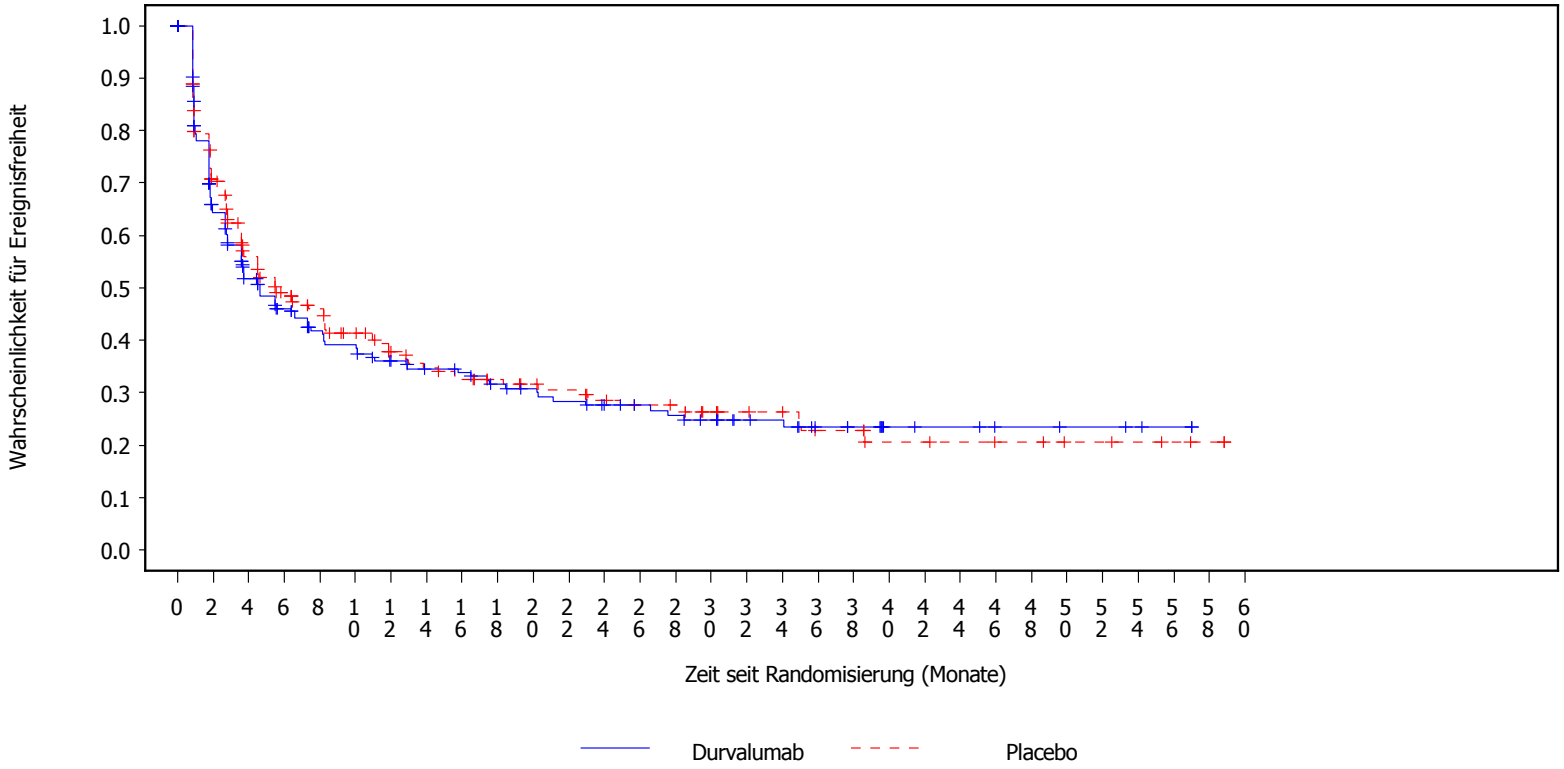
Figure 3.5.1.7 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	126	94	78	65	61	52	48	46	41	38	35	31	29	27	24	20	19	14	12	7	6	6	4	4	3	3	2	1	0	0	Durvalumab
266	136	100	83	72	61	51	45	41	37	34	32	28	25	24	20	17	16	12	12	8	8	7	6	6	4	4	3	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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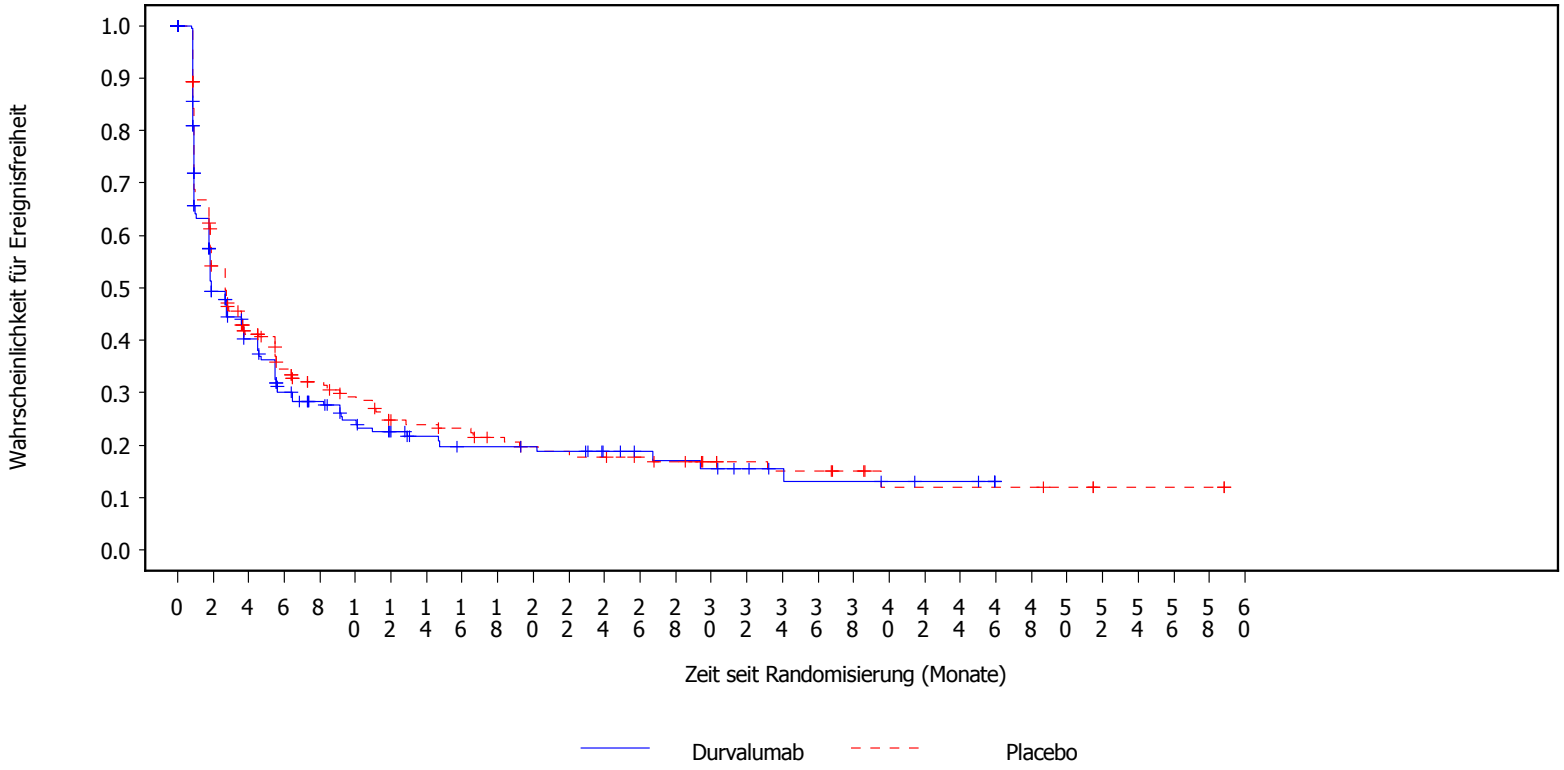
Figure 3.5.1.8 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	95	73	51	42	34	27	23	20	20	19	18	14	12	11	10	8	6	5	5	4	3	3	0	0	0	0	0	0	0	Durvalumab
266	106	73	56	46	40	32	30	28	24	21	20	19	17	15	12	10	9	9	7	4	4	4	4	4	3	1	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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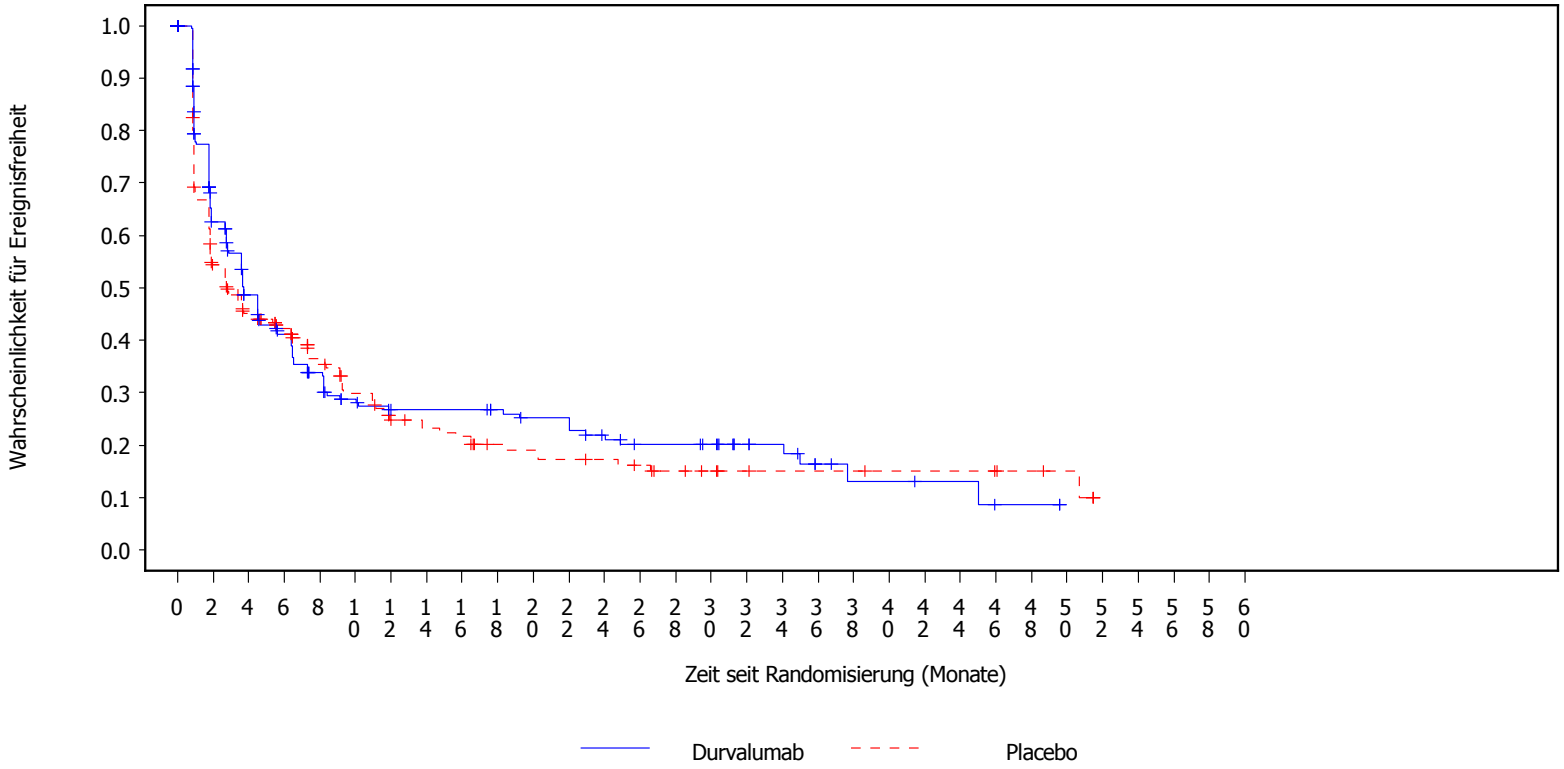
Figure 3.5.1.9 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	125	91	73	55	43	37	37	37	34	31	31	25	21	21	19	13	11	6	4	4	3	3	1	1	0	0	0	0	0	0	Durvalumab
266	107	84	72	56	43	33	29	27	21	20	18	17	15	12	10	8	7	7	7	6	6	6	5	4	3	0	0	0	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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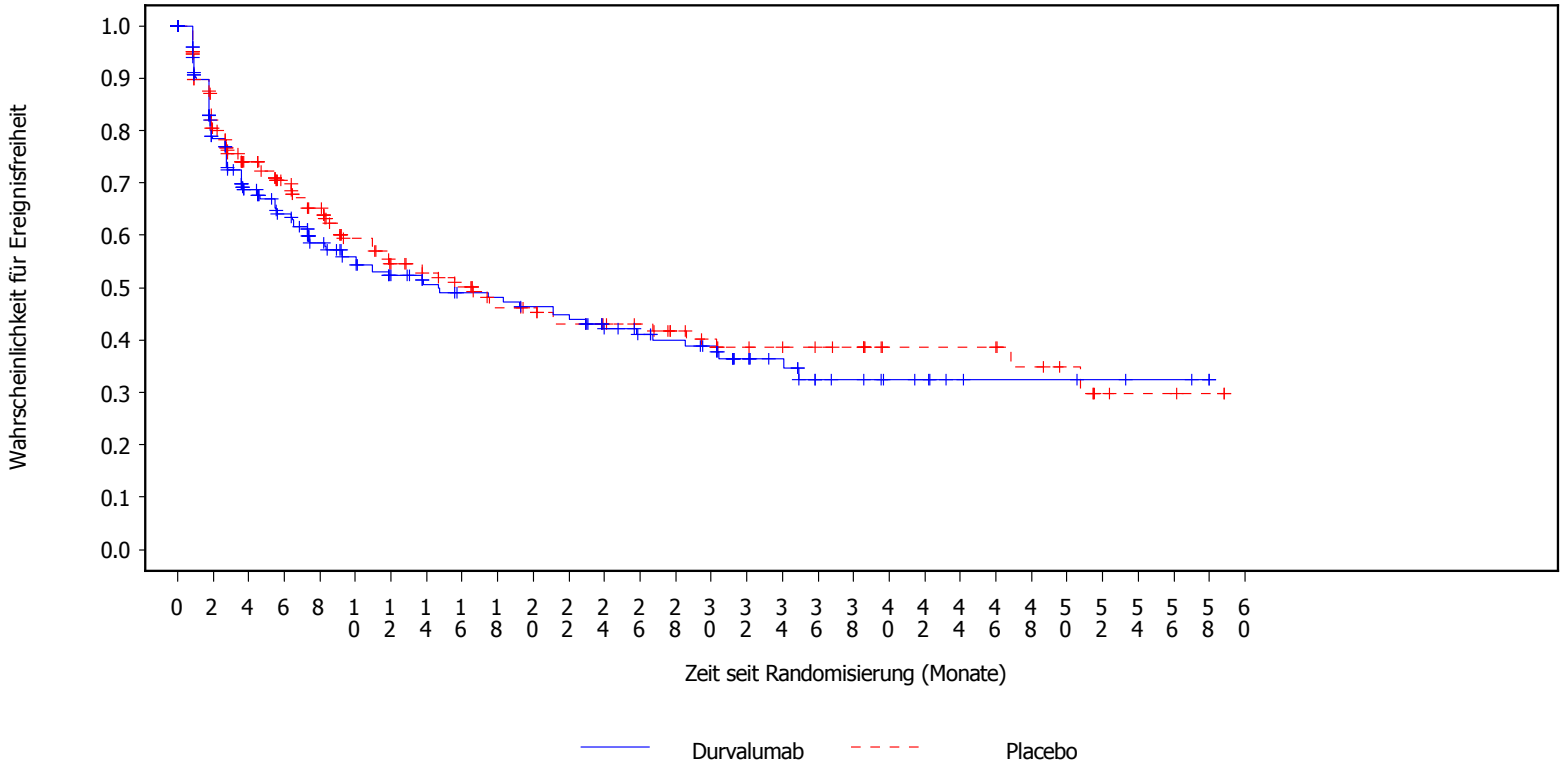
Figure 3.5.1.10 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	156	124	108	89	79	68	62	58	57	54	52	43	39	36	33	24	20	13	12	9	8	5	4	4	4	3	2	2	0	0	Durvalumab
266	153	127	110	96	76	66	60	55	46	44	39	36	34	29	26	22	21	19	18	12	12	12	11	9	7	3	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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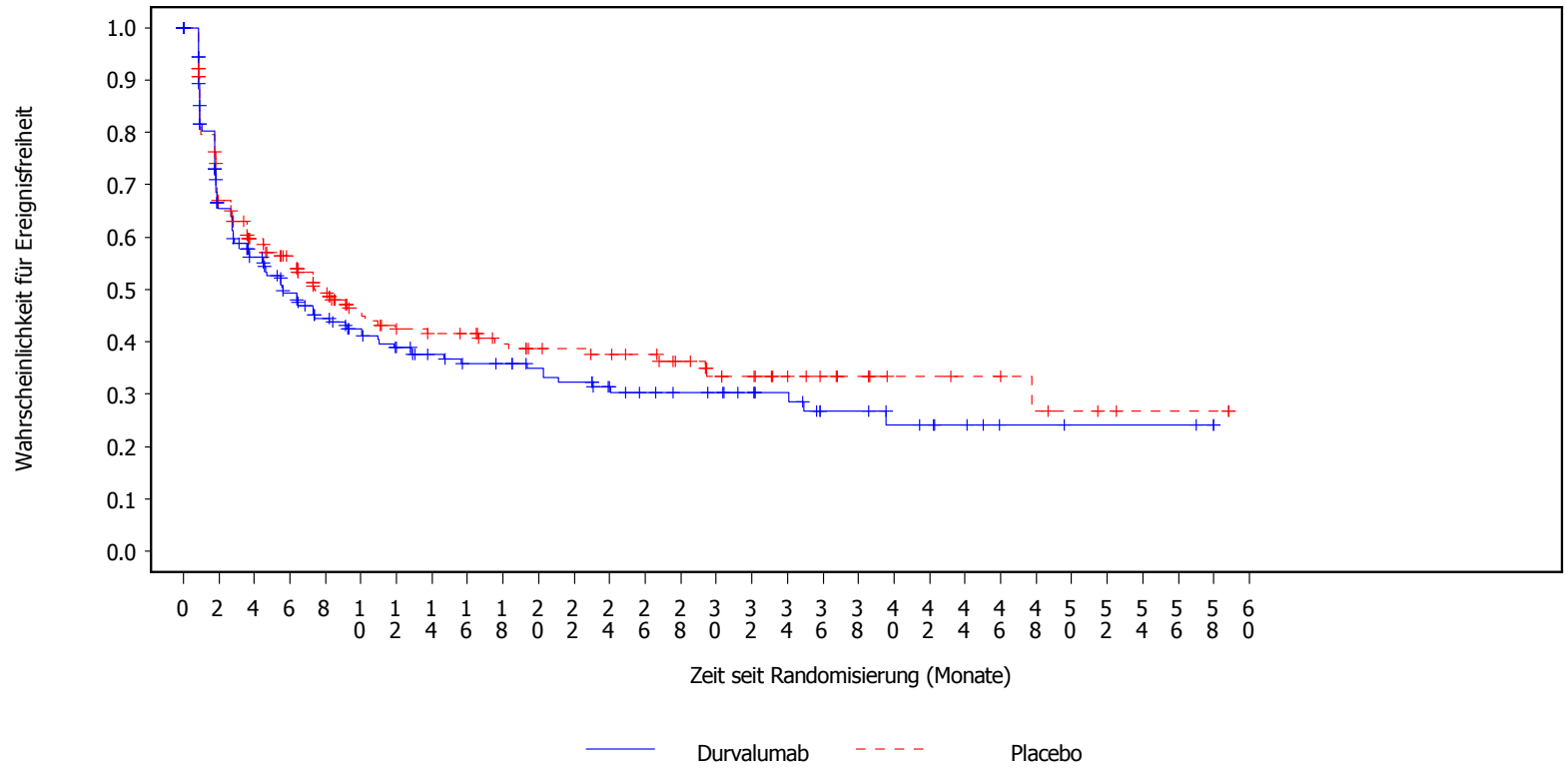
Figure 3.5.1.11 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	127	102	84	70	62	54	48	44	43	39	36	30	27	25	24	21	18	12	12	9	8	6	3	3	2	2	2	2	0	0	Durvalumab
266	131	107	93	73	58	51	48	47	41	37	36	34	32	27	22	20	16	13	11	7	7	6	5	4	3	2	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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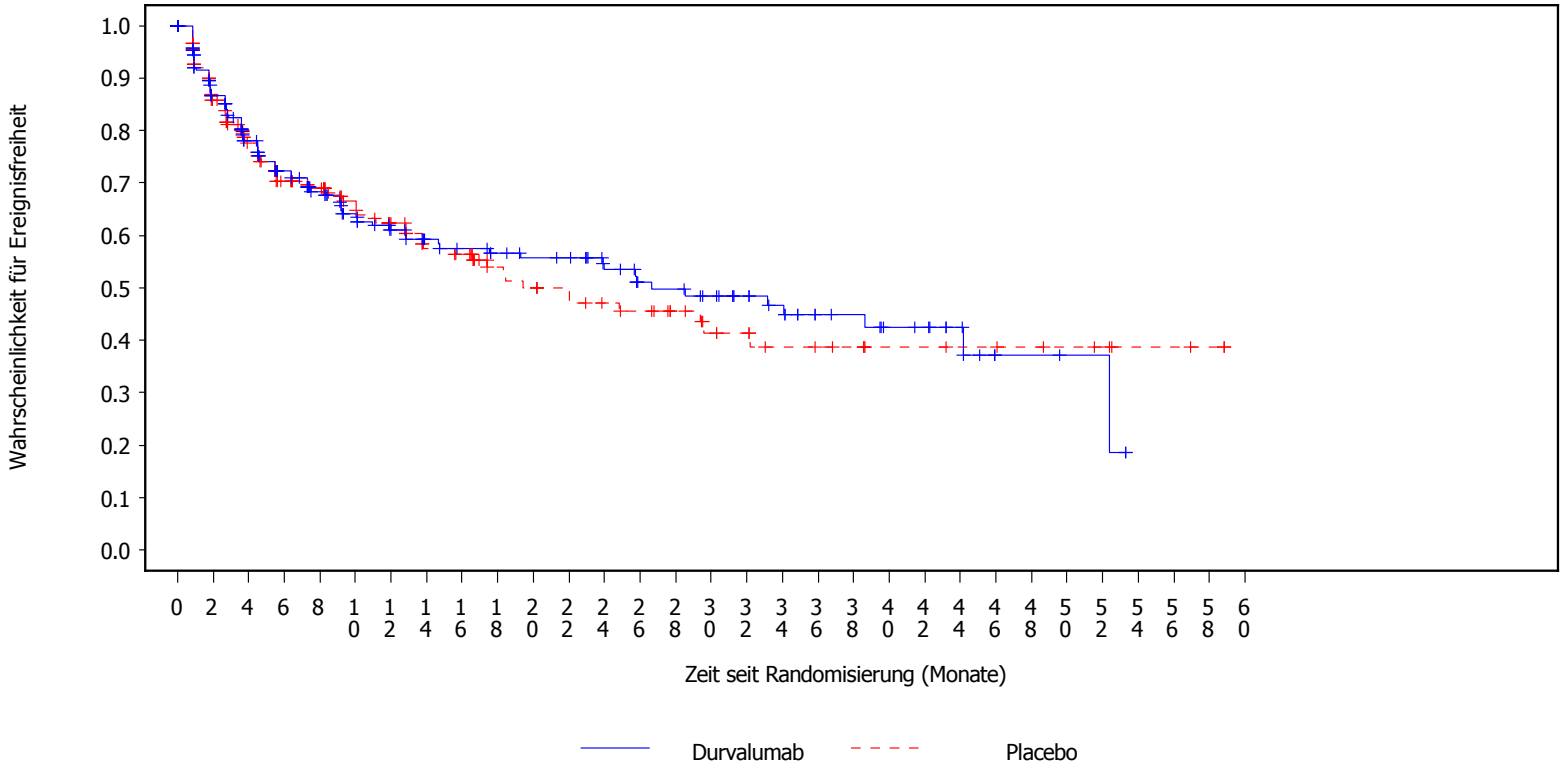
Figure 3.5.1.12 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	168	138	117	99	86	74	67	63	59	56	55	47	40	39	35	30	26	19	18	14	13	9	3	3	2	2	0	0	0	0	Durvalumab
266	163	131	108	96	80	68	56	53	41	38	35	31	29	24	19	17	13	12	11	8	8	7	7	6	5	4	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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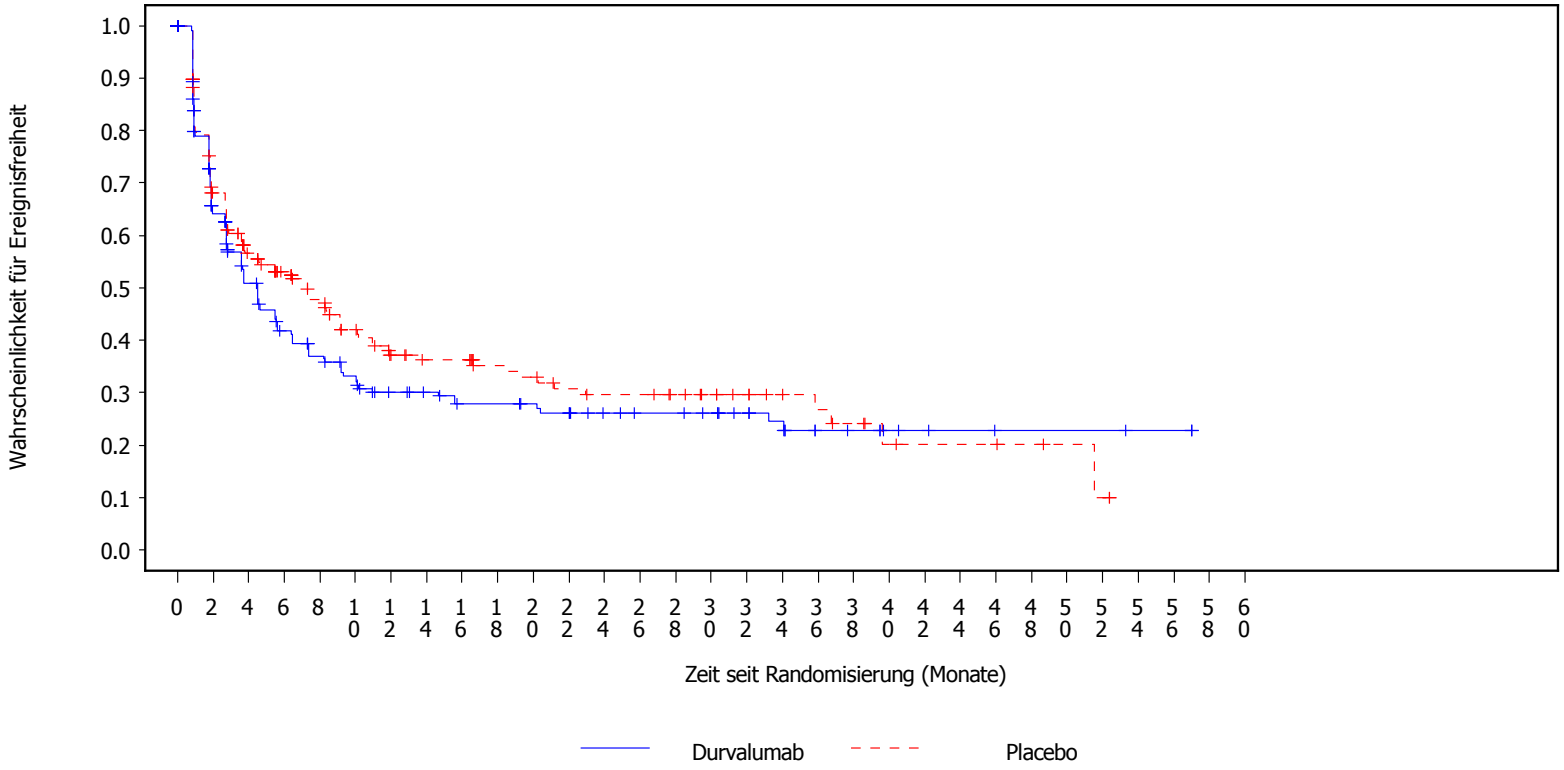
Figure 3.5.1.13 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	126	92	72	61	53	43	40	35	35	33	31	26	24	24	22	18	15	9	8	5	4	3	2	2	2	2	1	1	0	0	Durvalumab
266	132	101	84	69	55	44	39	39	32	30	26	24	24	21	18	15	12	10	8	5	4	4	4	3	2	1	0	0	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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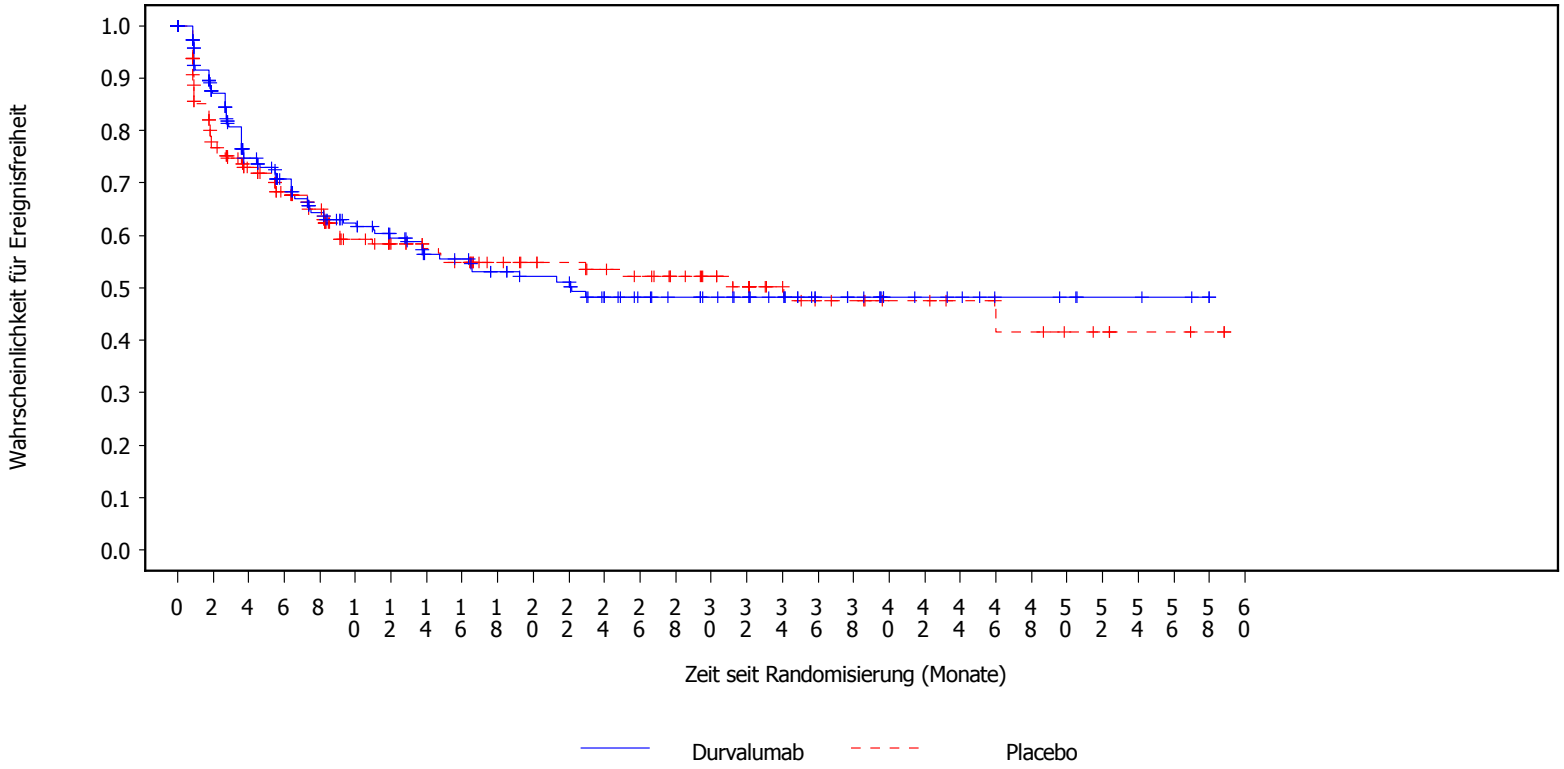
Figure 3.5.1.14 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	169	133	115	99	89	79	69	67	60	56	55	44	40	37	34	31	27	19	17	11	10	9	6	6	5	3	3	2	0	0	Durvalumab
266	146	128	112	97	74	68	62	58	50	47	45	42	39	34	30	25	19	15	14	11	11	9	8	7	5	4	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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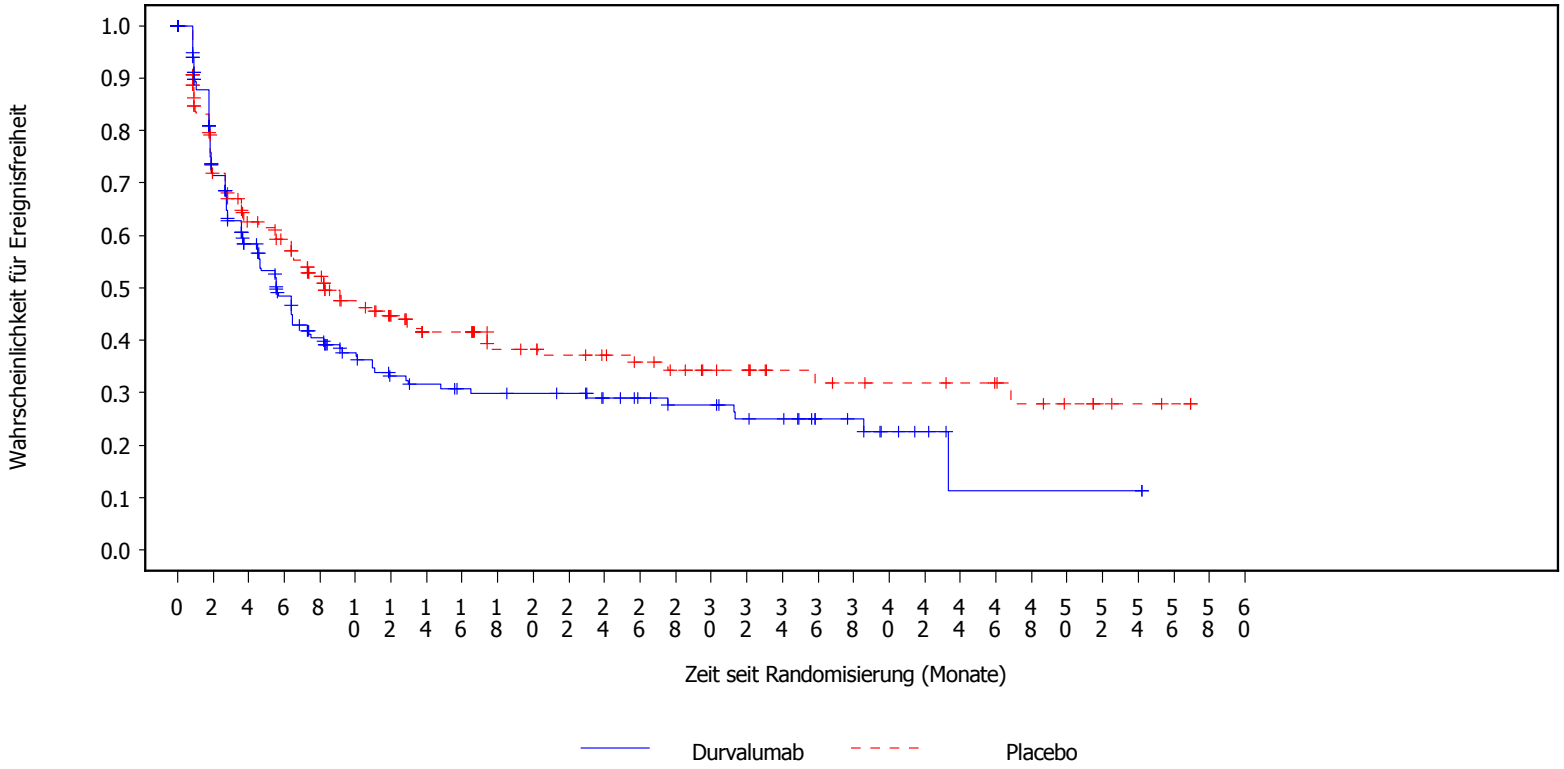
Figure 3.5.1.15 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	141	104	80	62	51	42	39	36	35	34	33	28	25	22	22	18	17	11	10	6	4	1	1	1	1	1	0	0	0	Durvalumab
266	136	113	103	84	68	58	46	46	35	34	31	29	26	23	20	19	14	13	12	11	11	10	9	7	5	3	2	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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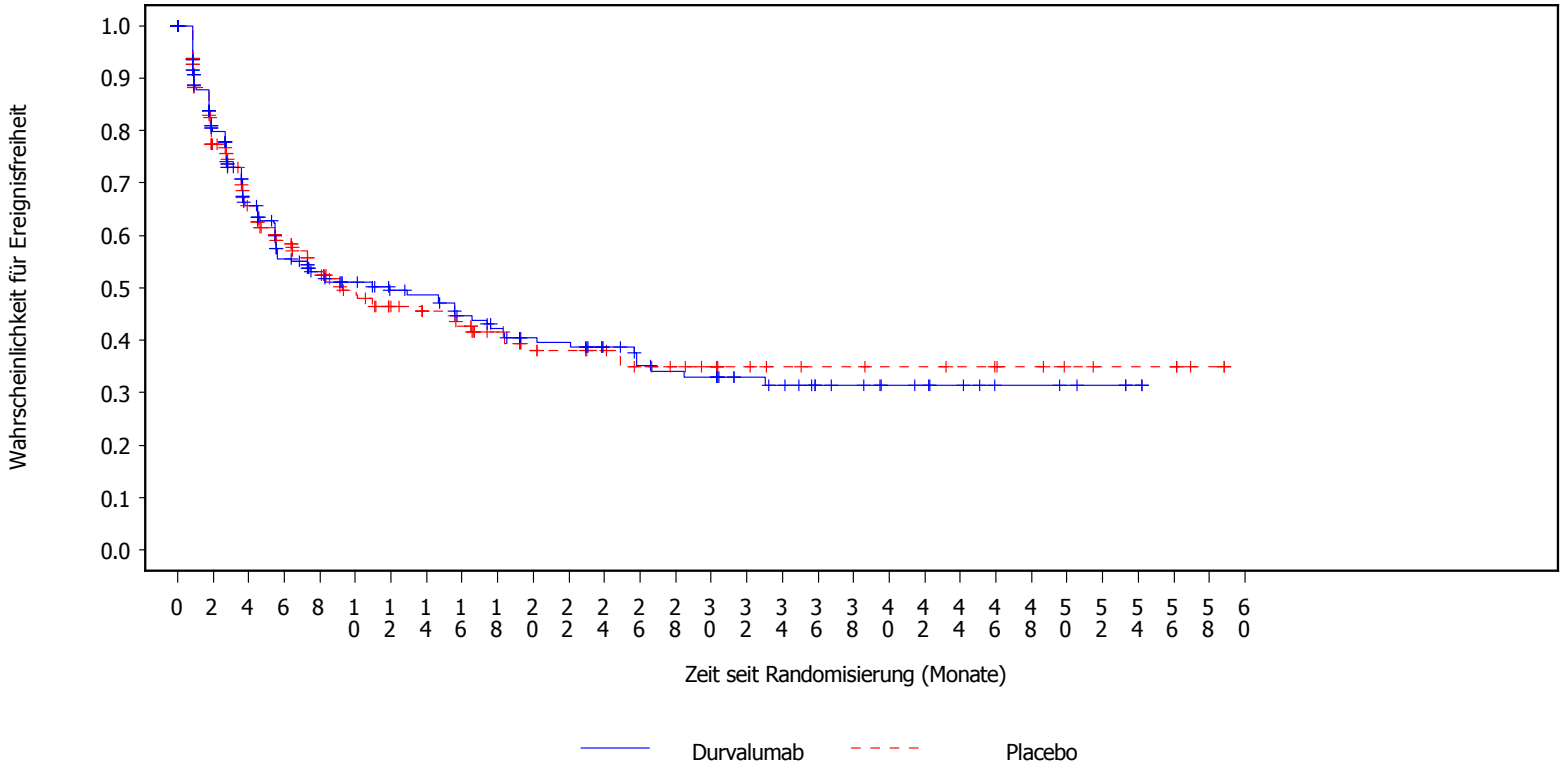
Figure 3.5.1.16 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	155	115	90	78	71	64	62	54	49	44	43	36	31	29	28	22	20	15	14	11	10	8	5	5	4	3	1	0	0	0	Durvalumab
266	145	113	94	78	65	55	49	44	37	30	28	26	22	20	18	14	12	11	11	10	10	9	8	7	5	4	4	4	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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Anhang 4-G6.2.2: EORTC QLQ-C30 - Subgruppenanalysen

Nutzenbewertung nach AMNOG

Table 3.6.1.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	19 (52,8)	1,8 [0,9; 3,6]	37	18 (48,6)	2,8 [0,9;12,1]	1,37	[0,71; 2,62]	0,3448
Stadium III	228	124 (54,4)	3,6 [2,7; 5,6]	229	112 (48,9)	4,5 [2,7; 8,2]	1,06	[0,82; 1,37]	0,6564
Interaktions p-Wert									0,4743
TNM Status (eCRF) - DEU									
Stadium I/II	33	18 (54,5)	1,8 [0,9; 3,6]	34	15 (44,1)	5,5 [1,0; NE]	1,56	[0,78; 3,14]	0,2043
Stadium III	231	125 (54,1)	3,6 [2,7; 5,5]	232	115 (49,6)	4,5 [2,7; 8,2]	1,04	[0,81; 1,34]	0,7479
Interaktions p-Wert									0,2804
Erhalt einer PCI (IVRS) - DEU									
Ja	142	81 (57,0)	2,8 [1,8; 4,5]	144	65 (45,1)	2,8 [1,8;16,6]	1,12	[0,81; 1,55]	0,5121
Nein	122	62 (50,8)	3,6 [2,7; 8,2]	122	65 (53,3)	6,4 [2,7; 9,1]	1,06	[0,74; 1,50]	0,7618
Interaktions p-Wert									0,8209
Erhalt einer PCI (eCRF) - DEU									
Ja	142	81 (57,0)	2,8 [1,8; 4,5]	143	65 (45,5)	2,8 [1,8;16,6]	1,12	[0,81; 1,55]	0,5121
Nein	122	62 (50,8)	3,6 [2,7; 8,2]	123	65 (52,8)	6,4 [2,7; 9,1]	1,06	[0,74; 1,50]	0,7618
Interaktions p-Wert									0,8209
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	20 (62,5)	2,7 [1,0;10,2]	32	14 (43,8)	8,3 [2,8; NE]	1,87	[0,95; 3,79]	0,0694
>=14 bis <28 Tage	79	36 (45,6)	9,1 [3,6;23,0]	80	40 (50,0)	6,4 [2,8;11,9]	0,87	[0,55; 1,37]	0,5524
>=28 Tage	153	87 (56,9)	2,8 [1,9; 3,6]	154	76 (49,4)	2,7 [1,8; 6,4]	1,07	[0,79; 1,46]	0,6479
Interaktions p-Wert									0,1828

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	12 (75,0)	1,8 [0,9; 3,6]	24	10 (41,7)	NE [NE; NE]	3,31	[1,43; 7,86]	0,0058*
>=28 bis <56 Tage	104	52 (50,0)	2,8 [1,9;10,1]	104	49 (47,1)	1,9 [1,8; 8,3]	0,87	[0,59; 1,29]	0,4817
>=56 bis <84 Tage	98	52 (53,1)	3,7 [1,9;11,1]	76	34 (44,7)	4,6 [2,7;36,9]	1,14	[0,74; 1,77]	0,5482
>=84 Tage	46	27 (58,7)	3,6 [1,0; 8,2]	62	37 (59,7)	2,8 [1,0;11,0]	1,07	[0,65; 1,76]	0,7826
Interaktions p-Wert									0,0477*
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	48 (52,7)	2,8 [1,9; 4,6]	88	48 (54,5)	2,8 [1,8; 8,2]	0,93	[0,63; 1,40]	0,7401
Cisplatin	173	95 (54,9)	3,6 [1,9; 6,4]	178	82 (46,1)	6,4 [2,7;12,1]	1,18	[0,88; 1,59]	0,2678
Interaktions p-Wert									0,3559
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	104 (53,3)	3,6 [2,7; 5,6]	187	82 (43,9)	5,5 [2,7;11,0]	1,17	[0,88; 1,57]	0,2825
Zweimal täglich	69	39 (56,5)	2,8 [1,8; 5,5]	79	48 (60,8)	3,7 [1,8; 9,1]	0,94	[0,62; 1,44]	0,7890
Interaktions p-Wert									0,4077
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	5,5 [0,9; NE]	34	16 (47,1)	1,9 [1,0; 2,8]	0,70	[0,33; 1,45]	0,3368
PR	191	107 (56,0)	2,8 [1,9; 3,6]	200	97 (48,5)	6,4 [2,8;11,0]	1,21	[0,92; 1,59]	0,1749
SD	42	23 (54,8)	9,1 [2,7;16,7]	32	17 (53,1)	1,8 [1,0; 9,1]	0,84	[0,45; 1,59]	0,5848
Interaktions p-Wert									0,2699
Geschlecht - DEU									
Männer	178	102 (57,3)	3,6 [2,8; 6,4]	188	92 (48,9)	6,4 [2,8;11,0]	1,18	[0,89; 1,57]	0,2405
Frauen	86	41 (47,7)	2,0 [1,8; 3,6]	78	38 (48,7)	1,8 [0,9; 2,9]	0,83	[0,53; 1,29]	0,4021

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,1816
Altersgruppe - DEU									
<65 Jahre	160	82 (51,3)	3,6 [2,0;10,1]	162	78 (48,1)	3,7 [1,8;11,9]	0,98	[0,72; 1,33]	0,8768
>=65 Jahre	104	61 (58,7)	2,8 [1,9; 3,7]	104	52 (50,0)	4,6 [2,7; 9,1]	1,30	[0,90; 1,89]	0,1647
Interaktions p-Wert									0,2448
PD-L1-Status - DEU									
TC and IC <1%	78	43 (55,1)	1,9 [1,8; 8,2]	73	39 (53,4)	2,8 [1,9;11,0]	1,16	[0,75; 1,80]	0,4988
TC or IC >=1%	84	57 (67,9)	2,8 [1,8; 3,6]	98	43 (43,9)	8,3 [2,8;37,7]	1,51	[1,02; 2,25]	0,0409*
Interaktions p-Wert									0,3830
Raucherstatus - DEU									
Raucher	241	126 (52,3)	3,6 [2,7; 5,5]	240	118 (49,2)	3,7 [1,9; 8,2]	1,03	[0,80; 1,33]	0,8088
Nichtraucher	23	17 (73,9)	2,7 [1,0; 4,5]	26	12 (46,2)	6,5 [0,9; NE]	1,85	[0,89; 3,96]	0,1014
Interaktions p-Wert									0,1414
Abstammung - DEU									
Weiß	130	64 (49,2)	2,8 [1,9; 3,6]	137	67 (48,9)	2,7 [1,8; 6,4]	0,93	[0,66; 1,31]	0,6773
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	2,3 [1,8; NE]	NC	[NC]	NC
Asiatisch	131	79 (60,3)	3,6 [1,9; 6,4]	121	61 (50,4)	8,3 [2,8;25,7]	1,26	[0,91; 1,77]	0,1686
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2086
Geographische Region - DEU									
Asien	129	79 (61,2)	3,6 [1,9; 6,4]	120	60 (50,0)	9,1 [2,9;25,7]	1,28	[0,92; 1,80]	0,1432
Europa	94	55 (58,5)	2,7 [1,8; 3,6]	112	59 (52,7)	1,9 [1,8; 6,4]	0,98	[0,68; 1,42]	0,9255

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	9 (22,0)	4,6 [1,0; NE]	34	11 (32,4)	2,8 [1,8; NE]	0,72	[0,29; 1,73]	0,4590
Interaktions p-Wert									0,3518
ECOG-Status zu Baseline - DEU									
0	133	71 (53,4)	3,6 [1,8; 4,6]	131	65 (49,6)	4,5 [1,9; 9,1]	1,17	[0,84; 1,64]	0,3610
1	131	72 (55,0)	3,6 [2,7; 8,2]	135	65 (48,1)	3,7 [1,8;11,0]	1,02	[0,73; 1,43]	0,9211
Interaktions p-Wert									0,5641

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	13 (36,1)	11,9 [2,7; NE]	37	17 (45,9)	6,4 [1,0;45,1]	0,72	[0,34; 1,48]	0,3748
Stadium III	228	112 (49,1)	8,2 [5,5;11,9]	229	107 (46,7)	7,3 [3,7;11,0]	0,96	[0,74; 1,25]	0,7581
Interaktions p-Wert									0,4680
TNM Status (eCRF) - DEU									
Stadium I/II	33	11 (33,3)	11,9 [2,8; NE]	34	16 (47,1)	1,8 [1,0;45,1]	0,58	[0,26; 1,25]	0,1669
Stadium III	231	114 (49,4)	8,2 [5,5;11,1]	232	108 (46,6)	7,3 [3,7;11,0]	0,98	[0,75; 1,28]	0,8880
Interaktions p-Wert									0,2079
Erhalt einer PCI (IVRS) - DEU									
Ja	142	72 (50,7)	5,5 [3,6;11,0]	144	65 (45,1)	3,6 [1,9; 9,2]	0,90	[0,64; 1,26]	0,5486
Nein	122	53 (43,4)	9,2 [5,5;14,8]	122	59 (48,4)	10,1 [6,4;11,9]	0,93	[0,64; 1,35]	0,7057
Interaktions p-Wert									0,9021
Erhalt einer PCI (eCRF) - DEU									
Ja	142	72 (50,7)	5,5 [3,6;11,0]	143	65 (45,5)	3,6 [1,9; 9,2]	0,90	[0,64; 1,26]	0,5486
Nein	122	53 (43,4)	9,2 [5,5;14,8]	123	59 (48,0)	10,1 [6,4;11,9]	0,93	[0,64; 1,35]	0,7057
Interaktions p-Wert									0,9021
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	16 (50,0)	12,0 [3,7;31,3]	32	15 (46,9)	9,1 [4,6;22,2]	0,94	[0,46; 1,91]	0,8523
>=14 bis <28 Tage	79	35 (44,3)	9,2 [4,5;20,2]	80	37 (46,3)	7,3 [2,8;11,9]	0,91	[0,57; 1,44]	0,6723
>=28 Tage	153	74 (48,4)	5,6 [3,7;11,0]	154	72 (46,8)	6,4 [2,7;11,9]	0,94	[0,68; 1,30]	0,6910
Interaktions p-Wert									0,9928

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	9 (56,3)	5,5 [1,8; NE]	24	11 (45,8)	11,9 [2,8; NE]	1,26	[0,51; 3,04]	0,6109
>=28 bis <56 Tage	104	45 (43,3)	11,0 [5,5;16,7]	104	44 (42,3)	6,4 [2,7;11,9]	0,83	[0,55; 1,26]	0,3734
>=56 bis <84 Tage	98	49 (50,0)	7,3 [2,8;11,9]	76	37 (48,7)	5,5 [1,9;10,1]	0,92	[0,60; 1,42]	0,6943
>=84 Tage	46	22 (47,8)	4,6 [1,8; NE]	62	32 (51,6)	9,2 [2,8;15,7]	0,96	[0,55; 1,64]	0,8716
Interaktions p-Wert									0,8630
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	7,3 [3,7;12,8]	88	37 (42,0)	8,3 [4,6;28,5]	1,15	[0,75; 1,79]	0,5218
Cisplatin	173	81 (46,8)	8,2 [4,6;11,9]	178	87 (48,9)	5,5 [2,8;10,1]	0,83	[0,61; 1,13]	0,2377
Interaktions p-Wert									0,2302
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	88 (45,1)	9,1 [5,5;12,0]	187	80 (42,8)	7,4 [3,8;11,9]	0,94	[0,69; 1,27]	0,6876
Zweimal täglich	69	37 (53,6)	3,7 [2,0;10,2]	79	44 (55,7)	4,6 [2,7;11,0]	0,93	[0,60; 1,43]	0,7342
Interaktions p-Wert									0,9604
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	5,5 [1,9; NE]	34	12 (35,3)	3,6 [1,8; NE]	0,94	[0,42; 2,08]	0,8676
PR	191	95 (49,7)	5,6 [4,5;11,1]	200	99 (49,5)	7,3 [3,6;11,0]	0,95	[0,72; 1,26]	0,7146
SD	42	17 (40,5)	16,7 [8,3;31,3]	32	13 (40,6)	8,3 [1,9; NE]	0,87	[0,42; 1,82]	0,7026
Interaktions p-Wert									0,9752
Geschlecht - DEU									
Männer	178	88 (49,4)	8,3 [5,5;13,7]	188	89 (47,3)	9,1 [5,5;11,9]	0,93	[0,69; 1,25]	0,6364
Frauen	86	37 (43,0)	5,5 [1,8;12,0]	78	35 (44,9)	2,8 [1,8; 6,4]	0,90	[0,56; 1,43]	0,6457

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,8937
Altersgruppe - DEU									
<65 Jahre	160	78 (48,8)	8,2 [5,5;12,0]	162	82 (50,6)	4,6 [2,7; 7,4]	0,78	[0,57; 1,06]	0,1165
>=65 Jahre	104	47 (45,2)	5,6 [3,7;20,2]	104	42 (40,4)	11,0 [4,6;28,5]	1,23	[0,81; 1,87]	0,3291
Interaktions p-Wert									0,0852
PD-L1-Status - DEU									
TC and IC <1%	78	36 (46,2)	11,1 [3,7;33,2]	73	36 (49,3)	6,4 [2,8;11,9]	0,80	[0,50; 1,27]	0,3421
TC or IC >=1%	84	48 (57,1)	5,6 [3,7;11,0]	98	45 (45,9)	11,9 [5,5;22,2]	1,20	[0,80; 1,81]	0,3721
Interaktions p-Wert									0,1929
Raucherstatus - DEU									
Raucher	241	115 (47,7)	8,2 [4,6;11,9]	240	114 (47,5)	7,3 [3,7;10,2]	0,93	[0,72; 1,21]	0,5839
Nichtraucher	23	10 (43,5)	6,5 [1,9; NE]	26	10 (38,5)	3,6 [1,8; NE]	0,90	[0,37; 2,19]	0,8126
Interaktions p-Wert									0,9425
Abstammung - DEU									
Weiß	130	57 (43,8)	5,6 [2,8;11,9]	137	60 (43,8)	5,5 [2,7;11,9]	1,00	[0,70; 1,44]	0,9948
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	68 (51,9)	9,1 [5,5;28,5]	121	63 (52,1)	8,3 [3,6;12,0]	0,88	[0,63; 1,25]	0,4830
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,6266
Geographische Region - DEU									
Asien	129	68 (52,7)	9,1 [5,5;28,5]	120	62 (51,7)	8,3 [3,6;12,0]	0,90	[0,64; 1,27]	0,5558
Europa	94	45 (47,9)	5,6 [2,8;11,9]	112	55 (49,1)	5,5 [2,7;11,0]	0,92	[0,62; 1,36]	0,6693

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Emotionale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	12 (29,3)	2,9 [1,8;16,7]	34	7 (20,6)	NE [NE; NE]	1,53	[0,61; 4,10]	0,3678
Interaktions p-Wert									0,5657
ECOG-Status zu Baseline - DEU									
0	133	62 (46,6)	5,6 [4,5;12,0]	131	63 (48,1)	6,4 [3,6;21,1]	0,96	[0,68; 1,37]	0,8410
1	131	63 (48,1)	8,2 [4,6;12,8]	135	61 (45,2)	7,4 [3,6;11,0]	0,89	[0,62; 1,27]	0,5117
Interaktions p-Wert									0,7462

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	17 (47,2)	6,4 [1,8;14,7]	37	19 (51,4)	4,7 [1,0;18,3]	0,93	[0,48; 1,80]	0,8401
Stadium III	228	123 (53,9)	4,6 [3,6; 6,4]	229	117 (51,1)	5,5 [3,7; 8,2]	0,98	[0,76; 1,26]	0,8608
Interaktions p-Wert									0,9006
TNM Status (eCRF) - DEU									
Stadium I/II	33	16 (48,5)	6,4 [1,8;14,7]	34	17 (50,0)	4,7 [1,0;10,1]	0,86	[0,43; 1,71]	0,6656
Stadium III	231	124 (53,7)	4,6 [3,6; 6,4]	232	119 (51,3)	5,5 [3,7; 8,2]	0,99	[0,77; 1,27]	0,9299
Interaktions p-Wert									0,7076
Erhalt einer PCI (IVRS) - DEU									
Ja	142	83 (58,5)	2,8 [1,9; 4,7]	144	71 (49,3)	4,6 [3,6; 9,1]	1,06	[0,77; 1,46]	0,7280
Nein	122	57 (46,7)	6,4 [5,5; 9,1]	122	65 (53,3)	6,4 [2,8;11,0]	0,87	[0,61; 1,24]	0,4317
Interaktions p-Wert									0,4132
Erhalt einer PCI (eCRF) - DEU									
Ja	142	83 (58,5)	2,8 [1,9; 4,7]	143	71 (49,7)	4,6 [3,6; 9,1]	1,06	[0,77; 1,46]	0,7280
Nein	122	57 (46,7)	6,4 [5,5; 9,1]	123	65 (52,8)	6,4 [2,8;11,0]	0,87	[0,61; 1,24]	0,4317
Interaktions p-Wert									0,4132
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	16 (50,0)	5,5 [2,7;34,1]	32	17 (53,1)	7,3 [1,8;23,1]	0,86	[0,43; 1,71]	0,6627
>=14 bis <28 Tage	79	38 (48,1)	7,4 [2,9;14,7]	80	38 (47,5)	8,1 [4,5;11,0]	0,95	[0,61; 1,50]	0,8326
>=28 Tage	153	86 (56,2)	3,7 [2,8; 5,5]	154	81 (52,6)	3,7 [2,7; 7,4]	1,01	[0,74; 1,37]	0,9654
Interaktions p-Wert									0,9118

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	10 (62,5)	4,5 [0,9;34,1]	24	12 (50,0)	5,5 [1,8;23,1]	1,07	[0,45; 2,49]	0,8733
>=28 bis <56 Tage	104	50 (48,1)	6,4 [4,5;12,9]	104	50 (48,1)	4,5 [1,9; 8,3]	0,85	[0,57; 1,26]	0,4246
>=56 bis <84 Tage	98	51 (52,0)	5,5 [2,8; 8,2]	76	38 (50,0)	7,3 [3,7;10,1]	0,97	[0,64; 1,48]	0,8760
>=84 Tage	46	29 (63,0)	3,6 [1,8; 4,6]	62	36 (58,1)	3,7 [1,8; 9,1]	1,29	[0,78; 2,09]	0,3183
Interaktions p-Wert									0,6405
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	49 (53,8)	5,5 [3,6; 8,2]	88	44 (50,0)	7,4 [4,5;10,1]	1,10	[0,73; 1,65]	0,6590
Cisplatin	173	91 (52,6)	4,5 [2,8; 6,6]	178	92 (51,7)	4,5 [2,8; 7,4]	0,91	[0,68; 1,22]	0,5425
Interaktions p-Wert									0,4757
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	97 (49,7)	5,5 [3,7; 7,5]	187	87 (46,5)	7,3 [3,7;10,1]	0,97	[0,73; 1,30]	0,8589
Zweimal täglich	69	43 (62,3)	3,7 [1,8; 7,4]	79	49 (62,0)	3,7 [1,9; 8,2]	1,00	[0,66; 1,50]	0,9955
Interaktions p-Wert									0,9219
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	5,5 [1,8; NE]	34	13 (38,2)	1,9 [1,0; 9,1]	0,62	[0,29; 1,36]	0,2288
PR	191	108 (56,5)	4,7 [3,6; 6,4]	200	106 (53,0)	5,5 [3,7; 8,2]	1,07	[0,82; 1,40]	0,6280
SD	42	19 (45,2)	5,6 [1,9; NE]	32	17 (53,1)	9,1 [1,9;11,0]	0,77	[0,40; 1,50]	0,4392
Interaktions p-Wert									0,3276
Geschlecht - DEU									
Männer	178	97 (54,5)	5,5 [3,6; 7,5]	188	97 (51,6)	7,3 [4,7; 9,1]	1,02	[0,77; 1,36]	0,8784
Frauen	86	43 (50,0)	4,5 [1,8; 7,4]	78	39 (50,0)	1,8 [0,9; 3,7]	0,77	[0,50; 1,19]	0,2377

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,2824
Altersgruppe - DEU									
<65 Jahre	160	81 (50,6)	5,5 [4,5;11,9]	162	84 (51,9)	4,6 [2,8; 7,4]	0,80	[0,59; 1,08]	0,1423
>=65 Jahre	104	59 (56,7)	3,7 [2,8; 5,6]	104	52 (50,0)	5,5 [3,7;11,0]	1,35	[0,93; 1,97]	0,1153
Interaktions p-Wert									0,0319*
PD-L1-Status - DEU									
TC and IC <1%	78	43 (55,1)	4,5 [2,7; 8,2]	73	45 (61,6)	2,8 [1,9; 5,5]	0,74	[0,49; 1,13]	0,1620
TC or IC >=1%	84	51 (60,7)	5,5 [2,8; 8,3]	98	45 (45,9)	9,1 [3,7;13,8]	1,22	[0,82; 1,82]	0,3359
Interaktions p-Wert									0,0934
Raucherstatus - DEU									
Raucher	241	125 (51,9)	5,5 [3,7; 7,4]	240	123 (51,3)	5,5 [3,7; 8,2]	0,95	[0,74; 1,22]	0,6890
Nichtraucher	23	15 (65,2)	3,6 [0,9; 5,5]	26	13 (50,0)	4,6 [1,8;15,6]	1,23	[0,59; 2,63]	0,5804
Interaktions p-Wert									0,5146
Abstammung - DEU									
Weiß	130	59 (45,4)	5,5 [2,8; 9,2]	137	63 (46,0)	5,5 [3,6; 9,1]	0,92	[0,65; 1,32]	0,6585
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	1,9 [1,1; NE]	NC	[NC]	NC
Asiatisch	131	81 (61,8)	4,7 [2,9; 7,4]	121	70 (57,9)	5,6 [3,6; 9,1]	1,04	[0,76; 1,44]	0,8090
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,6240
Geographische Region - DEU									
Asien	129	81 (62,8)	4,7 [2,9; 7,4]	120	69 (57,5)	6,5 [3,7; 9,1]	1,06	[0,77; 1,46]	0,7314
Europa	94	49 (52,1)	5,5 [2,8; 8,2]	112	56 (50,0)	4,6 [2,7; 9,1]	0,90	[0,61; 1,32]	0,5894

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	10 (24,4)	1,8 [1,0; NE]	34	11 (32,4)	8,1 [1,1;11,0]	0,81	[0,34; 1,93]	0,6363
Interaktions p-Wert									0,7451
ECOG-Status zu Baseline - DEU									
0	133	70 (52,6)	4,5 [2,8; 7,4]	131	68 (51,9)	5,5 [2,8; 8,4]	1,00	[0,72; 1,40]	0,9793
1	131	70 (53,4)	5,5 [2,8; 7,5]	135	68 (50,4)	5,6 [3,6; 9,1]	0,94	[0,67; 1,31]	0,7191
Interaktions p-Wert									0,7850

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	12 (33,3)	12,9 [4,6; NE]	37	17 (45,9)	8,2 [2,7;23,0]	0,69	[0,32; 1,43]	0,3141
Stadium III	228	122 (53,5)	4,6 [2,8; 5,6]	229	106 (46,3)	8,3 [5,5;11,1]	1,24	[0,95; 1,61]	0,1079
Interaktions p-Wert									0,1367
TNM Status (eCRF) - DEU									
Stadium I/II	33	11 (33,3)	12,9 [4,6; NE]	34	16 (47,1)	8,2 [2,7;23,0]	0,61	[0,27; 1,29]	0,1966
Stadium III	231	123 (53,2)	4,6 [2,8; 5,6]	232	107 (46,1)	8,3 [5,5;11,1]	1,25	[0,97; 1,63]	0,0864
Interaktions p-Wert									0,0755
Erhalt einer PCI (IVRS) - DEU									
Ja	142	75 (52,8)	4,6 [2,8;10,1]	144	64 (44,4)	8,2 [2,8;15,6]	1,04	[0,74; 1,45]	0,8298
Nein	122	59 (48,4)	5,5 [2,8; 8,2]	122	59 (48,4)	8,3 [5,5;16,6]	1,29	[0,90; 1,86]	0,1643
Interaktions p-Wert									0,3804
Erhalt einer PCI (eCRF) - DEU									
Ja	142	75 (52,8)	4,6 [2,8;10,1]	143	64 (44,8)	8,2 [2,8;15,6]	1,04	[0,74; 1,45]	0,8298
Nein	122	59 (48,4)	5,5 [2,8; 8,2]	123	59 (48,0)	8,3 [5,5;16,6]	1,29	[0,90; 1,86]	0,1643
Interaktions p-Wert									0,3804
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	19 (59,4)	3,7 [1,8;18,4]	32	16 (50,0)	6,5 [2,7; NE]	1,41	[0,72; 2,77]	0,3134
>=14 bis <28 Tage	79	40 (50,6)	5,7 [2,8;10,2]	80	37 (46,3)	9,1 [5,5;16,6]	1,22	[0,78; 1,91]	0,3875
>=28 Tage	153	75 (49,0)	4,6 [2,8; 9,2]	154	70 (45,5)	8,2 [3,6;15,6]	1,07	[0,77; 1,48]	0,6835
Interaktions p-Wert									0,7394
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	9 (56,3)	5,5 [1,8; NE]	24	11 (45,8)	10,1 [1,8; NE]	1,08	[0,43; 2,61]	0,8671
>=28 bis <56 Tage	104	44 (42,3)	7,4 [4,5;16,5]	104	46 (44,2)	5,5 [3,6;11,9]	0,91	[0,60; 1,38]	0,6518
>=56 bis <84 Tage	98	54 (55,1)	4,6 [1,9; 9,2]	76	37 (48,7)	8,2 [3,7;11,0]	1,21	[0,80; 1,85]	0,3729
>=84 Tage	46	27 (58,7)	2,7 [1,8; 5,5]	62	29 (46,8)	11,1 [3,6;24,9]	1,61	[0,95; 2,72]	0,0780
Interaktions p-Wert									0,4118
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	47 (51,6)	4,6 [2,8;10,1]	88	45 (51,1)	5,5 [2,7; 8,3]	1,00	[0,66; 1,50]	0,9849
Cisplatin	173	87 (50,3)	5,5 [2,8; 9,2]	178	78 (43,8)	10,1 [6,5;22,1]	1,24	[0,91; 1,69]	0,1676
Interaktions p-Wert									0,4006
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	94 (48,2)	5,6 [3,7;10,1]	187	87 (46,5)	7,3 [3,8; 9,2]	0,99	[0,74; 1,33]	0,9525
Zweimal täglich	69	40 (58,0)	3,6 [1,8; 5,6]	79	36 (45,6)	15,6 [5,5;37,7]	1,61	[1,02; 2,53]	0,0389*
Interaktions p-Wert									0,0772
Bestes Ansprechen auf cCRT - DEU									
CR	31	14 (45,2)	5,5 [1,8; NE]	34	11 (32,4)	9,2 [1,0; NE]	1,05	[0,48; 2,37]	0,8977
PR	191	99 (51,8)	4,6 [2,8; 6,4]	200	100 (50,0)	8,2 [5,5;11,0]	1,13	[0,86; 1,50]	0,3813
SD	42	21 (50,0)	7,4 [1,8;18,3]	32	12 (37,5)	10,1 [1,8; NE]	1,46	[0,73; 3,07]	0,2867
Interaktions p-Wert									0,7774
Geschlecht - DEU									
Männer	178	100 (56,2)	5,5 [3,6; 8,2]	188	90 (47,9)	8,3 [5,5;14,7]	1,24	[0,93; 1,65]	0,1438
Frauen	86	34 (39,5)	5,5 [1,9;18,3]	78	33 (42,3)	8,2 [1,8;15,6]	0,94	[0,58; 1,52]	0,7936
Interaktions p-Wert									0,3316
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	81 (50,6)	5,6 [3,7;10,1]	162	74 (45,7)	8,3 [5,5;16,6]	1,12	[0,82; 1,54]	0,4844
>=65 Jahre	104	53 (51,0)	4,5 [1,9; 6,4]	104	49 (47,1)	7,3 [3,6;11,0]	1,22	[0,82; 1,80]	0,3221
Interaktions p-Wert									0,7430
PD-L1-Status - DEU									
TC and IC <1%	78	42 (53,8)	5,5 [2,7;12,9]	73	38 (52,1)	8,2 [3,8;11,1]	1,11	[0,71; 1,72]	0,6497
TC or IC >=1%	84	47 (56,0)	4,6 [2,7;11,0]	98	45 (45,9)	11,0 [4,6;16,6]	1,22	[0,81; 1,85]	0,3335
Interaktions p-Wert									0,7434
Raucherstatus - DEU									
Raucher	241	121 (50,2)	5,5 [3,7; 8,2]	240	109 (45,4)	8,3 [5,5;11,9]	1,17	[0,90; 1,51]	0,2447
Nichtraucher	23	13 (56,5)	2,8 [0,9; NE]	26	14 (53,8)	4,6 [1,8;24,9]	1,07	[0,50; 2,28]	0,8646
Interaktions p-Wert									0,8289
Abstammung - DEU									
Weiß	130	51 (39,2)	9,2 [3,7;18,3]	137	60 (43,8)	5,5 [2,7;11,0]	0,88	[0,60; 1,27]	0,4879
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	83 (63,4)	4,5 [2,8; 5,5]	121	62 (51,2)	10,1 [5,5;16,5]	1,40	[1,01; 1,95]	0,0443*
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,0646
Geographische Region - DEU									
Asien	129	83 (64,3)	4,5 [2,8; 5,5]	120	61 (50,8)	10,1 [5,5;16,6]	1,43	[1,03; 1,99]	0,0340*
Europa	94	44 (46,8)	5,6 [1,9;18,3]	112	54 (48,2)	3,7 [2,7; 9,1]	0,90	[0,60; 1,33]	0,5846
Nordamerika	41	7 (17,1)	NE [NE; NE]	34	8 (23,5)	22,1 [1,8; NE]	0,86	[0,30; 2,39]	0,7693
Interaktions p-Wert									0,1743
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Körperfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	68 (51,1)	4,6 [2,8; 8,2]	131	57 (43,5)	8,3 [5,5;24,9]	1,36	[0,96; 1,94]	0,0849
1	131	66 (50,4)	5,5 [3,6;10,1]	135	66 (48,9)	8,2 [3,6;11,0]	0,98	[0,69; 1,38]	0,9005
Interaktions p-Wert									0,1860

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	16 (44,4)	2,8 [1,8; NE]	37	14 (37,8)	8,3 [1,8; NE]	1,21	[0,59; 2,52]	0,5999
Stadium III	228	122 (53,5)	5,5 [2,8; 7,4]	229	125 (54,6)	3,7 [2,7; 5,5]	0,81	[0,63; 1,04]	0,0971
Interaktions p-Wert									0,2978
TNM Status (eCRF) - DEU									
Stadium I/II	33	14 (42,4)	12,9 [1,9; NE]	34	12 (35,3)	8,3 [1,8; NE]	1,19	[0,55; 2,62]	0,6548
Stadium III	231	124 (53,7)	4,7 [2,8; 7,3]	232	127 (54,7)	3,7 [2,7; 5,5]	0,82	[0,64; 1,05]	0,1078
Interaktions p-Wert									0,3585
Erhalt einer PCI (IVRS) - DEU									
Ja	142	78 (54,9)	4,5 [2,7; 9,1]	144	69 (47,9)	2,8 [1,8; 5,5]	0,83	[0,60; 1,15]	0,2677
Nein	122	60 (49,2)	5,5 [3,6; 8,2]	122	70 (57,4)	5,5 [2,8; 8,3]	0,87	[0,61; 1,23]	0,4240
Interaktions p-Wert									0,8583
Erhalt einer PCI (eCRF) - DEU									
Ja	142	78 (54,9)	4,5 [2,7; 9,1]	143	69 (48,3)	2,8 [1,8; 5,5]	0,83	[0,60; 1,15]	0,2677
Nein	122	60 (49,2)	5,5 [3,6; 8,2]	123	70 (56,9)	5,5 [2,8; 8,3]	0,87	[0,61; 1,23]	0,4240
Interaktions p-Wert									0,8583
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	18 (56,3)	3,6 [1,8;34,1]	32	15 (46,9)	8,3 [2,8; NE]	1,25	[0,63; 2,52]	0,5217
>=14 bis <28 Tage	79	35 (44,3)	9,2 [4,5;12,9]	80	46 (57,5)	5,5 [2,8; 8,2]	0,65	[0,42; 1,004]	0,0522
>=28 Tage	153	85 (55,6)	2,9 [2,7; 6,5]	154	78 (50,6)	1,9 [1,8; 6,4]	0,90	[0,66; 1,22]	0,4808
Interaktions p-Wert									0,2463
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	10 (62,5)	3,6 [1,8; NE]	24	11 (45,8)	8,4 [3,6; NE]	1,35	[0,56; 3,20]	0,4962
>=28 bis <56 Tage	104	49 (47,1)	7,5 [2,8;11,0]	104	53 (51,0)	3,6 [1,8; 7,4]	0,71	[0,48; 1,05]	0,0842
>=56 bis <84 Tage	98	50 (51,0)	4,6 [2,8; 8,2]	76	38 (50,0)	4,5 [1,9; 8,2]	0,90	[0,59; 1,38]	0,6332
>=84 Tage	46	29 (63,0)	2,8 [1,8; 8,2]	62	37 (59,7)	1,8 [1,0; 6,5]	0,95	[0,58; 1,55]	0,8505
Interaktions p-Wert									0,5327
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	43 (47,3)	9,2 [3,6;12,9]	88	51 (58,0)	3,7 [2,7; 5,5]	0,65	[0,43; 0,97]	0,0372*
Cisplatin	173	95 (54,9)	3,6 [2,8; 5,5]	178	88 (49,4)	4,5 [1,8; 7,3]	0,99	[0,74; 1,32]	0,9192
Interaktions p-Wert									0,1023
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	96 (49,2)	5,5 [2,9; 8,2]	187	93 (49,7)	3,8 [2,7; 6,5]	0,82	[0,61; 1,09]	0,1635
Zweimal täglich	69	42 (60,9)	2,8 [1,8; 9,1]	79	46 (58,2)	4,6 [1,8; 7,3]	0,96	[0,63; 1,46]	0,8501
Interaktions p-Wert									0,5294
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	7,3 [1,8; NE]	34	15 (44,1)	1,8 [1,0; 6,4]	0,58	[0,27; 1,23]	0,1573
PR	191	104 (54,5)	3,6 [2,8; 6,5]	200	107 (53,5)	5,5 [2,8; 7,3]	0,96	[0,74; 1,26]	0,7925
SD	42	21 (50,0)	7,4 [2,8;12,8]	32	17 (53,1)	1,8 [1,0; 8,2]	0,53	[0,28; 1,03]	0,0594
Interaktions p-Wert									0,1507
Geschlecht - DEU									
Männer	178	100 (56,2)	5,5 [2,8; 9,1]	188	103 (54,8)	5,5 [2,8; 7,3]	0,88	[0,66; 1,15]	0,3432
Frauen	86	38 (44,2)	3,6 [1,8; 7,3]	78	36 (46,2)	1,9 [1,0; 5,5]	0,78	[0,49; 1,24]	0,2884
Interaktions p-Wert									0,6738
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	82 (51,3)	7,3 [4,5;10,2]	162	84 (51,9)	3,7 [1,9; 6,5]	0,80	[0,59; 1,09]	0,1536
>=65 Jahre	104	56 (53,8)	2,8 [1,9; 4,6]	104	55 (52,9)	5,5 [1,8; 6,4]	0,95	[0,66; 1,39]	0,8006
Interaktions p-Wert									0,4791
PD-L1-Status - DEU									
TC and IC <1%	78	47 (60,3)	6,6 [2,7;11,0]	73	41 (56,2)	3,7 [1,8; 8,2]	0,88	[0,58; 1,34]	0,5388
TC or IC >=1%	84	46 (54,8)	4,7 [2,8;11,0]	98	48 (49,0)	6,4 [1,9; 9,2]	0,92	[0,61; 1,37]	0,6709
Interaktions p-Wert									0,8823
Raucherstatus - DEU									
Raucher	241	123 (51,0)	4,5 [2,8; 8,2]	240	125 (52,1)	4,5 [2,7; 6,4]	0,84	[0,65; 1,07]	0,1627
Nichtraucher	23	15 (65,2)	6,5 [1,8; 9,2]	26	14 (53,8)	2,8 [1,0; 6,5]	1,02	[0,49; 2,14]	0,9515
Interaktions p-Wert									0,6106
Abstammung - DEU									
Weiß	130	59 (45,4)	3,6 [2,7; 9,1]	137	65 (47,4)	2,7 [1,8; 6,5]	0,78	[0,55; 1,11]	0,1612
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	1,0 [0,9; NE]	NC	[NC]	NC
Asiatisch	131	79 (60,3)	5,5 [2,8; 8,2]	121	70 (57,9)	5,5 [3,6; 7,4]	0,96	[0,70; 1,33]	0,8123
Andere	2	0	NE [NE; NE]	5	2 (40,0)	1,8 [0,9; NE]	NC	[NC]	NC
Interaktions p-Wert									0,3821
Geographische Region - DEU									
Asien	129	79 (61,2)	5,5 [2,8; 8,2]	120	70 (58,3)	5,5 [3,6; 7,4]	0,96	[0,70; 1,33]	0,8058
Europa	94	49 (52,1)	3,6 [2,7; 9,1]	112	58 (51,8)	1,9 [1,8; 5,5]	0,76	[0,52; 1,11]	0,1593
Nordamerika	41	10 (24,4)	4,5 [1,1; NE]	34	11 (32,4)	2,3 [0,9;11,9]	0,68	[0,28; 1,62]	0,3849
Interaktions p-Wert									0,5713
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Rollenfunktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	66 (49,6)	3,7 [2,7; 6,6]	131	70 (53,4)	4,5 [2,7; 6,4]	0,91	[0,65; 1,28]	0,5869
1	131	72 (55,0)	5,6 [2,8; 9,2]	135	69 (51,1)	3,7 [1,8; 8,2]	0,80	[0,57; 1,11]	0,1842
Interaktions p-Wert									0,5864

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	15 (41,7)	6,4 [0,9; NE]	37	18 (48,6)	8,4 [1,9;34,9]	1,04	[0,52; 2,06]	0,9127
Stadium III	228	125 (54,8)	4,6 [3,6; 7,3]	229	114 (49,8)	5,5 [3,6; 8,3]	1,05	[0,81; 1,36]	0,7044
Interaktions p-Wert									0,9770
TNM Status (eCRF) - DEU									
Stadium I/II	33	14 (42,4)	6,4 [1,9; NE]	34	16 (47,1)	8,3 [1,8;34,9]	0,98	[0,47; 2,01]	0,9485
Stadium III	231	126 (54,5)	4,6 [3,6; 7,3]	232	116 (50,0)	5,5 [3,7; 8,3]	1,06	[0,83; 1,37]	0,6340
Interaktions p-Wert									0,8267
Erhalt einer PCI (IVRS) - DEU									
Ja	142	82 (57,7)	2,8 [1,9; 5,5]	144	68 (47,2)	3,7 [2,7; 8,4]	1,10	[0,80; 1,52]	0,5502
Nein	122	58 (47,5)	7,3 [3,7;10,1]	122	64 (52,5)	8,2 [4,5;11,9]	0,99	[0,69; 1,41]	0,9360
Interaktions p-Wert									0,6455
Erhalt einer PCI (eCRF) - DEU									
Ja	142	82 (57,7)	2,8 [1,9; 5,5]	143	68 (47,6)	3,7 [2,7; 8,4]	1,10	[0,80; 1,52]	0,5502
Nein	122	58 (47,5)	7,3 [3,7;10,1]	123	64 (52,0)	8,2 [4,5;11,9]	0,99	[0,69; 1,41]	0,9360
Interaktions p-Wert									0,6455
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	17 (53,1)	12,9 [2,7;34,1]	32	17 (53,1)	8,3 [2,7;23,1]	0,92	[0,46; 1,81]	0,7997
>=14 bis <28 Tage	79	41 (51,9)	5,5 [2,7;11,0]	80	36 (45,0)	11,9 [4,6;24,9]	1,31	[0,84; 2,07]	0,2303
>=28 Tage	153	82 (53,6)	3,7 [2,7; 6,6]	154	79 (51,3)	3,7 [2,8; 8,2]	0,97	[0,71; 1,32]	0,8477
Interaktions p-Wert									0,5019
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	7 (43,8)	34,1 [0,9; NE]	24	13 (54,2)	6,5 [2,7; NE]	0,68	[0,25; 1,66]	0,3988
>=28 bis <56 Tage	104	56 (53,8)	5,5 [2,7;10,1]	104	51 (49,0)	4,6 [3,6;11,0]	1,02	[0,70; 1,50]	0,9033
>=56 bis <84 Tage	98	50 (51,0)	4,6 [2,7;17,4]	76	36 (47,4)	5,6 [3,6;12,8]	1,04	[0,68; 1,61]	0,8495
>=84 Tage	46	27 (58,7)	3,6 [1,8; 5,5]	62	32 (51,6)	6,4 [2,7;20,3]	1,36	[0,81; 2,27]	0,2449
Interaktions p-Wert									0,6005
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	47 (51,6)	7,3 [2,8;15,8]	88	45 (51,1)	4,5 [2,7; 8,3]	0,94	[0,62; 1,41]	0,7574
Cisplatin	173	93 (53,8)	3,7 [2,8; 6,6]	178	87 (48,9)	7,3 [3,7;11,1]	1,12	[0,84; 1,51]	0,4372
Interaktions p-Wert									0,4823
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	99 (50,8)	5,5 [3,7; 8,3]	187	86 (46,0)	5,6 [3,6;11,0]	1,05	[0,79; 1,41]	0,7257
Zweimal täglich	69	41 (59,4)	3,6 [1,8; 7,3]	79	46 (58,2)	4,6 [2,8;11,9]	1,09	[0,71; 1,65]	0,7015
Interaktions p-Wert									0,9062
Bestes Ansprechen auf cCRT - DEU									
CR	31	14 (45,2)	11,1 [1,8;27,5]	34	14 (41,2)	2,7 [1,8; NE]	0,84	[0,40; 1,77]	0,6383
PR	191	104 (54,5)	4,5 [2,8; 6,6]	200	102 (51,0)	5,6 [3,7; 8,3]	1,11	[0,85; 1,46]	0,4412
SD	42	22 (52,4)	7,3 [2,7;20,3]	32	16 (50,0)	7,4 [1,8; NE]	0,94	[0,50; 1,83]	0,8579
Interaktions p-Wert									0,7264
Geschlecht - DEU									
Männer	178	98 (55,1)	6,4 [3,7;10,1]	188	98 (52,1)	7,3 [4,5;11,1]	1,00	[0,76; 1,32]	0,9979
Frauen	86	42 (48,8)	1,9 [1,7; 5,5]	78	34 (43,6)	3,6 [2,7; 8,3]	1,22	[0,78; 1,93]	0,3835
Interaktions p-Wert									0,4583
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	86 (53,8)	6,6 [3,6;10,1]	162	86 (53,1)	4,6 [2,8; 8,3]	0,88	[0,65; 1,18]	0,3895
>=65 Jahre	104	54 (51,9)	2,8 [1,8; 5,5]	104	46 (44,2)	6,4 [3,7;18,3]	1,46	[0,98; 2,16]	0,0613
Interaktions p-Wert									0,0444*
PD-L1-Status - DEU									
TC and IC <1%	78	40 (51,3)	8,2 [2,7;22,9]	73	43 (58,9)	4,5 [2,7; 7,3]	0,71	[0,46; 1,10]	0,1218
TC or IC >=1%	84	54 (64,3)	3,7 [2,7; 6,4]	98	46 (46,9)	11,0 [4,6;15,6]	1,53	[1,03; 2,27]	0,0354*
Interaktions p-Wert									0,0106*
Raucherstatus - DEU									
Raucher	241	124 (51,5)	5,5 [3,6; 8,2]	240	119 (49,6)	6,4 [3,7; 8,4]	1,02	[0,79; 1,31]	0,8674
Nichtraucher	23	16 (69,6)	1,9 [1,0; 4,7]	26	13 (50,0)	3,6 [1,9; NE]	1,48	[0,71; 3,14]	0,2915
Interaktions p-Wert									0,3458
Abstammung - DEU									
Weiß	130	64 (49,2)	3,7 [2,7; 7,3]	137	65 (47,4)	4,6 [3,6;11,0]	1,03	[0,73; 1,45]	0,8784
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	76 (58,0)	5,5 [3,6;10,1]	121	66 (54,5)	6,4 [3,6;12,9]	1,07	[0,77; 1,49]	0,6883
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8679
Geographische Region - DEU									
Asien	129	76 (58,9)	5,5 [3,6;10,1]	120	66 (55,0)	6,4 [3,6;12,9]	1,07	[0,77; 1,50]	0,6761
Europa	94	51 (54,3)	4,5 [2,7; 8,3]	112	58 (51,8)	4,5 [2,8;11,0]	0,95	[0,65; 1,38]	0,7727
Nordamerika	41	13 (31,7)	3,6 [0,9;17,5]	34	8 (23,5)	5,6 [1,9; NE]	1,87	[0,79; 4,72]	0,1576
Interaktions p-Wert									0,3690
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	69 (51,9)	4,5 [2,7; 6,6]	131	67 (51,1)	6,5 [3,6;11,9]	1,11	[0,79; 1,56]	0,5401
1	131	71 (54,2)	6,4 [2,8;10,1]	135	65 (48,1)	5,5 [3,6;11,0]	1,01	[0,72; 1,41]	0,9685
Interaktions p-Wert									0,6855

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	18 (50,0)	2,8 [1,8;10,1]	37	19 (51,4)	2,7 [1,0;11,1]	1,00	[0,52; 1,90]	0,9890
Stadium III	228	141 (61,8)	1,8 [1,8; 3,6]	229	134 (58,5)	2,8 [1,9; 3,6]	1,10	[0,87; 1,39]	0,4290
Interaktions p-Wert									0,7754
TNM Status (eCRF) - DEU									
Stadium I/II	33	16 (48,5)	2,8 [1,8;12,9]	34	18 (52,9)	1,9 [0,9;11,1]	0,82	[0,42; 1,62]	0,5712
Stadium III	231	143 (61,9)	1,8 [1,8; 3,6]	232	135 (58,2)	2,8 [1,9; 3,6]	1,13	[0,89; 1,43]	0,3158
Interaktions p-Wert									0,3867
Erhalt einer PCI (IVRS) - DEU									
Ja	142	87 (61,3)	1,8 [1,1; 3,6]	144	83 (57,6)	1,9 [1,8; 2,8]	0,88	[0,65; 1,19]	0,4151
Nein	122	72 (59,0)	2,7 [1,8; 4,6]	122	70 (57,4)	4,6 [2,7; 8,2]	1,33	[0,95; 1,84]	0,0945
Interaktions p-Wert									0,0747
Erhalt einer PCI (eCRF) - DEU									
Ja	142	87 (61,3)	1,8 [1,1; 3,6]	143	83 (58,0)	1,9 [1,8; 2,8]	0,88	[0,65; 1,19]	0,4151
Nein	122	72 (59,0)	2,7 [1,8; 4,6]	123	70 (56,9)	4,6 [2,7; 8,2]	1,33	[0,95; 1,84]	0,0945
Interaktions p-Wert									0,0747
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	23 (71,9)	1,8 [1,0; 3,6]	32	18 (56,3)	5,5 [1,0;33,1]	1,68	[0,91; 3,15]	0,0990
>=14 bis <28 Tage	79	48 (60,8)	2,8 [1,8; 4,6]	80	47 (58,8)	3,7 [1,9; 7,3]	1,17	[0,78; 1,75]	0,4517
>=28 Tage	153	88 (57,5)	1,8 [1,8; 3,7]	154	88 (57,1)	1,9 [1,8; 2,8]	0,94	[0,70; 1,27]	0,6970
Interaktions p-Wert									0,2329
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	13 (81,3)	1,3 [0,9; 5,5]	24	14 (58,3)	6,5 [1,8; NE]	2,16	[1,004; 4,63]	0,0490*
>=28 bis <56 Tage	104	58 (55,8)	3,7 [1,8; 5,5]	104	51 (49,0)	2,7 [1,8; 3,6]	0,98	[0,67; 1,44]	0,9294
>=56 bis <84 Tage	98	59 (60,2)	1,9 [1,8; 3,6]	76	47 (61,8)	2,8 [1,8; 5,5]	1,07	[0,73; 1,57]	0,7420
>=84 Tage	46	29 (63,0)	1,8 [1,0; 3,6]	62	41 (66,1)	2,8 [1,0; 5,5]	1,09	[0,67; 1,75]	0,7107
Interaktions p-Wert									0,3395
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	51 (56,0)	2,8 [1,8; 5,5]	88	52 (59,1)	2,7 [1,8; 3,8]	0,97	[0,66; 1,43]	0,8721
Cisplatin	173	108 (62,4)	1,8 [1,8; 3,6]	178	101 (56,7)	2,8 [1,8; 5,5]	1,15	[0,88; 1,51]	0,3146
Interaktions p-Wert									0,4780
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	110 (56,4)	3,6 [1,8; 4,6]	187	102 (54,5)	2,7 [1,8; 5,5]	0,99	[0,76; 1,30]	0,9495
Zweimal täglich	69	49 (71,0)	1,8 [1,0; 1,9]	79	51 (64,6)	2,8 [1,0; 3,7]	1,42	[0,96; 2,11]	0,0824
Interaktions p-Wert									0,1413
Bestes Ansprechen auf cCRT - DEU									
CR	31	16 (51,6)	2,7 [1,8;11,0]	34	19 (55,9)	1,0 [0,9; 1,9]	0,49	[0,25; 0,96]	0,0379*
PR	191	119 (62,3)	1,9 [1,8; 3,7]	200	121 (60,5)	2,8 [1,9; 3,7]	1,12	[0,87; 1,44]	0,3786
SD	42	24 (57,1)	1,9 [0,9; 4,5]	32	13 (40,6)	12,8 [1,0; NE]	1,75	[0,91; 3,54]	0,0966
Interaktions p-Wert									0,0246*
Geschlecht - DEU									
Männer	178	119 (66,9)	2,7 [1,8; 3,7]	188	112 (59,6)	3,6 [2,7; 5,5]	1,20	[0,93; 1,56]	0,1596
Frauen	86	40 (46,5)	1,8 [1,0; 5,5]	78	41 (52,6)	1,8 [1,0; 2,7]	0,78	[0,50; 1,21]	0,2686
Interaktions p-Wert									0,0956
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	99 (61,9)	1,8 [1,8; 3,7]	162	96 (59,3)	1,9 [1,8; 3,6]	1,00	[0,76; 1,33]	0,9792
>=65 Jahre	104	60 (57,7)	2,7 [1,8; 4,6]	104	57 (54,8)	2,8 [2,7; 5,6]	1,23	[0,86; 1,78]	0,2553
Interaktions p-Wert									0,3769
PD-L1-Status - DEU									
TC and IC <1%	78	49 (62,8)	1,8 [1,0; 4,5]	73	44 (60,3)	2,7 [1,8; 6,4]	1,15	[0,77; 1,73]	0,4997
TC or IC >=1%	84	56 (66,7)	3,6 [1,8; 5,5]	98	54 (55,1)	3,7 [2,7; 8,2]	1,12	[0,77; 1,63]	0,5587
Interaktions p-Wert									0,9198
Raucherstatus - DEU									
Raucher	241	145 (60,2)	1,9 [1,8; 3,7]	240	137 (57,1)	2,8 [1,9; 3,8]	1,10	[0,87; 1,39]	0,4119
Nichtraucher	23	14 (60,9)	1,0 [0,9;12,9]	26	16 (61,5)	2,7 [0,9; 5,5]	0,96	[0,46; 1,97]	0,9074
Interaktions p-Wert									0,7151
Abstammung - DEU									
Weiß	130	68 (52,3)	1,9 [1,1; 4,7]	137	71 (51,8)	1,9 [1,8; 2,8]	0,98	[0,70; 1,37]	0,9148
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	91 (69,5)	1,9 [1,8; 3,6]	121	79 (65,3)	3,6 [2,7; 5,6]	1,18	[0,87; 1,60]	0,2761
Andere	2	0	NE [NE; NE]	5	2 (40,0)	1,8 [0,9; NE]	NC	[NC]	NC
Interaktions p-Wert									0,4182
Geographische Region - DEU									
Asien	129	91 (70,5)	1,9 [1,8; 3,6]	120	79 (65,8)	3,6 [2,7; 5,6]	1,17	[0,87; 1,59]	0,2963
Europa	94	56 (59,6)	2,7 [1,0; 5,5]	112	63 (56,3)	1,9 [1,8; 2,8]	0,97	[0,67; 1,38]	0,8508
Nordamerika	41	12 (29,3)	1,8 [1,0; 9,1]	34	11 (32,4)	2,3 [1,0; NE]	1,16	[0,51; 2,67]	0,7259
Interaktions p-Wert									0,7100
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	81 (60,9)	1,9 [1,8; 3,7]	131	82 (62,6)	1,9 [1,8; 2,8]	0,99	[0,73; 1,35]	0,9518
1	131	78 (59,5)	1,8 [1,8; 4,5]	135	71 (52,6)	3,6 [1,9; 5,6]	1,20	[0,87; 1,65]	0,2736
Interaktions p-Wert									0,4047

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	17 (47,2)	6,4 [1,8;24,0]	37	17 (45,9)	11,1 [1,8; NE]	1,22	[0,62; 2,41]	0,5644
Stadium III	228	138 (60,5)	3,7 [2,8; 4,6]	229	137 (59,8)	2,8 [1,8; 4,5]	0,85	[0,67; 1,08]	0,1887
Interaktions p-Wert									0,3274
TNM Status (eCRF) - DEU									
Stadium I/II	33	15 (45,5)	7,3 [2,7;24,0]	34	15 (44,1)	11,1 [1,8; NE]	1,14	[0,55; 2,36]	0,7172
Stadium III	231	140 (60,6)	3,7 [2,8; 4,6]	232	139 (59,9)	2,7 [1,8; 3,7]	0,87	[0,68; 1,10]	0,2313
Interaktions p-Wert									0,4732
Erhalt einer PCI (IVRS) - DEU									
Ja	142	87 (61,3)	3,7 [2,8; 5,6]	144	83 (57,6)	3,6 [1,8; 7,3]	0,84	[0,62; 1,14]	0,2582
Nein	122	68 (55,7)	3,7 [2,7; 6,4]	122	71 (58,2)	2,7 [1,8; 6,5]	0,98	[0,70; 1,37]	0,9097
Interaktions p-Wert									0,4994
Erhalt einer PCI (eCRF) - DEU									
Ja	142	87 (61,3)	3,7 [2,8; 5,6]	143	83 (58,0)	3,6 [1,8; 7,3]	0,84	[0,62; 1,14]	0,2582
Nein	122	68 (55,7)	3,7 [2,7; 6,4]	123	71 (57,7)	2,7 [1,8; 6,5]	0,98	[0,70; 1,37]	0,9097
Interaktions p-Wert									0,4994
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	20 (62,5)	3,6 [2,8;11,9]	32	21 (65,6)	1,8 [0,9; 8,3]	0,69	[0,37; 1,28]	0,2400
>=14 bis <28 Tage	79	43 (54,4)	4,5 [1,9; 8,2]	80	43 (53,8)	5,4 [1,8;11,0]	1,02	[0,67; 1,56]	0,9203
>=28 Tage	153	92 (60,1)	3,7 [2,7; 5,6]	154	90 (58,4)	2,8 [1,8; 5,5]	0,90	[0,67; 1,20]	0,4595
Interaktions p-Wert									0,5911
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	12 (75,0)	2,7 [1,8; 5,5]	24	14 (58,3)	1,8 [0,9; NE]	1,43	[0,65; 3,11]	0,3643
>=28 bis <56 Tage	104	51 (49,0)	6,4 [3,6; 8,2]	104	52 (50,0)	2,7 [1,8; 5,4]	0,72	[0,49; 1,06]	0,0981
>=56 bis <84 Tage	98	61 (62,2)	3,6 [1,9; 5,6]	76	46 (60,5)	6,4 [1,8; 8,2]	0,98	[0,67; 1,45]	0,9206
>=84 Tage	46	31 (67,4)	3,7 [1,8; 4,6]	62	42 (67,7)	3,6 [1,8; 5,6]	1,01	[0,63; 1,61]	0,9522
Interaktions p-Wert									0,3848
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	52 (57,1)	4,5 [1,8; 6,5]	88	54 (61,4)	1,8 [1,8; 5,4]	0,83	[0,57; 1,22]	0,3387
Cisplatin	173	103 (59,5)	3,7 [2,8; 5,6]	178	100 (56,2)	3,6 [1,9; 7,3]	0,94	[0,71; 1,24]	0,6716
Interaktions p-Wert									0,5978
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	106 (54,4)	4,5 [3,6; 6,4]	187	97 (51,9)	2,8 [1,8; 7,4]	0,90	[0,69; 1,19]	0,4696
Zweimal täglich	69	49 (71,0)	3,6 [1,8; 4,5]	79	57 (72,2)	2,8 [1,0; 5,6]	0,94	[0,64; 1,38]	0,7604
Interaktions p-Wert									0,8602
Bestes Ansprechen auf cCRT - DEU									
CR	31	18 (58,1)	3,7 [1,8; 6,5]	34	15 (44,1)	5,4 [0,9;26,6]	1,10	[0,55; 2,21]	0,7950
PR	191	115 (60,2)	4,5 [2,8; 6,4]	200	120 (60,0)	2,8 [1,8; 5,5]	0,88	[0,68; 1,14]	0,3440
SD	42	22 (52,4)	1,9 [1,8;18,3]	32	19 (59,4)	4,5 [0,9; 8,3]	0,89	[0,48; 1,66]	0,7036
Interaktions p-Wert									0,8459
Geschlecht - DEU									
Männer	178	111 (62,4)	3,7 [3,6; 5,6]	188	110 (58,5)	5,5 [2,8; 7,4]	0,99	[0,76; 1,30]	0,9664
Frauen	86	44 (51,2)	3,6 [1,8; 6,5]	78	44 (56,4)	1,0 [0,9; 1,8]	0,64	[0,42; 0,98]	0,0380*
Interaktions p-Wert									0,0829
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	100 (62,5)	4,5 [2,9; 6,4]	162	97 (59,9)	2,7 [1,8; 3,7]	0,85	[0,64; 1,13]	0,2587
>=65 Jahre	104	55 (52,9)	3,6 [2,7; 5,6]	104	57 (54,8)	4,5 [1,8; 9,2]	0,99	[0,68; 1,43]	0,9462
Interaktions p-Wert									0,5304
PD-L1-Status - DEU									
TC and IC <1%	78	46 (59,0)	4,5 [1,9; 7,3]	73	42 (57,5)	1,9 [1,8; 9,1]	0,87	[0,57; 1,33]	0,5272
TC or IC >=1%	84	59 (70,2)	3,6 [1,9; 5,6]	98	61 (62,2)	3,2 [1,9; 7,4]	0,98	[0,68; 1,40]	0,9009
Interaktions p-Wert									0,6899
Raucherstatus - DEU									
Raucher	241	141 (58,5)	3,7 [3,6; 5,6]	240	140 (58,3)	2,8 [1,8; 5,6]	0,90	[0,71; 1,13]	0,3610
Nichtraucher	23	14 (60,9)	2,7 [0,9; 6,5]	26	14 (53,8)	1,8 [0,9; NE]	1,00	[0,47; 2,11]	0,9971
Interaktions p-Wert									0,7853
Abstammung - DEU									
Weiß	130	69 (53,1)	2,9 [1,8; 5,5]	137	75 (54,7)	1,8 [1,8; 2,8]	0,86	[0,62; 1,19]	0,3526
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	86 (65,6)	4,5 [3,6; 6,5]	121	78 (64,5)	3,7 [2,7; 8,3]	0,93	[0,68; 1,26]	0,6345
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7249
Geographische Region - DEU									
Asien	129	86 (66,7)	4,5 [3,6; 6,5]	120	77 (64,2)	3,7 [2,7; 8,3]	0,93	[0,69; 1,27]	0,6585
Europa	94	57 (60,6)	3,6 [1,8; 5,6]	112	64 (57,1)	1,8 [1,8; 5,5]	0,90	[0,63; 1,28]	0,5547
Nordamerika	41	12 (29,3)	1,9 [1,0;19,3]	34	13 (38,2)	1,8 [1,0; 9,2]	0,85	[0,38; 1,87]	0,6839
Interaktions p-Wert									0,9709
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schmerzen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	73 (54,9)	4,5 [2,8; 6,5]	131	78 (59,5)	3,6 [1,8; 7,4]	0,92	[0,67; 1,26]	0,5974
1	131	82 (62,6)	3,7 [2,8; 4,7]	135	76 (56,3)	2,7 [1,8; 5,6]	0,88	[0,64; 1,20]	0,4062
Interaktions p-Wert									0,8384

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	10 (27,8)	30,3 [9,2; NE]	37	10 (27,0)	NE [NE; NE]	1,26	[0,52; 3,08]	0,6021
Stadium III	228	99 (43,4)	13,7 [7,4;22,0]	229	86 (37,6)	15,6 [9,1;21,2]	1,07	[0,80; 1,43]	0,6444
Interaktions p-Wert									0,7256
TNM Status (eCRF) - DEU									
Stadium I/II	33	9 (27,3)	30,3 [9,2; NE]	34	8 (23,5)	NE [NE; NE]	1,38	[0,53; 3,67]	0,5093
Stadium III	231	100 (43,3)	13,7 [7,4;22,0]	232	88 (37,9)	15,6 [9,1;21,2]	1,06	[0,80; 1,42]	0,6721
Interaktions p-Wert									0,6102
Erhalt einer PCI (IVRS) - DEU									
Ja	142	60 (42,3)	17,4 [7,4;28,5]	144	51 (35,4)	15,6 [7,3;30,3]	0,94	[0,65; 1,37]	0,7565
Nein	122	49 (40,2)	11,9 [7,3;30,3]	122	45 (36,9)	16,6 [9,2; NE]	1,32	[0,88; 1,98]	0,1827
Interaktions p-Wert									0,2344
Erhalt einer PCI (eCRF) - DEU									
Ja	142	60 (42,3)	17,4 [7,4;28,5]	143	51 (35,7)	15,6 [7,3;30,3]	0,94	[0,65; 1,37]	0,7565
Nein	122	49 (40,2)	11,9 [7,3;30,3]	123	45 (36,6)	16,6 [9,2; NE]	1,32	[0,88; 1,98]	0,1827
Interaktions p-Wert									0,2344
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	12 (37,5)	30,5 [6,4; NE]	32	11 (34,4)	NE [NE; NE]	1,00	[0,44; 2,31]	0,9986
>=14 bis <28 Tage	79	32 (40,5)	14,7 [5,5; NE]	80	33 (41,3)	11,9 [9,1;16,6]	1,00	[0,61; 1,62]	0,9867
>=28 Tage	153	65 (42,5)	11,0 [6,5;22,9]	154	52 (33,8)	21,1 [11,0; NE]	1,20	[0,83; 1,73]	0,3279
Interaktions p-Wert									0,8093

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	8 (50,0)	6,4 [1,8; NE]	24	9 (37,5)	14,7 [6,4; NE]	1,30	[0,49; 3,42]	0,5874
>=28 bis <56 Tage	104	40 (38,5)	14,7 [11,0;30,3]	104	32 (30,8)	21,1 [8,3; NE]	1,12	[0,70; 1,79]	0,6363
>=56 bis <84 Tage	98	42 (42,9)	18,3 [5,5;34,9]	76	27 (35,5)	16,6 [8,2; NE]	1,16	[0,72; 1,90]	0,5455
>=84 Tage	46	19 (41,3)	9,2 [3,6; NE]	62	28 (45,2)	17,4 [6,4;50,7]	0,99	[0,55; 1,77]	0,9830
Interaktions p-Wert									0,9639
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	40 (44,0)	13,8 [4,5;26,7]	88	34 (38,6)	11,0 [5,5; NE]	1,12	[0,71; 1,78]	0,6315
Cisplatin	173	69 (39,9)	18,3 [8,3;30,3]	178	62 (34,8)	17,4 [11,9;30,3]	1,09	[0,78; 1,55]	0,6050
Interaktions p-Wert									0,9415
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	85 (43,6)	11,0 [7,3;21,1]	187	63 (33,7)	17,5 [11,0;30,3]	1,24	[0,90; 1,72]	0,1956
Zweimal täglich	69	24 (34,8)	NE [NE; NE]	79	33 (41,8)	11,9 [8,2; NE]	0,80	[0,47; 1,34]	0,3949
Interaktions p-Wert									0,1596
Bestes Ansprechen auf cCRT - DEU									
CR	31	9 (29,0)	26,7 [6,5; NE]	34	10 (29,4)	9,1 [1,9; NE]	0,69	[0,28; 1,72]	0,4275
PR	191	86 (45,0)	11,9 [6,5;21,1]	200	77 (38,5)	15,7 [11,0;28,6]	1,17	[0,86; 1,60]	0,3080
SD	42	14 (33,3)	28,5 [7,3; NE]	32	9 (28,1)	20,2 [11,0; NE]	1,20	[0,53; 2,89]	0,6623
Interaktions p-Wert									0,5498
Geschlecht - DEU									
Männer	178	73 (41,0)	22,9 [11,0;34,1]	188	65 (34,6)	20,2 [13,8;50,7]	1,14	[0,82; 1,60]	0,4438
Frauen	86	36 (41,9)	6,5 [3,6;14,8]	78	31 (39,7)	7,3 [2,0;11,9]	0,97	[0,60; 1,58]	0,9168

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,6013
Altersgruppe - DEU									
<65 Jahre	160	73 (45,6)	13,8 [7,3;22,9]	162	63 (38,9)	11,9 [7,3;20,2]	1,02	[0,73; 1,43]	0,9265
>=65 Jahre	104	36 (34,6)	21,1 [8,3; NE]	104	33 (31,7)	30,3 [14,7;50,7]	1,23	[0,76; 1,98]	0,3946
Interaktions p-Wert									0,5233
PD-L1-Status - DEU									
TC and IC <1%	78	34 (43,6)	22,9 [5,6; NE]	73	29 (39,7)	13,8 [8,2;28,6]	0,99	[0,60; 1,63]	0,9567
TC or IC >=1%	84	43 (51,2)	11,0 [6,4;22,0]	98	34 (34,7)	20,2 [11,0; NE]	1,46	[0,94; 2,31]	0,0950
Interaktions p-Wert									0,2485
Raucherstatus - DEU									
Raucher	241	99 (41,1)	14,8 [9,2;25,8]	240	88 (36,7)	15,7 [11,0;26,7]	1,09	[0,82; 1,46]	0,5400
Nichtraucher	23	10 (43,5)	7,4 [2,0; NE]	26	8 (30,8)	NE [NE; NE]	1,22	[0,48; 3,19]	0,6751
Interaktions p-Wert									0,8269
Abstammung - DEU									
Weiß	130	53 (40,8)	10,1 [3,6;17,4]	137	49 (35,8)	11,9 [5,5;30,3]	1,22	[0,83; 1,80]	0,3142
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	56 (42,7)	23,9 [8,3;34,9]	121	46 (38,0)	17,5 [13,8;50,7]	1,04	[0,71; 1,55]	0,8315
Andere	2	0	NE [NE; NE]	5	1 (20,0)	2,7 [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5767
Geographische Region - DEU									
Asien	129	56 (43,4)	23,9 [8,3;34,9]	120	45 (37,5)	17,5 [13,8;50,7]	1,07	[0,72; 1,59]	0,7521
Europa	94	42 (44,7)	11,0 [4,5;21,1]	112	42 (37,5)	11,9 [4,6;46,9]	1,14	[0,74; 1,75]	0,5455

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Übelkeit und Erbrechen
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	11 (26,8)	2,8 [1,0; NE]	34	9 (26,5)	11,0 [1,9; NE]	1,66	[0,68; 4,11]	0,2616
Interaktions p-Wert									0,6695
ECOG-Status zu Baseline - DEU									
0	133	50 (37,6)	17,4 [7,3; NE]	131	49 (37,4)	13,8 [8,4; NE]	0,95	[0,64; 1,41]	0,7823
1	131	59 (45,0)	11,0 [7,3;25,8]	135	47 (34,8)	17,5 [11,0;46,9]	1,28	[0,88; 1,89]	0,2026
Interaktions p-Wert									0,2780

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	18 (50,0)	2,7 [1,8;24,0]	37	15 (40,5)	18,3 [1,8; NE]	1,51	[0,76; 3,04]	0,2378
Stadium III	228	113 (49,6)	6,4 [4,5;10,1]	229	100 (43,7)	7,3 [4,6;11,0]	1,09	[0,83; 1,42]	0,5438
Interaktions p-Wert									0,3810
TNM Status (eCRF) - DEU									
Stadium I/II	33	17 (51,5)	2,7 [1,8;24,0]	34	14 (41,2)	18,3 [1,8; NE]	1,39	[0,68; 2,87]	0,3613
Stadium III	231	114 (49,4)	6,4 [4,5; 9,2]	232	101 (43,5)	7,3 [4,6;11,0]	1,10	[0,84; 1,44]	0,4736
Interaktions p-Wert									0,5492
Erhalt einer PCI (IVRS) - DEU									
Ja	142	78 (54,9)	2,7 [1,8; 4,6]	144	62 (43,1)	3,6 [1,9; 8,2]	1,12	[0,80; 1,56]	0,5201
Nein	122	53 (43,4)	10,1 [5,6;20,2]	122	53 (43,4)	10,2 [7,3;29,4]	1,10	[0,75; 1,62]	0,6145
Interaktions p-Wert									0,9649
Erhalt einer PCI (eCRF) - DEU									
Ja	142	78 (54,9)	2,7 [1,8; 4,6]	143	62 (43,4)	3,6 [1,9; 8,2]	1,12	[0,80; 1,56]	0,5201
Nein	122	53 (43,4)	10,1 [5,6;20,2]	123	53 (43,1)	10,2 [7,3;29,4]	1,10	[0,75; 1,62]	0,6145
Interaktions p-Wert									0,9649
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	15 (46,9)	5,5 [3,7;34,9]	32	13 (40,6)	10,1 [7,4; NE]	1,20	[0,57; 2,57]	0,6256
>=14 bis <28 Tage	79	39 (49,4)	6,5 [4,6;11,9]	80	37 (46,3)	9,1 [3,6;18,3]	1,09	[0,70; 1,72]	0,6997
>=28 Tage	153	77 (50,3)	2,9 [1,9; 8,2]	154	65 (42,2)	6,5 [1,9;22,9]	1,14	[0,82; 1,59]	0,4442
Interaktions p-Wert									0,9751
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	8 (50,0)	7,3 [1,8; NE]	24	12 (50,0)	10,1 [2,7; NE]	0,92	[0,36; 2,24]	0,8638
>=28 bis <56 Tage	104	45 (43,3)	9,2 [4,7;23,0]	104	41 (39,4)	7,4 [4,6;22,9]	0,96	[0,63; 1,47]	0,8596
>=56 bis <84 Tage	98	53 (54,1)	4,6 [2,0; 7,4]	76	34 (44,7)	4,6 [1,9;29,5]	1,20	[0,78; 1,86]	0,4014
>=84 Tage	46	25 (54,3)	2,7 [1,0; 8,2]	62	28 (45,2)	8,2 [1,9; NE]	1,47	[0,85; 2,52]	0,1675
Interaktions p-Wert									0,6353
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	48 (52,7)	4,6 [1,8; 9,2]	88	39 (44,3)	7,3 [3,6;11,0]	1,26	[0,83; 1,93]	0,2838
Cisplatin	173	83 (48,0)	6,5 [3,7;12,8]	178	76 (42,7)	7,4 [4,5;22,9]	1,07	[0,79; 1,47]	0,6523
Interaktions p-Wert									0,5524
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	90 (46,2)	7,3 [5,5;14,7]	187	81 (43,3)	7,4 [4,6;11,9]	0,96	[0,71; 1,30]	0,7830
Zweimal täglich	69	41 (59,4)	1,9 [1,8; 2,9]	79	34 (43,0)	8,2 [2,7; NE]	1,74	[1,11; 2,76]	0,0168*
Interaktions p-Wert									0,0319*
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	5,6 [2,8; NE]	34	14 (41,2)	1,8 [0,9;29,5]	0,57	[0,26; 1,22]	0,1480
PR	191	97 (50,8)	5,5 [2,8;11,0]	200	88 (44,0)	9,1 [6,4;17,5]	1,25	[0,93; 1,66]	0,1361
SD	42	21 (50,0)	6,4 [2,7;20,3]	32	13 (40,6)	4,5 [1,8; NE]	1,07	[0,54; 2,20]	0,8430
Interaktions p-Wert									0,1701
Geschlecht - DEU									
Männer	178	98 (55,1)	5,5 [3,6;10,1]	188	81 (43,1)	10,2 [6,4;22,9]	1,26	[0,94; 1,70]	0,1220
Frauen	86	33 (38,4)	5,6 [1,8;23,0]	78	34 (43,6)	3,6 [1,9; 7,3]	0,83	[0,52; 1,35]	0,4611
Interaktions p-Wert									0,1514
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	83 (51,9)	5,6 [2,8;10,1]	162	73 (45,1)	6,4 [2,8;11,9]	1,07	[0,78; 1,46]	0,6847
>=65 Jahre	104	48 (46,2)	5,5 [2,8;12,8]	104	42 (40,4)	10,1 [6,4;29,4]	1,24	[0,82; 1,89]	0,3035
Interaktions p-Wert									0,5668
PD-L1-Status - DEU									
TC and IC <1%	78	40 (51,3)	5,5 [2,0;20,2]	73	38 (52,1)	6,4 [1,9; 7,3]	0,93	[0,60; 1,46]	0,7608
TC or IC >=1%	84	49 (58,3)	5,5 [2,7;11,0]	98	41 (41,8)	10,2 [3,6; NE]	1,30	[0,86; 1,98]	0,2137
Interaktions p-Wert									0,2851
Raucherstatus - DEU									
Raucher	241	117 (48,5)	6,4 [3,7;10,1]	240	105 (43,8)	7,4 [4,6;11,9]	1,07	[0,82; 1,40]	0,6003
Nichtraucher	23	14 (60,9)	3,7 [1,8; 7,3]	26	10 (38,5)	NE [NE; NE]	1,93	[0,86; 4,48]	0,1094
Interaktions p-Wert									0,1747
Abstammung - DEU									
Weiß	130	56 (43,1)	6,4 [2,7;11,0]	137	60 (43,8)	6,4 [2,7;10,1]	0,98	[0,68; 1,41]	0,9230
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	1,3 [0,9; NE]	NC	[NC]	NC
Asiatisch	131	75 (57,3)	5,5 [3,7;11,9]	121	53 (43,8)	11,9 [6,4; NE]	1,33	[0,94; 1,89]	0,1138
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2447
Geographische Region - DEU									
Asien	129	75 (58,1)	5,5 [3,7;11,9]	120	52 (43,3)	13,8 [7,3; NE]	1,36	[0,95; 1,94]	0,0893
Europa	94	45 (47,9)	6,4 [1,9;11,0]	112	54 (48,2)	6,4 [2,7; 9,2]	0,94	[0,63; 1,39]	0,7417
Nordamerika	41	11 (26,8)	7,3 [1,1; NE]	34	9 (26,5)	5,5 [1,0; NE]	1,07	[0,44; 2,65]	0,8804
Interaktions p-Wert									0,3843
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	58 (43,6)	6,4 [4,5;14,7]	131	59 (45,0)	7,3 [3,6;18,3]	0,97	[0,67; 1,39]	0,8593
1	131	73 (55,7)	4,6 [2,7; 8,2]	135	56 (41,5)	8,3 [4,6;17,5]	1,31	[0,93; 1,87]	0,1240
Interaktions p-Wert									0,2339

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.11 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	7 (19,4)	NE [NE; NE]	37	10 (27,0)	NE [NE; NE]	0,91	[0,33; 2,37]	0,8443
Stadium III	228	80 (35,1)	26,6 [12,8;44,2]	229	72 (31,4)	19,4 [13,8;29,6]	0,94	[0,68; 1,30]	0,7137
Interaktions p-Wert									0,9435
TNM Status (eCRF) - DEU									
Stadium I/II	33	7 (21,2)	NE [NE; NE]	34	9 (26,5)	NE [NE; NE]	0,96	[0,34; 2,58]	0,9371
Stadium III	231	80 (34,6)	26,6 [12,8;44,2]	232	73 (31,5)	19,4 [13,8;29,6]	0,94	[0,68; 1,29]	0,7006
Interaktions p-Wert									0,9658
Erhalt einer PCI (IVRS) - DEU									
Ja	142	46 (32,4)	33,2 [23,9; NE]	144	44 (30,6)	18,5 [13,7;29,6]	0,81	[0,53; 1,23]	0,3137
Nein	122	41 (33,6)	17,5 [9,2; NE]	122	38 (31,1)	32,2 [10,1; NE]	1,17	[0,75; 1,83]	0,4825
Interaktions p-Wert									0,2290
Erhalt einer PCI (eCRF) - DEU									
Ja	142	46 (32,4)	33,2 [23,9; NE]	143	44 (30,8)	18,5 [13,7;29,6]	0,81	[0,53; 1,23]	0,3137
Nein	122	41 (33,6)	17,5 [9,2; NE]	123	38 (30,9)	32,2 [10,1; NE]	1,17	[0,75; 1,83]	0,4825
Interaktions p-Wert									0,2290
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	14 (43,8)	17,5 [7,3;34,1]	32	9 (28,1)	17,4 [5,5; NE]	1,46	[0,64; 3,52]	0,3687
>=14 bis <28 Tage	79	27 (34,2)	23,9 [9,2; NE]	80	24 (30,0)	32,2 [10,1; NE]	1,09	[0,63; 1,89]	0,7708
>=28 Tage	153	46 (30,1)	44,2 [24,0; NE]	154	49 (31,8)	19,4 [12,8;29,6]	0,81	[0,54; 1,21]	0,2975
Interaktions p-Wert									0,3877
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.11 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	9 (56,3)	17,5 [5,5;34,1]	24	8 (33,3)	17,4 [5,5; NE]	1,39	[0,53; 3,71]	0,4985
>=28 bis <56 Tage	104	30 (28,8)	38,7 [17,5; NE]	104	30 (28,8)	19,4 [11,0; NE]	0,78	[0,47; 1,29]	0,3312
>=56 bis <84 Tage	98	32 (32,7)	33,2 [9,1; NE]	76	27 (35,5)	13,7 [8,3;29,4]	0,79	[0,48; 1,34]	0,3828
>=84 Tage	46	16 (34,8)	23,9 [7,3; NE]	62	17 (27,4)	NE [NE; NE]	1,41	[0,71; 2,81]	0,3258
Interaktions p-Wert									0,4015
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	29 (31,9)	33,2 [14,7; NE]	88	29 (33,0)	17,4 [5,5; NE]	0,78	[0,46; 1,31]	0,3404
Cisplatin	173	58 (33,5)	25,8 [11,0; NE]	178	53 (29,8)	22,0 [13,8; NE]	1,06	[0,73; 1,54]	0,7606
Interaktions p-Wert									0,3407
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	65 (33,3)	25,8 [12,8;38,7]	187	53 (28,3)	22,0 [13,7; NE]	1,03	[0,72; 1,49]	0,8749
Zweimal täglich	69	22 (31,9)	NE [NE; NE]	79	29 (36,7)	19,4 [10,1; NE]	0,79	[0,45; 1,37]	0,4069
Interaktions p-Wert									0,4353
Bestes Ansprechen auf cCRT - DEU									
CR	31	10 (32,3)	33,2 [3,6; NE]	34	5 (14,7)	NE [NE; NE]	2,11	[0,75; 6,78]	0,1600
PR	191	61 (31,9)	26,6 [14,7; NE]	200	65 (32,5)	19,4 [12,8; NE]	0,88	[0,62; 1,25]	0,4616
SD	42	16 (38,1)	9,2 [4,5; NE]	32	12 (37,5)	9,2 [4,6;29,4]	0,83	[0,39; 1,79]	0,6213
Interaktions p-Wert									0,2751
Geschlecht - DEU									
Männer	178	64 (36,0)	33,2 [12,8; NE]	188	54 (28,7)	29,4 [15,6; NE]	1,18	[0,82; 1,70]	0,3723
Frauen	86	23 (26,7)	24,0 [11,0; NE]	78	28 (35,9)	9,1 [3,7;22,0]	0,53	[0,30; 0,92]	0,0251*
Interaktions p-Wert									0,0181*
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.11 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	54 (33,8)	26,6 [12,8; NE]	162	47 (29,0)	22,0 [13,7; NE]	0,99	[0,67; 1,46]	0,9442
>=65 Jahre	104	33 (31,7)	28,5 [9,2;44,2]	104	35 (33,7)	19,4 [10,1;32,2]	0,91	[0,57; 1,48]	0,7131
Interaktions p-Wert									0,8103
PD-L1-Status - DEU									
TC and IC <1%	78	24 (30,8)	33,2 [24,0; NE]	73	21 (28,8)	29,4 [10,1; NE]	0,81	[0,45; 1,48]	0,4919
TC or IC >=1%	84	33 (39,3)	14,7 [7,3; NE]	98	38 (38,8)	16,6 [10,1;32,2]	0,90	[0,56; 1,44]	0,6587
Interaktions p-Wert									0,7907
Raucherstatus - DEU									
Raucher	241	80 (33,2)	25,8 [14,7;44,2]	240	74 (30,8)	22,0 [13,8;32,2]	1,00	[0,73; 1,37]	0,9923
Nichtraucher	23	7 (30,4)	52,4 [7,5; NE]	26	8 (30,8)	10,1 [3,7; NE]	0,61	[0,21; 1,71]	0,3457
Interaktions p-Wert									0,3694
Abstammung - DEU									
Weiß	130	40 (30,8)	23,9 [9,2; NE]	137	40 (29,2)	19,4 [11,0; NE]	0,98	[0,63; 1,52]	0,9273
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	8,3 [NE; NE]	NC	[NC]	NC
Asiatisch	131	47 (35,9)	34,1 [19,3; NE]	121	41 (33,9)	29,4 [13,8; NE]	0,95	[0,62; 1,45]	0,8086
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9189
Geographische Region - DEU									
Asien	129	47 (36,4)	34,1 [19,3; NE]	120	41 (34,2)	29,4 [13,7; NE]	0,94	[0,62; 1,44]	0,7750
Europa	94	33 (35,1)	23,9 [7,3; NE]	112	35 (31,3)	18,5 [10,1; NE]	0,97	[0,60; 1,57]	0,9151
Nordamerika	41	7 (17,1)	17,5 [3,7; NE]	34	6 (17,6)	19,4 [7,3; NE]	1,11	[0,37; 3,46]	0,8484
Interaktions p-Wert									0,9603
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.11 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	40 (30,1)	38,7 [14,7; NE]	131	38 (29,0)	32,2 [12,8; NE]	0,98	[0,63; 1,54]	0,9354
1	131	47 (35,9)	24,0 [10,1;44,2]	135	44 (32,6)	17,4 [10,1;22,0]	0,92	[0,61; 1,40]	0,7024
Interaktions p-Wert									0,8410

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.1.12 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	15 (41,7)	4,6 [2,7; NE]	37	17 (45,9)	4,5 [1,8;51,5]	0,97	[0,48; 1,94]	0,9235
Stadium III	228	127 (55,7)	3,7 [2,8; 5,6]	229	108 (47,2)	7,3 [3,8; 9,1]	1,19	[0,92; 1,53]	0,1929
Interaktions p-Wert									0,5886
TNM Status (eCRF) - DEU									
Stadium I/II	33	14 (42,4)	5,5 [2,7; NE]	34	15 (44,1)	3,2 [1,8;51,5]	0,93	[0,45; 1,94]	0,8525
Stadium III	231	128 (55,4)	3,7 [2,8; 5,6]	232	110 (47,4)	7,3 [4,5; 9,1]	1,19	[0,92; 1,54]	0,1770
Interaktions p-Wert									0,5350
Erhalt einer PCI (IVRS) - DEU									
Ja	142	81 (57,0)	3,7 [2,7; 6,4]	144	59 (41,0)	7,4 [3,6;18,4]	1,30	[0,93; 1,83]	0,1215
Nein	122	61 (50,0)	4,6 [3,6; 7,4]	122	66 (54,1)	7,3 [2,8; 9,1]	1,02	[0,72; 1,45]	0,8960
Interaktions p-Wert									0,3292
Erhalt einer PCI (eCRF) - DEU									
Ja	142	81 (57,0)	3,7 [2,7; 6,4]	143	59 (41,3)	7,4 [3,6;18,4]	1,30	[0,93; 1,83]	0,1215
Nein	122	61 (50,0)	4,6 [3,6; 7,4]	123	66 (53,7)	7,3 [2,8; 9,1]	1,02	[0,72; 1,45]	0,8960
Interaktions p-Wert									0,3292
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	15 (46,9)	4,5 [2,8; NE]	32	17 (53,1)	5,5 [2,7;11,9]	0,75	[0,37; 1,51]	0,4199
>=14 bis <28 Tage	79	41 (51,9)	4,5 [2,7; 7,4]	80	41 (51,3)	8,2 [2,8;11,0]	1,16	[0,75; 1,79]	0,5084
>=28 Tage	153	86 (56,2)	3,6 [2,7; 6,4]	154	67 (43,5)	7,3 [2,9;13,8]	1,28	[0,93; 1,77]	0,1288
Interaktions p-Wert									0,3942
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.12 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	12 (75,0)	2,8 [1,8;15,6]	24	14 (58,3)	4,7 [1,9;39,6]	1,24	[0,56; 2,68]	0,5907
>=28 bis <56 Tage	104	50 (48,1)	5,5 [3,6; 7,4]	104	37 (35,6)	9,1 [3,8; NE]	1,37	[0,90; 2,11]	0,1440
>=56 bis <84 Tage	98	51 (52,0)	4,5 [2,8;10,1]	76	44 (57,9)	3,6 [2,7; 8,2]	0,80	[0,54; 1,21]	0,2916
>=84 Tage	46	29 (63,0)	2,7 [1,8; 5,5]	62	30 (48,4)	8,3 [1,9;35,8]	1,61	[0,96; 2,69]	0,0714
Interaktions p-Wert									0,1529
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	46 (50,5)	4,6 [2,8; 9,2]	88	41 (46,6)	7,4 [2,7;11,9]	1,10	[0,72; 1,68]	0,6543
Cisplatin	173	96 (55,5)	3,7 [2,8; 5,6]	178	84 (47,2)	7,3 [3,6;10,2]	1,19	[0,89; 1,60]	0,2430
Interaktions p-Wert									0,7653
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	98 (50,3)	4,6 [3,6; 6,5]	187	84 (44,9)	7,3 [2,8;10,1]	1,07	[0,80; 1,44]	0,6352
Zweimal täglich	69	44 (63,8)	2,8 [1,8; 5,5]	79	41 (51,9)	7,3 [3,6;18,4]	1,39	[0,91; 2,13]	0,1326
Interaktions p-Wert									0,3302
Bestes Ansprechen auf cCRT - DEU									
CR	31	12 (38,7)	4,5 [1,8; NE]	34	14 (41,2)	6,4 [1,1;35,8]	0,72	[0,32; 1,55]	0,3947
PR	191	106 (55,5)	4,5 [2,8; 6,4]	200	97 (48,5)	7,4 [3,8;10,2]	1,17	[0,89; 1,55]	0,2572
SD	42	24 (57,1)	2,7 [1,0; 4,6]	32	14 (43,8)	4,5 [1,0; NE]	1,52	[0,80; 3,02]	0,2046
Interaktions p-Wert									0,3365
Geschlecht - DEU									
Männer	178	103 (57,9)	3,7 [2,8; 5,5]	188	87 (46,3)	8,4 [6,4;13,8]	1,29	[0,97; 1,72]	0,0774
Frauen	86	39 (45,3)	6,4 [1,8; 9,2]	78	38 (48,7)	2,7 [1,0; 3,7]	0,83	[0,53; 1,30]	0,4126
Interaktions p-Wert									0,1019
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.12 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	84 (52,5)	5,5 [3,6; 8,3]	162	76 (46,9)	7,3 [3,7;13,8]	1,08	[0,79; 1,47]	0,6457
>=65 Jahre	104	58 (55,8)	3,6 [1,9; 4,6]	104	49 (47,1)	8,3 [2,8;10,1]	1,32	[0,90; 1,94]	0,1542
Interaktions p-Wert									0,4170
PD-L1-Status - DEU									
TC and IC <1%	78	48 (61,5)	3,6 [1,8; 6,5]	73	33 (45,2)	9,1 [3,6;36,7]	1,59	[1,03; 2,50]	0,0383*
TC or IC >=1%	84	50 (59,5)	3,6 [2,0; 5,6]	98	48 (49,0)	7,3 [2,7;13,8]	1,24	[0,83; 1,85]	0,2969
Interaktions p-Wert									0,4064
Raucherstatus - DEU									
Raucher	241	127 (52,7)	4,5 [3,6; 5,6]	240	107 (44,6)	8,4 [6,4;11,9]	1,23	[0,95; 1,59]	0,1173
Nichtraucher	23	15 (65,2)	2,0 [1,0; 6,4]	26	18 (69,2)	2,7 [0,9; 2,9]	0,72	[0,36; 1,43]	0,3518
Interaktions p-Wert									0,1554
Abstammung - DEU									
Weiß	130	62 (47,7)	3,7 [2,7; 6,4]	137	58 (42,3)	4,5 [2,7; 9,1]	1,18	[0,83; 1,70]	0,3579
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	1,0 [0,9; NE]	NC	[NC]	NC
Asiatisch	131	80 (61,1)	4,5 [3,6; 6,5]	121	64 (52,9)	8,2 [5,5;11,0]	1,19	[0,85; 1,65]	0,3083
Andere	2	0	NE [NE; NE]	5	1 (20,0)	3,6 [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9918
Geographische Region - DEU									
Asien	129	80 (62,0)	4,5 [3,6; 6,5]	120	63 (52,5)	8,2 [5,5;11,9]	1,20	[0,86; 1,67]	0,2854
Europa	94	53 (56,4)	2,8 [1,9; 5,5]	112	49 (43,8)	4,5 [2,7;16,6]	1,35	[0,91; 1,99]	0,1331
Nordamerika	41	9 (22,0)	7,4 [1,8; NE]	34	13 (38,2)	3,7 [1,0; 9,1]	0,55	[0,23; 1,27]	0,1588
Interaktions p-Wert									0,1592
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.12 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	71 (53,4)	4,5 [2,8; 7,4]	131	65 (49,6)	4,7 [2,7; 8,4]	1,08	[0,77; 1,52]	0,6440
1	131	71 (54,2)	3,7 [2,7; 6,5]	135	60 (44,4)	9,1 [4,5;11,9]	1,25	[0,88; 1,76]	0,2084
Interaktions p-Wert									0,5657

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.13 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	5 (13,9)	NE [NE; NE]	37	7 (18,9)	NE [NE; NE]	0,80	[0,24; 2,52]	0,7068
Stadium III	228	82 (36,0)	19,3 [12,0; NE]	229	77 (33,6)	24,9 [9,1; NE]	0,93	[0,68; 1,27]	0,6316
Interaktions p-Wert									0,8132
TNM Status (eCRF) - DEU									
Stadium I/II	33	6 (18,2)	NE [NE; NE]	34	5 (14,7)	NE [NE; NE]	1,31	[0,39; 4,53]	0,6582
Stadium III	231	81 (35,1)	19,3 [12,0; NE]	232	79 (34,1)	22,9 [9,1; NE]	0,90	[0,66; 1,23]	0,5001
Interaktions p-Wert									0,5492
Erhalt einer PCI (IVRS) - DEU									
Ja	142	49 (34,5)	22,9 [12,9; NE]	144	39 (27,1)	34,1 [14,7; NE]	1,03	[0,68; 1,58]	0,8825
Nein	122	38 (31,1)	22,0 [10,1; NE]	122	45 (36,9)	14,8 [8,2; NE]	0,85	[0,55; 1,31]	0,4669
Interaktions p-Wert									0,5324
Erhalt einer PCI (eCRF) - DEU									
Ja	142	49 (34,5)	22,9 [12,9; NE]	143	39 (27,3)	34,1 [14,7; NE]	1,03	[0,68; 1,58]	0,8825
Nein	122	38 (31,1)	22,0 [10,1; NE]	123	45 (36,6)	14,8 [8,2; NE]	0,85	[0,55; 1,31]	0,4669
Interaktions p-Wert									0,5324
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	15 (46,9)	5,5 [2,8; NE]	32	12 (37,5)	9,1 [3,6; NE]	1,24	[0,58; 2,71]	0,5776
>=14 bis <28 Tage	79	23 (29,1)	NE [NE; NE]	80	23 (28,8)	NE [NE; NE]	0,95	[0,53; 1,71]	0,8709
>=28 Tage	153	49 (32,0)	22,9 [13,7; NE]	154	49 (31,8)	34,1 [9,1; NE]	0,86	[0,58; 1,28]	0,4495
Interaktions p-Wert									0,6984

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.13 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	6 (37,5)	22,0 [5,5; NE]	24	10 (41,7)	8,2 [3,6; NE]	0,75	[0,25; 2,02]	0,5712
>=28 bis <56 Tage	104	34 (32,7)	NE [NE; NE]	104	32 (30,8)	22,9 [7,3; NE]	0,89	[0,55; 1,44]	0,6251
>=56 bis <84 Tage	98	31 (31,6)	NE [NE; NE]	76	20 (26,3)	31,2 [13,8; NE]	1,09	[0,62; 1,94]	0,7730
>=84 Tage	46	16 (34,8)	13,8 [7,3; NE]	62	22 (35,5)	34,1 [9,1; NE]	0,99	[0,51; 1,88]	0,9734
Interaktions p-Wert									0,9123
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	28 (30,8)	NE [NE; NE]	88	26 (29,5)	NE [NE; NE]	0,92	[0,54; 1,58]	0,7574
Cisplatin	173	59 (34,1)	21,3 [12,9; NE]	178	58 (32,6)	31,2 [13,8; NE]	0,94	[0,66; 1,36]	0,7529
Interaktions p-Wert									0,9371
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	63 (32,3)	21,3 [11,1; NE]	187	52 (27,8)	NE [NE; NE]	1,02	[0,70; 1,47]	0,9317
Zweimal täglich	69	24 (34,8)	NE [NE; NE]	79	32 (40,5)	24,9 [7,4; NE]	0,79	[0,46; 1,34]	0,3848
Interaktions p-Wert									0,4462
Bestes Ansprechen auf cCRT - DEU									
CR	31	10 (32,3)	16,5 [2,8; NE]	34	10 (29,4)	7,4 [1,9; NE]	0,73	[0,30; 1,79]	0,4897
PR	191	63 (33,0)	22,9 [11,1; NE]	200	64 (32,0)	34,1 [14,7; NE]	0,99	[0,69; 1,40]	0,9340
SD	42	14 (33,3)	21,3 [7,3; NE]	32	10 (31,3)	9,1 [3,6; NE]	0,78	[0,35; 1,82]	0,5578
Interaktions p-Wert									0,7577
Geschlecht - DEU									
Männer	178	69 (38,8)	16,6 [11,0; NE]	188	63 (33,5)	31,2 [14,7; NE]	1,02	[0,72; 1,44]	0,9139
Frauen	86	18 (20,9)	NE [NE; NE]	78	21 (26,9)	34,1 [7,4; NE]	0,71	[0,38; 1,34]	0,2897

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.13 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,3262
Altersgruppe - DEU									
<65 Jahre	160	52 (32,5)	22,9 [14,8; NE]	162	56 (34,6)	24,9 [9,1; NE]	0,78	[0,53; 1,14]	0,1927
>=65 Jahre	104	35 (33,7)	13,8 [5,5; NE]	104	28 (26,9)	NE [NE; NE]	1,28	[0,78; 2,12]	0,3304
Interaktions p-Wert									0,1178
PD-L1-Status - DEU									
TC and IC <1%	78	27 (34,6)	22,0 [9,3; NE]	73	18 (24,7)	34,1 [24,9; NE]	1,33	[0,74; 2,46]	0,3429
TC or IC >=1%	84	33 (39,3)	22,1 [8,2; NE]	98	34 (34,7)	NE [NE; NE]	0,85	[0,53; 1,38]	0,5166
Interaktions p-Wert									0,2521
Raucherstatus - DEU									
Raucher	241	78 (32,4)	22,0 [13,7; NE]	240	78 (32,5)	31,2 [11,0; NE]	0,89	[0,65; 1,22]	0,4808
Nichtraucher	23	9 (39,1)	NE [NE; NE]	26	6 (23,1)	NE [NE; NE]	1,50	[0,54; 4,48]	0,4364
Interaktions p-Wert									0,3412
Abstammung - DEU									
Weiß	130	36 (27,7)	22,1 [12,9; NE]	137	47 (34,3)	11,0 [7,3;31,2]	0,69	[0,44; 1,06]	0,0903
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	51 (38,9)	21,3 [9,3; NE]	121	36 (29,8)	46,0 [34,1; NE]	1,25	[0,82; 1,93]	0,3045
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,0539
Geographische Region - DEU									
Asien	129	51 (39,5)	21,3 [9,3; NE]	120	36 (30,0)	46,0 [34,1; NE]	1,25	[0,82; 1,93]	0,3064
Europa	94	31 (33,0)	22,1 [10,1; NE]	112	44 (39,3)	8,2 [5,5;22,9]	0,64	[0,40; 1,01]	0,0534

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.13 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Finanzielle Schwierigkeiten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	5 (12,2)	22,0 [6,4; NE]	34	4 (11,8)	NE [NE; NE]	1,31	[0,35; 5,31]	0,6835
Interaktions p-Wert									0,0942
ECOG-Status zu Baseline - DEU									
0	133	39 (29,3)	NE [NE; NE]	131	43 (32,8)	34,1 [9,1; NE]	0,85	[0,55; 1,32]	0,4716
1	131	48 (36,6)	16,6 [10,1; NE]	135	41 (30,4)	31,2 [9,1; NE]	1,01	[0,67; 1,54]	0,9545
Interaktions p-Wert									0,5765

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.14 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	14 (38,9)	10,1 [3,6; NE]	37	16 (43,2)	9,1 [1,9; NE]	0,96	[0,46; 1,98]	0,9218
Stadium III	228	120 (52,6)	5,5 [3,7; 6,5]	229	98 (42,8)	8,2 [6,4;13,7]	1,29	[0,99; 1,69]	0,0589
Interaktions p-Wert									0,4517
TNM Status (eCRF) - DEU									
Stadium I/II	33	13 (39,4)	10,1 [3,6; NE]	34	16 (47,1)	8,3 [1,9;25,7]	0,81	[0,38; 1,68]	0,5688
Stadium III	231	121 (52,4)	5,5 [3,7; 6,5]	232	98 (42,2)	8,3 [6,4;17,4]	1,32	[1,01; 1,73]	0,0388*
Interaktions p-Wert									0,2129
Erhalt einer PCI (IVRS) - DEU									
Ja	142	75 (52,8)	4,7 [3,6; 6,4]	144	57 (39,6)	9,1 [5,5;17,5]	1,30	[0,92; 1,84]	0,1395
Nein	122	59 (48,4)	6,4 [4,5;10,1]	122	57 (46,7)	8,2 [5,5;17,4]	1,20	[0,83; 1,73]	0,3263
Interaktions p-Wert									0,7654
Erhalt einer PCI (eCRF) - DEU									
Ja	142	75 (52,8)	4,7 [3,6; 6,4]	143	57 (39,9)	9,1 [5,5;17,5]	1,30	[0,92; 1,84]	0,1395
Nein	122	59 (48,4)	6,4 [4,5;10,1]	123	57 (46,3)	8,2 [5,5;17,4]	1,20	[0,83; 1,73]	0,3263
Interaktions p-Wert									0,7654
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	17 (53,1)	4,6 [1,9;27,5]	32	15 (46,9)	6,5 [4,6; NE]	1,22	[0,61; 2,47]	0,5822
>=14 bis <28 Tage	79	40 (50,6)	5,5 [3,6;10,1]	80	36 (45,0)	9,1 [3,6;17,5]	1,17	[0,75; 1,85]	0,4853
>=28 Tage	153	77 (50,3)	5,7 [3,7; 7,5]	154	63 (40,9)	8,3 [5,6;25,7]	1,30	[0,93; 1,82]	0,1226
Interaktions p-Wert									0,9359
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.14 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	9 (56,3)	9,1 [1,8; NE]	24	11 (45,8)	13,7 [2,7; NE]	1,06	[0,43; 2,56]	0,8985
>=28 bis <56 Tage	104	47 (45,2)	7,3 [4,7;10,9]	104	41 (39,4)	8,3 [3,6;27,5]	1,09	[0,71; 1,66]	0,7020
>=56 bis <84 Tage	98	53 (54,1)	3,7 [2,8; 6,4]	76	36 (47,4)	7,4 [3,7;12,9]	1,24	[0,82; 1,91]	0,3120
>=84 Tage	46	25 (54,3)	5,5 [2,7;11,1]	62	26 (41,9)	10,2 [5,5; NE]	1,57	[0,90; 2,72]	0,1111
Interaktions p-Wert									0,7536
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	5,6 [3,6;10,9]	88	44 (50,0)	6,4 [2,8; 9,1]	0,98	[0,64; 1,49]	0,9220
Cisplatin	173	90 (52,0)	5,5 [3,7; 7,4]	178	70 (39,3)	11,9 [7,3;27,5]	1,42	[1,04; 1,95]	0,0281*
Interaktions p-Wert									0,1640
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	96 (49,2)	6,4 [4,5; 8,2]	187	73 (39,0)	9,1 [6,4;17,4]	1,32	[0,98; 1,80]	0,0724
Zweimal täglich	69	38 (55,1)	5,5 [3,6; 7,4]	79	41 (51,9)	8,3 [4,6;17,4]	1,11	[0,71; 1,73]	0,6359
Interaktions p-Wert									0,5295
Bestes Ansprechen auf cCRT - DEU									
CR	31	17 (54,8)	4,5 [1,8; 6,4]	34	13 (38,2)	12,9 [1,9;25,7]	1,69	[0,82; 3,55]	0,1550
PR	191	96 (50,3)	6,4 [4,6; 8,2]	200	87 (43,5)	8,3 [6,4;17,5]	1,20	[0,90; 1,61]	0,2216
SD	42	21 (50,0)	4,5 [1,8;16,5]	32	14 (43,8)	7,3 [1,9; NE]	1,20	[0,62; 2,41]	0,5968
Interaktions p-Wert									0,6847
Geschlecht - DEU									
Männer	178	101 (56,7)	5,5 [3,6; 6,5]	188	78 (41,5)	11,9 [7,3;35,8]	1,52	[1,13; 2,06]	0,0052*
Frauen	86	33 (38,4)	6,4 [3,7;12,9]	78	36 (46,2)	6,4 [3,6; 8,2]	0,72	[0,45; 1,16]	0,1751
Interaktions p-Wert									0,0086*
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.14 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	88 (55,0)	5,6 [3,6; 8,2]	162	67 (41,4)	9,1 [5,5;25,7]	1,33	[0,97; 1,83]	0,0819
>=65 Jahre	104	46 (44,2)	5,5 [3,7; 7,4]	104	47 (45,2)	8,2 [6,4;17,4]	1,13	[0,75; 1,71]	0,5464
Interaktions p-Wert									0,5533
PD-L1-Status - DEU									
TC and IC <1%	78	42 (53,8)	5,5 [2,8;10,9]	73	34 (46,6)	6,4 [3,6;20,3]	1,17	[0,75; 1,86]	0,4867
TC or IC >=1%	84	42 (50,0)	7,3 [4,6;12,8]	98	47 (48,0)	8,2 [4,6;12,9]	0,96	[0,63; 1,45]	0,8326
Interaktions p-Wert									0,5127
Raucherstatus - DEU									
Raucher	241	123 (51,0)	5,5 [3,7; 6,4]	240	99 (41,3)	9,1 [6,4;17,4]	1,35	[1,04; 1,77]	0,0249*
Nichtraucher	23	11 (47,8)	9,2 [2,7; NE]	26	15 (57,7)	5,6 [1,8;17,4]	0,62	[0,28; 1,35]	0,2280
Interaktions p-Wert									0,0618
Abstammung - DEU									
Weiß	130	58 (44,6)	6,4 [3,6;10,1]	137	55 (40,1)	6,4 [2,8;12,9]	1,14	[0,78; 1,65]	0,4984
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	76 (58,0)	5,5 [4,5; 7,4]	121	57 (47,1)	10,1 [7,3;20,3]	1,37	[0,97; 1,94]	0,0711
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,4662
Geographische Region - DEU									
Asien	129	76 (58,9)	5,5 [4,5; 7,4]	120	56 (46,7)	10,1 [6,5;25,7]	1,38	[0,98; 1,96]	0,0646
Europa	94	48 (51,1)	6,4 [3,6;10,1]	112	48 (42,9)	5,5 [2,7;12,9]	1,10	[0,74; 1,65]	0,6297
Nordamerika	41	10 (24,4)	4,5 [1,8; NE]	34	10 (29,4)	10,2 [1,1; NE]	1,22	[0,50; 2,97]	0,6626
Interaktions p-Wert									0,7030
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.14 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	67 (50,4)	5,6 [3,7; 8,2]	131	56 (42,7)	9,1 [5,5;20,3]	1,28	[0,90; 1,83]	0,1702
1	131	67 (51,1)	5,5 [3,6; 7,5]	135	58 (43,0)	8,3 [6,4;17,4]	1,22	[0,86; 1,74]	0,2727
Interaktions p-Wert									0,8400

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.1.15 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	11 (30,6)	25,8 [3,6; NE]	37	12 (32,4)	NE [NE; NE]	1,11	[0,48; 2,52]	0,8111
Stadium III	228	102 (44,7)	8,3 [5,5;16,6]	229	93 (40,6)	9,1 [5,6;15,7]	0,98	[0,74; 1,30]	0,8715
Interaktions p-Wert									0,7805
TNM Status (eCRF) - DEU									
Stadium I/II	33	12 (36,4)	25,8 [2,8; NE]	34	12 (35,3)	15,6 [3,7; NE]	1,10	[0,49; 2,48]	0,8111
Stadium III	231	101 (43,7)	11,0 [5,5;17,4]	232	93 (40,1)	9,3 [6,4;16,5]	0,99	[0,74; 1,31]	0,9213
Interaktions p-Wert									0,7962
Erhalt einer PCI (IVRS) - DEU									
Ja	142	68 (47,9)	8,2 [4,5;20,2]	144	55 (38,2)	7,4 [4,5;15,6]	0,96	[0,68; 1,38]	0,8429
Nein	122	45 (36,9)	12,9 [5,5;25,8]	122	50 (41,0)	11,0 [6,4; NE]	1,02	[0,68; 1,52]	0,9415
Interaktions p-Wert									0,8522
Erhalt einer PCI (eCRF) - DEU									
Ja	142	68 (47,9)	8,2 [4,5;20,2]	143	55 (38,5)	7,4 [4,5;15,6]	0,96	[0,68; 1,38]	0,8429
Nein	122	45 (36,9)	12,9 [5,5;25,8]	123	50 (40,7)	11,0 [6,4; NE]	1,02	[0,68; 1,52]	0,9415
Interaktions p-Wert									0,8522
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	14 (43,8)	14,7 [2,7; NE]	32	14 (43,8)	7,4 [3,6; NE]	1,06	[0,50; 2,24]	0,8830
>=14 bis <28 Tage	79	36 (45,6)	11,0 [4,5;20,2]	80	29 (36,3)	15,7 [6,4; NE]	1,27	[0,78; 2,08]	0,3438
>=28 Tage	153	63 (41,2)	8,2 [5,5;25,8]	154	62 (40,3)	8,4 [4,5;16,5]	0,87	[0,61; 1,24]	0,4448
Interaktions p-Wert									0,4719
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.15 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	9 (56,3)	11,9 [0,9; NE]	24	9 (37,5)	NE [NE; NE]	1,72	[0,67; 4,41]	0,2531
>=28 bis <56 Tage	104	42 (40,4)	12,9 [5,5;20,2]	104	36 (34,6)	9,3 [6,4;19,3]	1,08	[0,69; 1,69]	0,7352
>=56 bis <84 Tage	98	42 (42,9)	15,6 [4,5;26,7]	76	29 (38,2)	10,1 [3,7; NE]	0,89	[0,56; 1,44]	0,6274
>=84 Tage	46	20 (43,5)	7,3 [2,7; NE]	62	31 (50,0)	6,5 [3,6;24,9]	0,89	[0,50; 1,55]	0,6809
Interaktions p-Wert									0,6102
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	43 (47,3)	15,6 [5,5;18,4]	88	39 (44,3)	9,1 [3,7;16,5]	0,95	[0,62; 1,48]	0,8268
Cisplatin	173	70 (40,5)	8,2 [5,5;26,7]	178	66 (37,1)	11,0 [7,3; NE]	1,03	[0,73; 1,44]	0,8854
Interaktions p-Wert									0,7939
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	78 (40,0)	14,7 [5,6;18,4]	187	64 (34,2)	15,6 [7,3; NE]	1,07	[0,77; 1,49]	0,6948
Zweimal täglich	69	35 (50,7)	5,5 [2,8;26,7]	79	41 (51,9)	7,4 [3,7;13,7]	0,92	[0,58; 1,44]	0,7108
Interaktions p-Wert									0,5953
Bestes Ansprechen auf cCRT - DEU									
CR	31	12 (38,7)	14,7 [3,6; NE]	34	10 (29,4)	10,1 [1,9; NE]	0,95	[0,41; 2,24]	0,8983
PR	191	82 (42,9)	12,9 [5,5;20,2]	200	84 (42,0)	10,1 [6,5;18,4]	0,98	[0,72; 1,33]	0,8797
SD	42	19 (45,2)	6,4 [2,7; NE]	32	11 (34,4)	5,5 [3,6; NE]	1,16	[0,56; 2,53]	0,6924
Interaktions p-Wert									0,9071
Geschlecht - DEU									
Männer	178	81 (45,5)	8,2 [5,5;22,1]	188	73 (38,8)	11,0 [7,3;24,9]	1,11	[0,81; 1,53]	0,5071
Frauen	86	32 (37,2)	15,6 [5,5;20,2]	78	32 (41,0)	6,5 [1,9;15,6]	0,74	[0,45; 1,21]	0,2266
Interaktions p-Wert									0,1687
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.1.15 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	68 (42,5)	14,7 [5,5;25,8]	162	68 (42,0)	7,4 [4,6;15,6]	0,86	[0,61; 1,20]	0,3694
>=65 Jahre	104	45 (43,3)	8,2 [5,5;18,3]	104	37 (35,6)	15,7 [5,5; NE]	1,29	[0,84; 2,01]	0,2456
Interaktions p-Wert									0,1421
PD-L1-Status - DEU									
TC and IC <1%	78	31 (39,7)	17,6 [5,4; NE]	73	32 (43,8)	5,6 [2,8;24,9]	0,73	[0,45; 1,21]	0,2200
TC or IC >=1%	84	42 (50,0)	14,7 [5,5;20,2]	98	39 (39,8)	15,6 [5,5; NE]	1,18	[0,76; 1,83]	0,4607
Interaktions p-Wert									0,1591
Raucherstatus - DEU									
Raucher	241	102 (42,3)	11,9 [5,6;18,3]	240	94 (39,2)	9,3 [6,4;16,5]	1,01	[0,76; 1,34]	0,9454
Nichtraucher	23	11 (47,8)	7,5 [1,9; NE]	26	11 (42,3)	18,4 [1,9; NE]	0,94	[0,40; 2,19]	0,8762
Interaktions p-Wert									0,8654
Abstammung - DEU									
Weiß	130	47 (36,2)	14,7 [5,6;20,2]	137	50 (36,5)	7,4 [3,7;16,5]	0,88	[0,59; 1,31]	0,5177
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	66 (50,4)	8,2 [4,5;22,1]	121	55 (45,5)	9,3 [5,6;19,3]	1,08	[0,75; 1,55]	0,6776
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,4477
Geographische Region - DEU									
Asien	129	66 (51,2)	8,2 [4,5;22,1]	120	55 (45,8)	9,3 [5,6;19,3]	1,07	[0,75; 1,53]	0,7179
Europa	94	40 (42,6)	14,7 [5,6;20,2]	112	43 (38,4)	7,3 [3,6;18,4]	0,86	[0,55; 1,32]	0,4796
Nordamerika	41	7 (17,1)	7,3 [3,8; NE]	34	7 (20,6)	15,7 [7,4; NE]	1,34	[0,46; 3,91]	0,5871
Interaktions p-Wert									0,6300
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.1.15 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-C30 Verstopfung
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	57 (42,9)	8,2 [4,5;20,2]	131	57 (43,5)	6,4 [3,7;15,6]	0,90	[0,62; 1,30]	0,5670
1	131	56 (42,7)	14,7 [5,5;25,8]	135	48 (35,6)	15,6 [7,4; NE]	1,13	[0,77; 1,66]	0,5486
Interaktions p-Wert									0,4069

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Anhang 4-G6.2.3: EORTC QLQ-C30 - Subgruppenanalysen Kaplan-Meier-Plot

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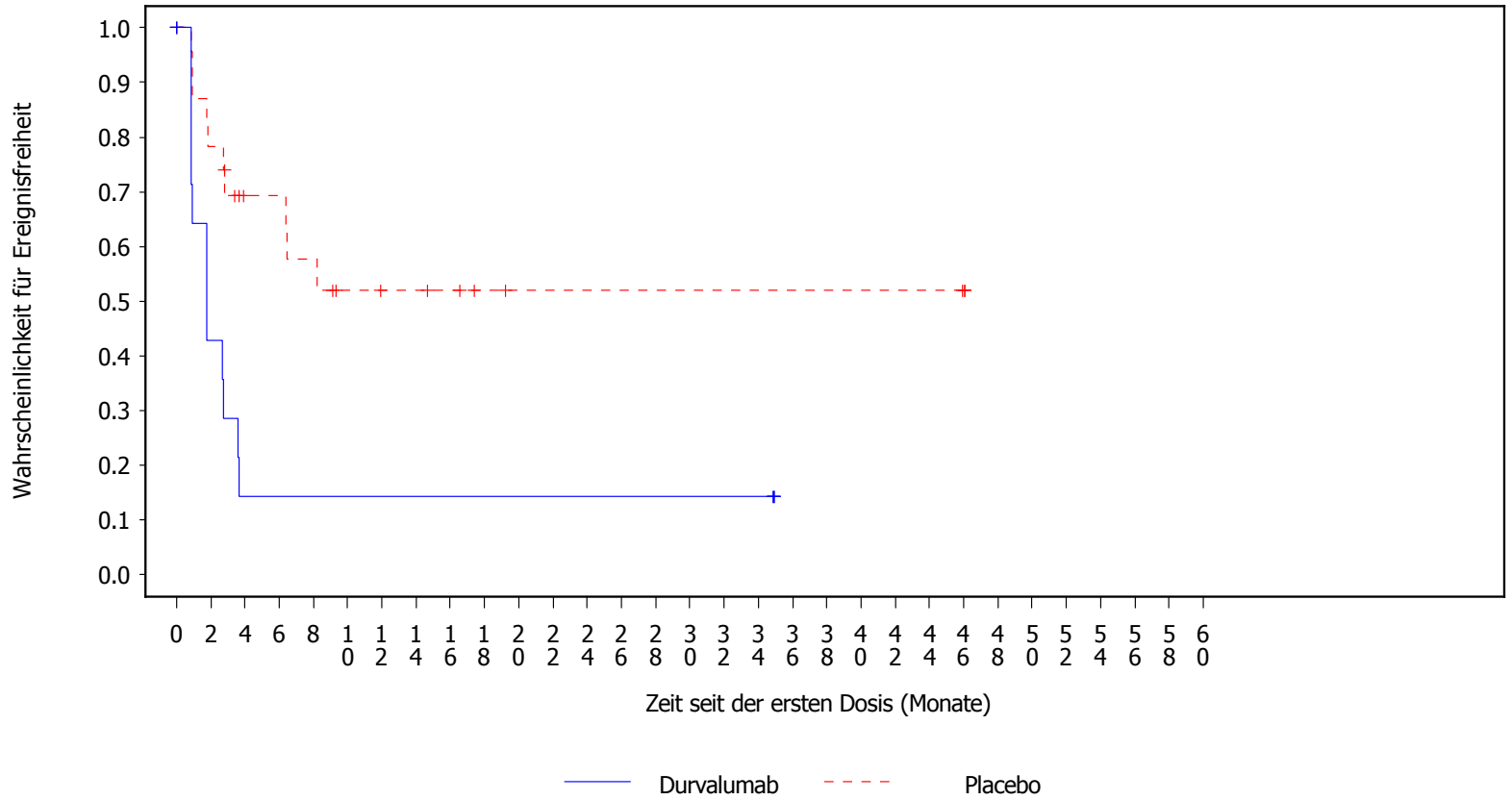
Figure 3.6.1.16 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus for Zeit vom Ende der Radiotherapie bis Randomisierung - DEU=<28 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

16	6	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
24	18	12	12	10	7	6	6	5	3	2	2	2	2	2	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreaa 07NOV2024:14:41

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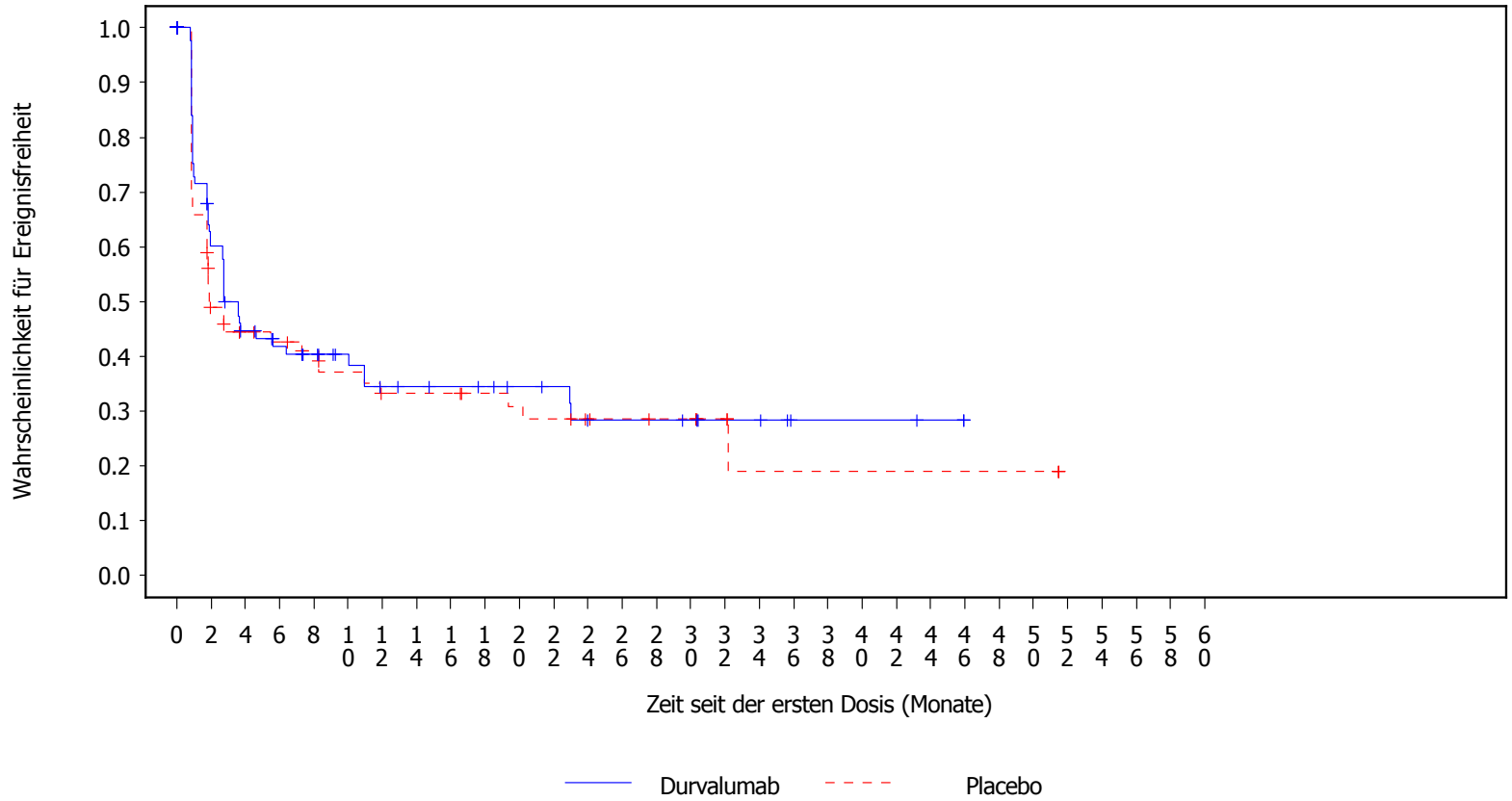
Figure 3.6.1.17 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus for Zeit vom Ende der Radiotherapie bis Randomisierung - DEU=>=28 bis <56 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

104	47	33	28	25	21	17	16	15	14	12	11	8	8	8	7	5	5	2	2	2	2	1	0	0	0	0	0	0	0	Durvalumab
104	33	27	25	22	19	16	16	16	14	13	12	10	9	8	8	5	2	2	2	2	2	2	2	2	2	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreab 07NOV2024:14:41

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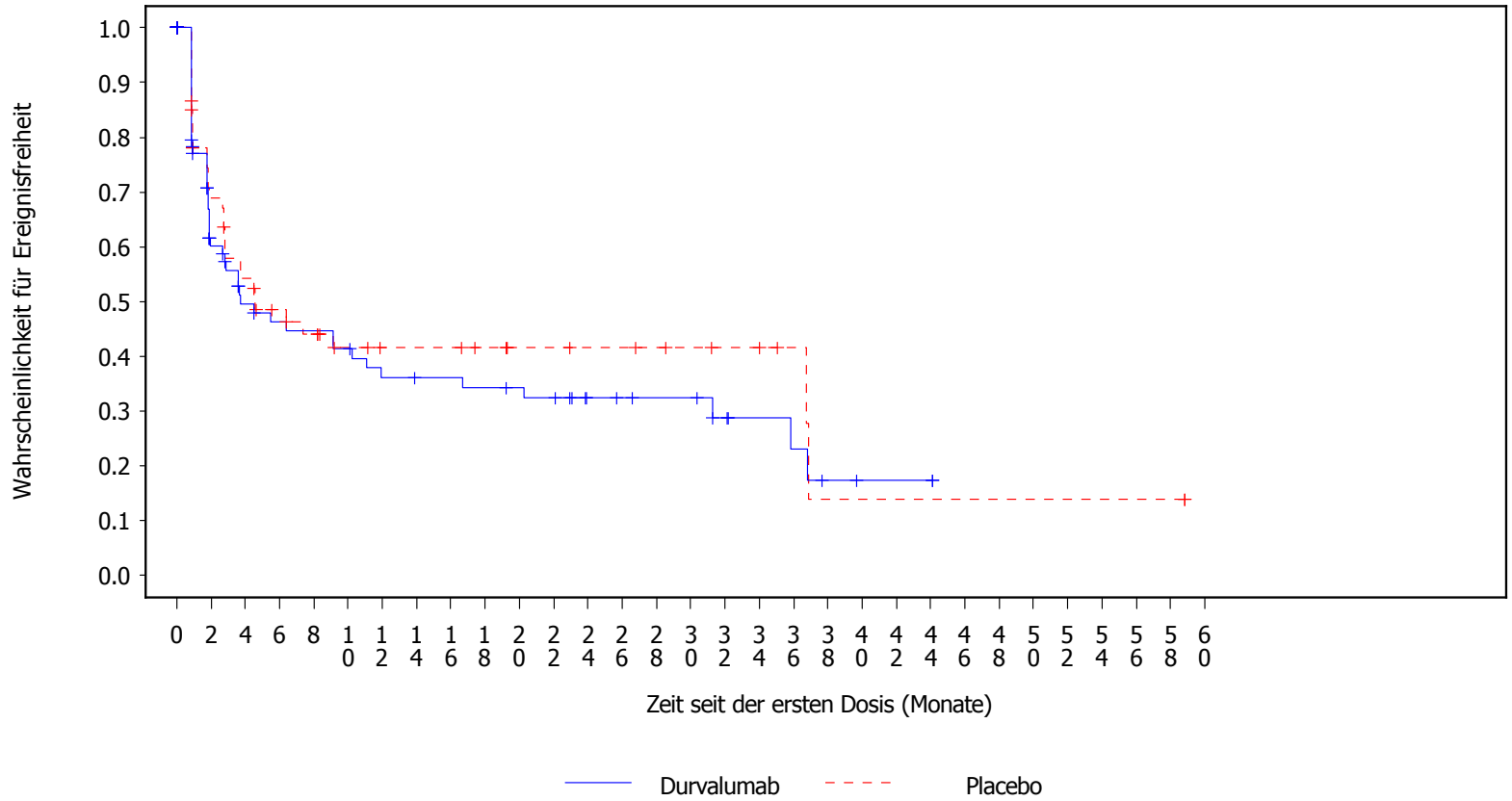
Figure 3.6.1.18 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus for Zeit vom Ende der Radiotherapie bis Randomisierung - DEU=>=56 bis <84 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

98	42	31	28	27	25	21	20	20	19	18	17	12	11	10	10	7	5	4	2	1	1	1	0	0	0	0	0	0	0	Durvalumab
76	38	29	23	20	15	13	13	13	11	9	9	8	8	7	6	5	5	3	1	1	1	1	1	1	1	1	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreac 07NOV2024:14:41

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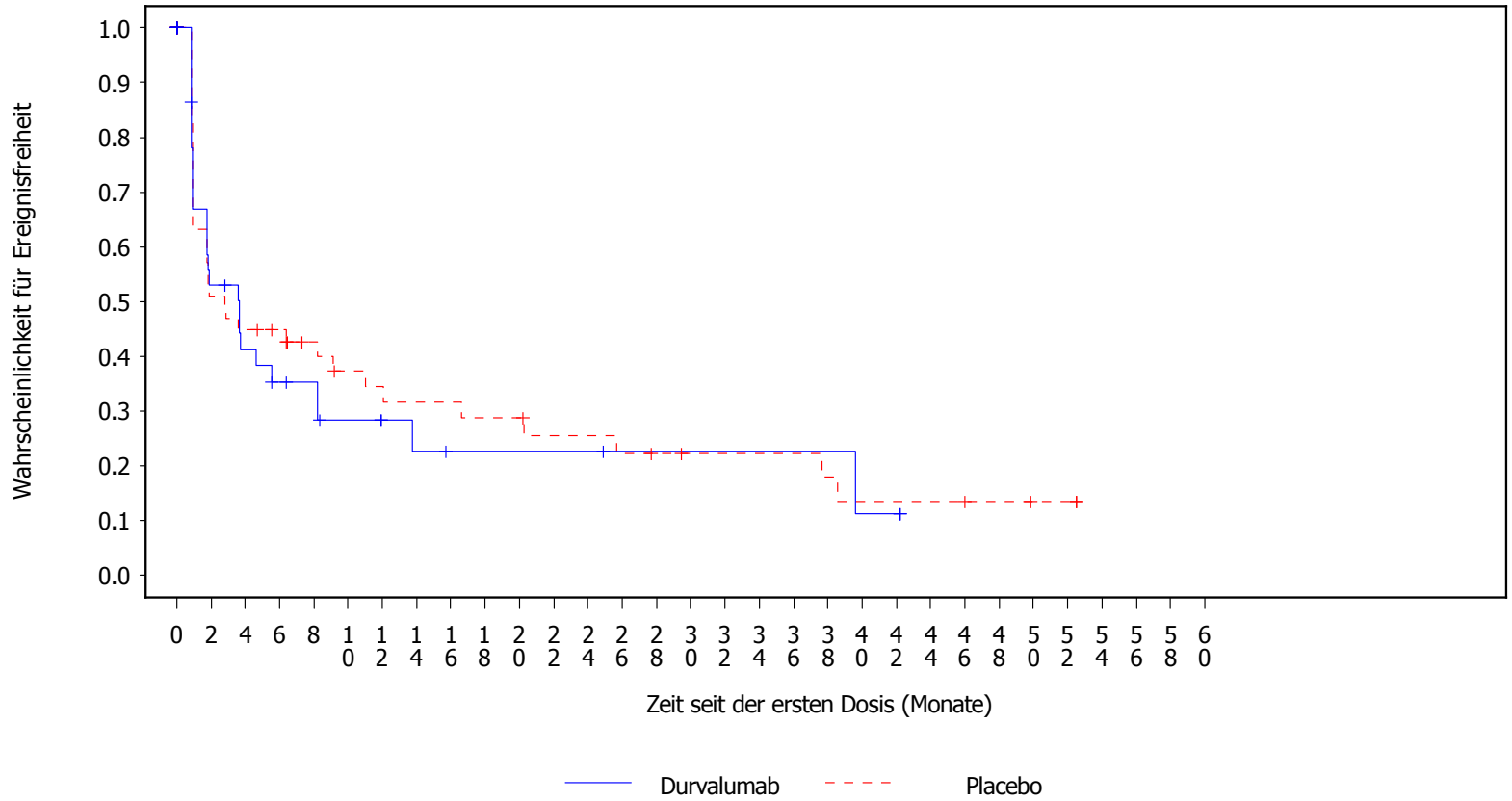
Figure 3.6.1.19 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Globaler Gesundheitsstatus for Zeit vom Ende der Radiotherapie bis Randomisierung - DEU=>=84 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

46	19	14	11	10	7	5	4	3	3	3	3	3	2	2	2	2	2	2	2	1	1	0	0	0	0	0	0	0	Durvalumab
62	25	22	20	16	13	12	11	11	10	10	8	8	7	6	5	5	5	5	4	3	3	3	2	2	1	1	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpread 07NOV2024:14:41

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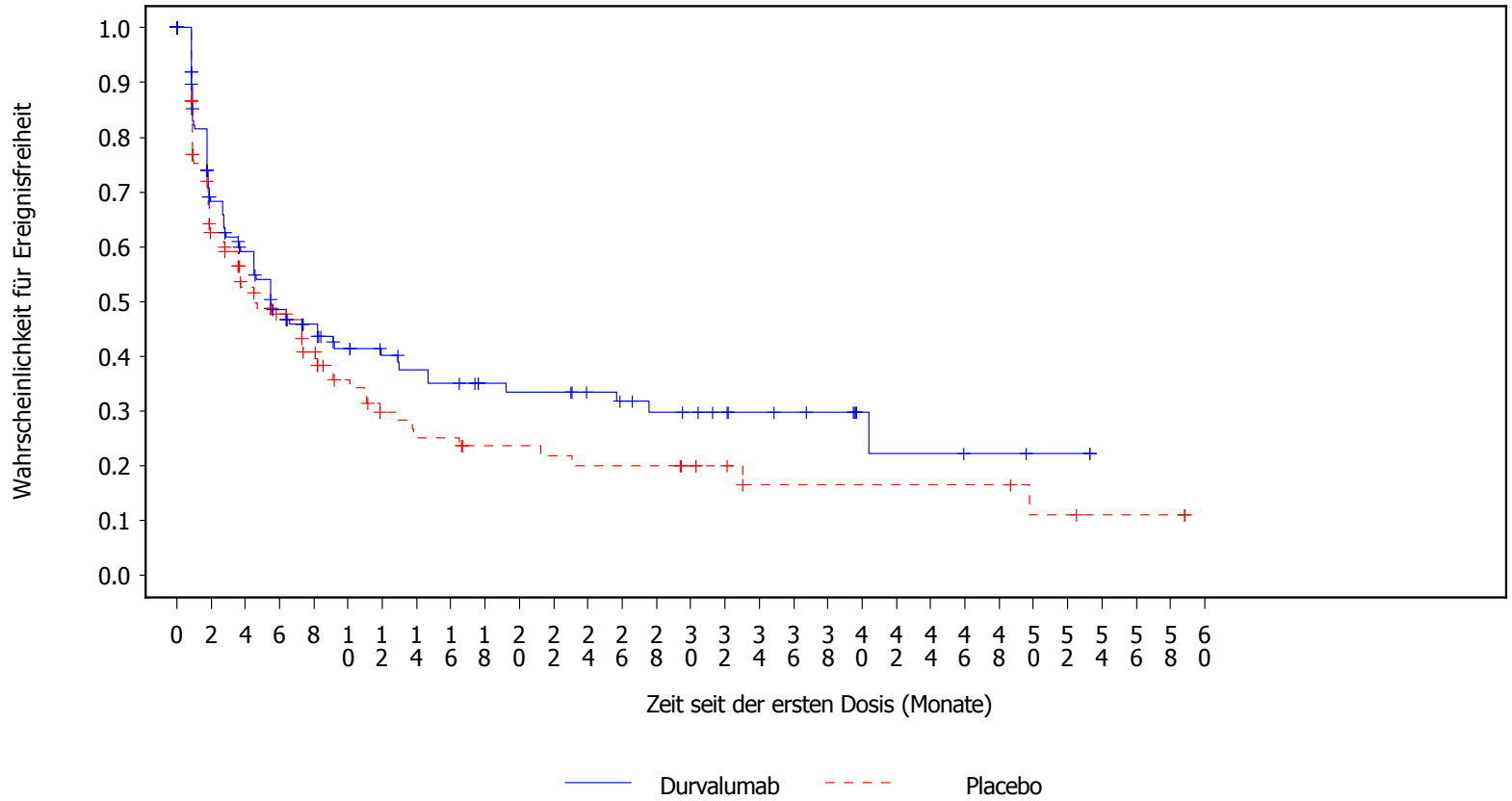
Figure 3.6.1.20 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion for Altersgruppe - DEU=<65 Jahre
Full Analysis Set, DCO 15JAN2024

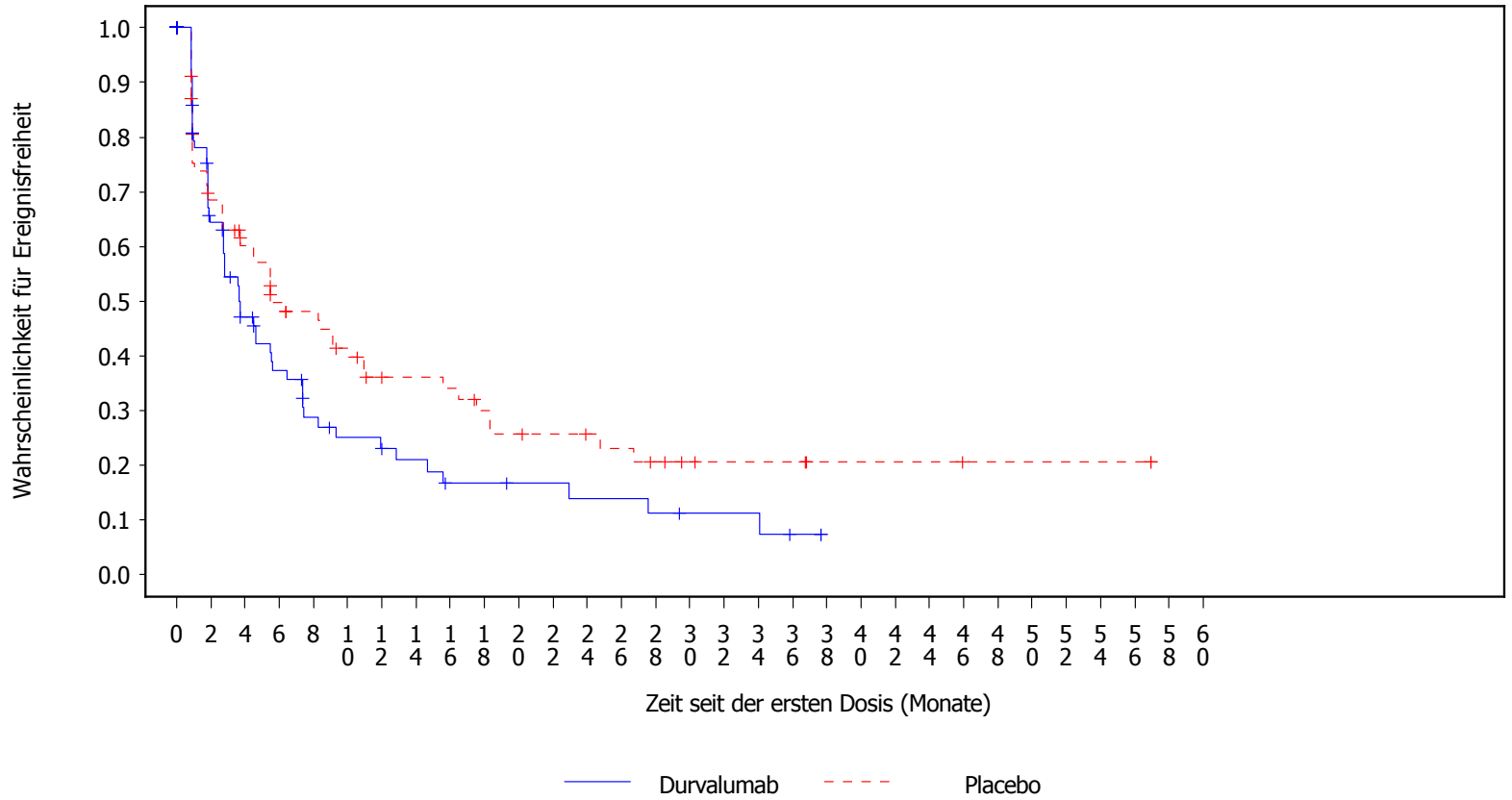


Anzahl an Patienten unter Risiko:

1608	3	68	53	44	36	32	29	27	23	22	22	19	17	15	14	12	10	9	8	4	3	3	2	2	1	1	0	0	0	0	Durvalumab
1627	2	55	45	34	25	19	16	16	13	13	12	11	11	11	9	7	4	4	4	4	4	4	4	4	2	2	1	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreae 07NOV2024:14:41

Figure 3.6.1.21 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Kognitive Funktion for Altersgruppe - DEU=>=65 Jahre
Full Analysis Set, DCO 15JAN2024

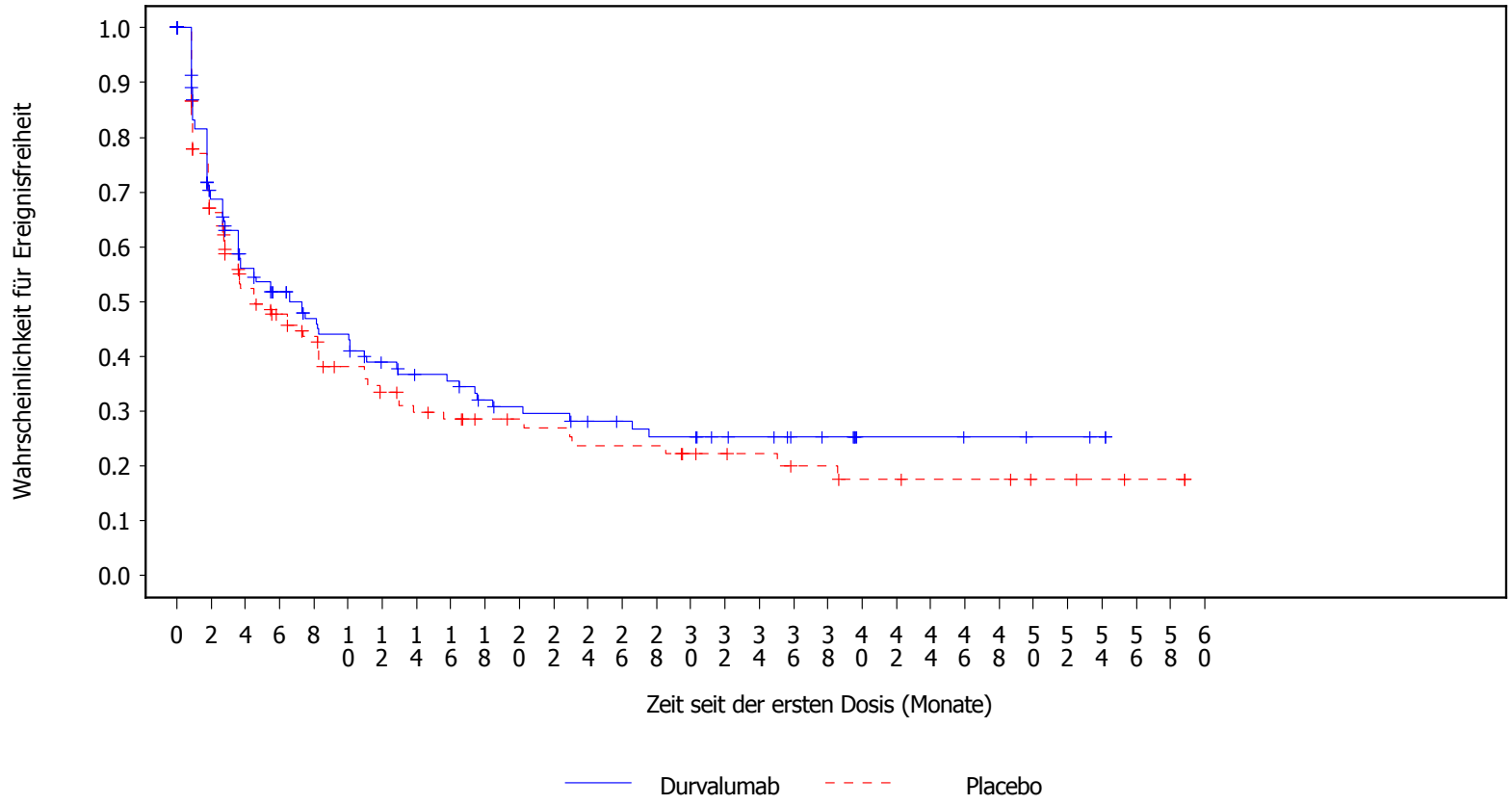


Anzahl an Patienten unter Risiko:

10446	31	23	16	13	11	10	7	7	6	6	5	5	4	3	3	3	1	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
10450	41	32	29	24	19	18	17	14	12	11	10	9	7	5	4	4	4	2	2	2	2	1	1	1	1	1	1	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreaf 07NOV2024:14:41

Figure 3.6.1.22 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion for Altersgruppe - DEU=<65 Jahre
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

160	85	65	56	47	44	36	32	31	26	24	23	20	19	17	17	14	13	10	9	4	4	4	3	3	2	2	1	0	0	0	Durvalumab
162	79	57	48	41	33	28	24	22	19	18	17	15	15	15	12	11	10	8	8	6	6	5	5	5	3	3	2	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreag 07NOV2024:14:41

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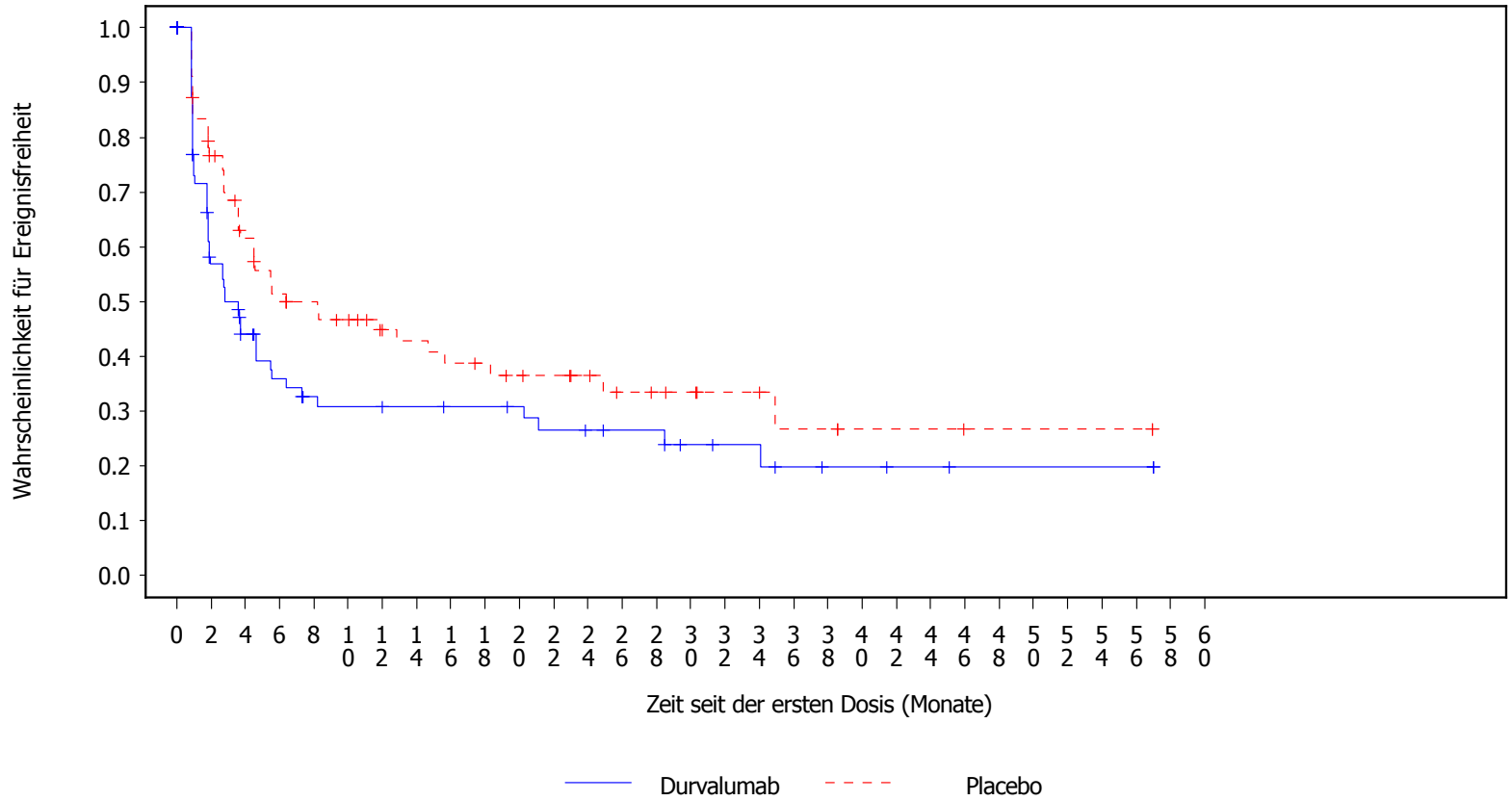
Figure 3.6.1.23 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion for Altersgruppe - DEU=>=65 Jahre
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

1044	1	29	22	18	17	16	16	15	15	14	12	11	10	10	7	6	6	4	3	3	2	2	1	1	1	1	1	1	0	0	Durvalumab
1045	7	43	35	31	28	23	21	19	18	16	15	13	10	9	8	6	6	4	4	2	2	2	1	1	1	1	1	1	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreah 07NOV2024:14:41

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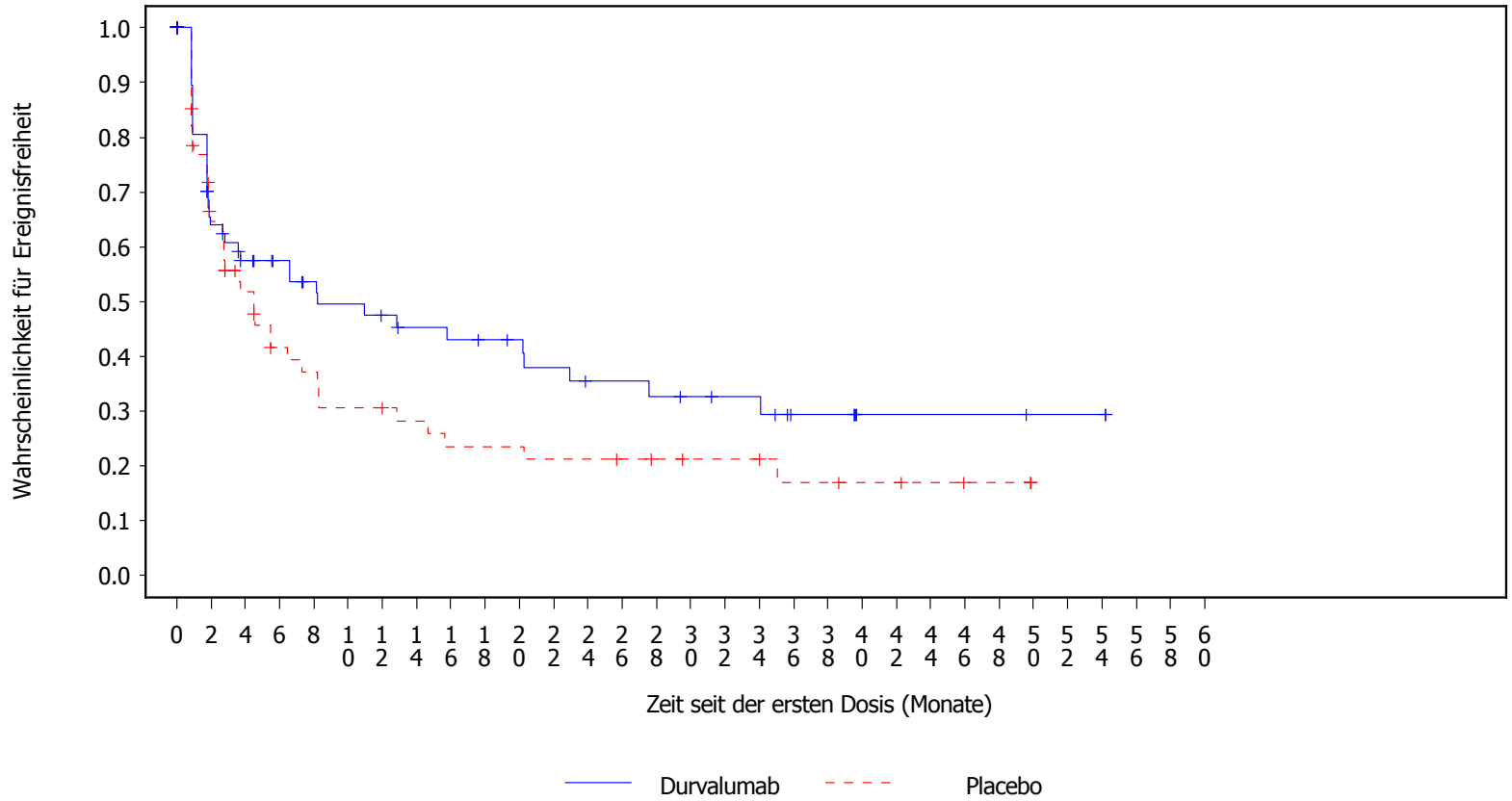
Figure 3.6.1.24 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion for PD-L1-Status - DEU=TC and IC <1%
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

78	41	34	30	26	24	22	20	19	18	17	15	13	13	12	11	10	10	6	6	2	2	2	2	2	1	1	1	0	0	0	Durvalumab
73	36	26	19	17	14	14	12	10	10	10	9	9	8	7	6	6	6	4	4	3	3	2	1	1	0	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreai ttesubpreai

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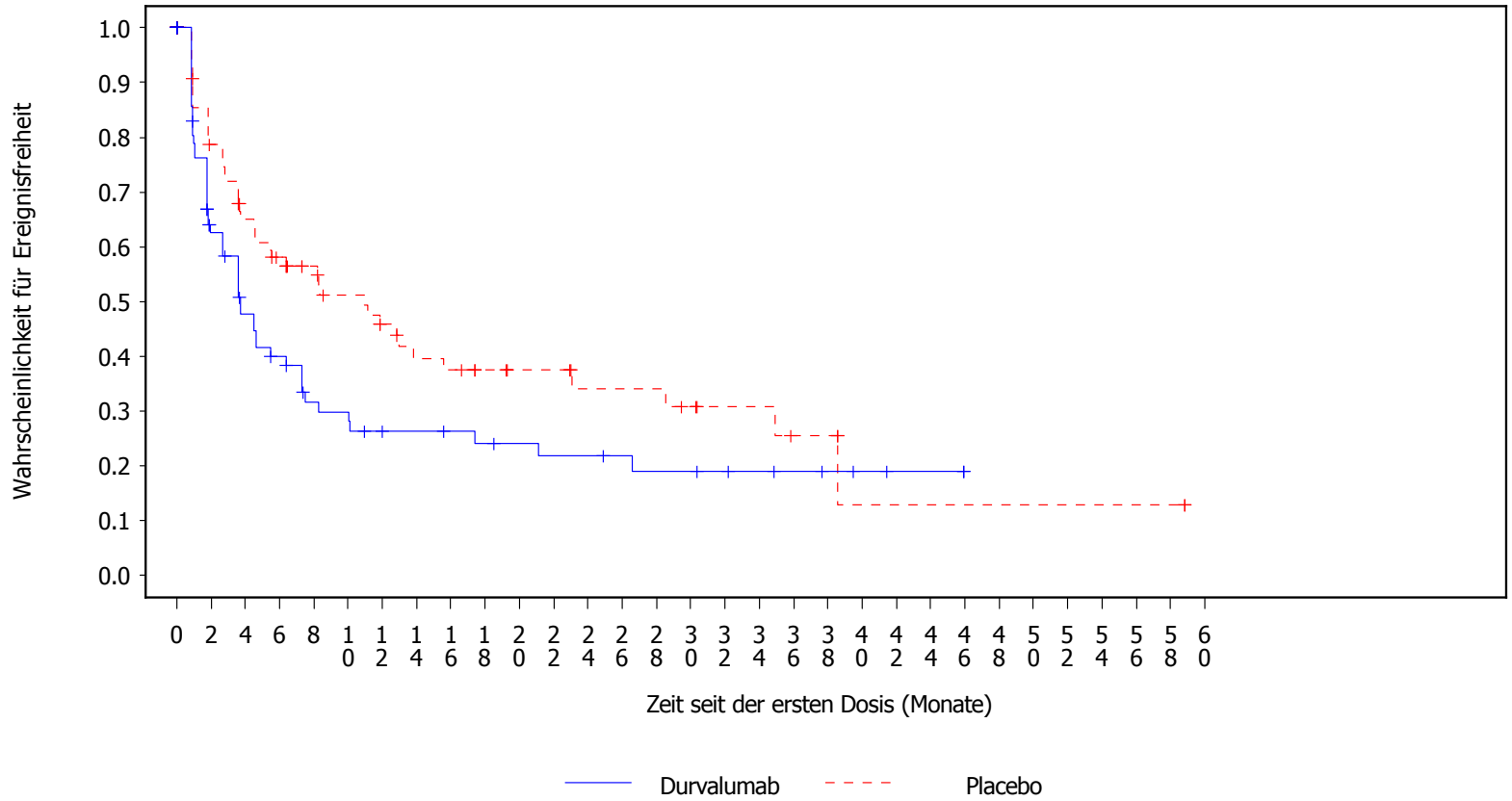
Figure 3.6.1.25 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Soziale Funktion for PD-L1-Status - DEU=TC or IC >=1%
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

84	43	31	25	18	17	13	13	12	11	10	9	9	8	7	7	6	5	4	3	2	1	1	0	0	0	0	0	0	0	Durvalumab
98	58	46	39	33	28	23	19	18	15	13	13	10	10	10	8	6	6	4	4	1	1	1	1	1	1	1	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreaj ttesubpreaj

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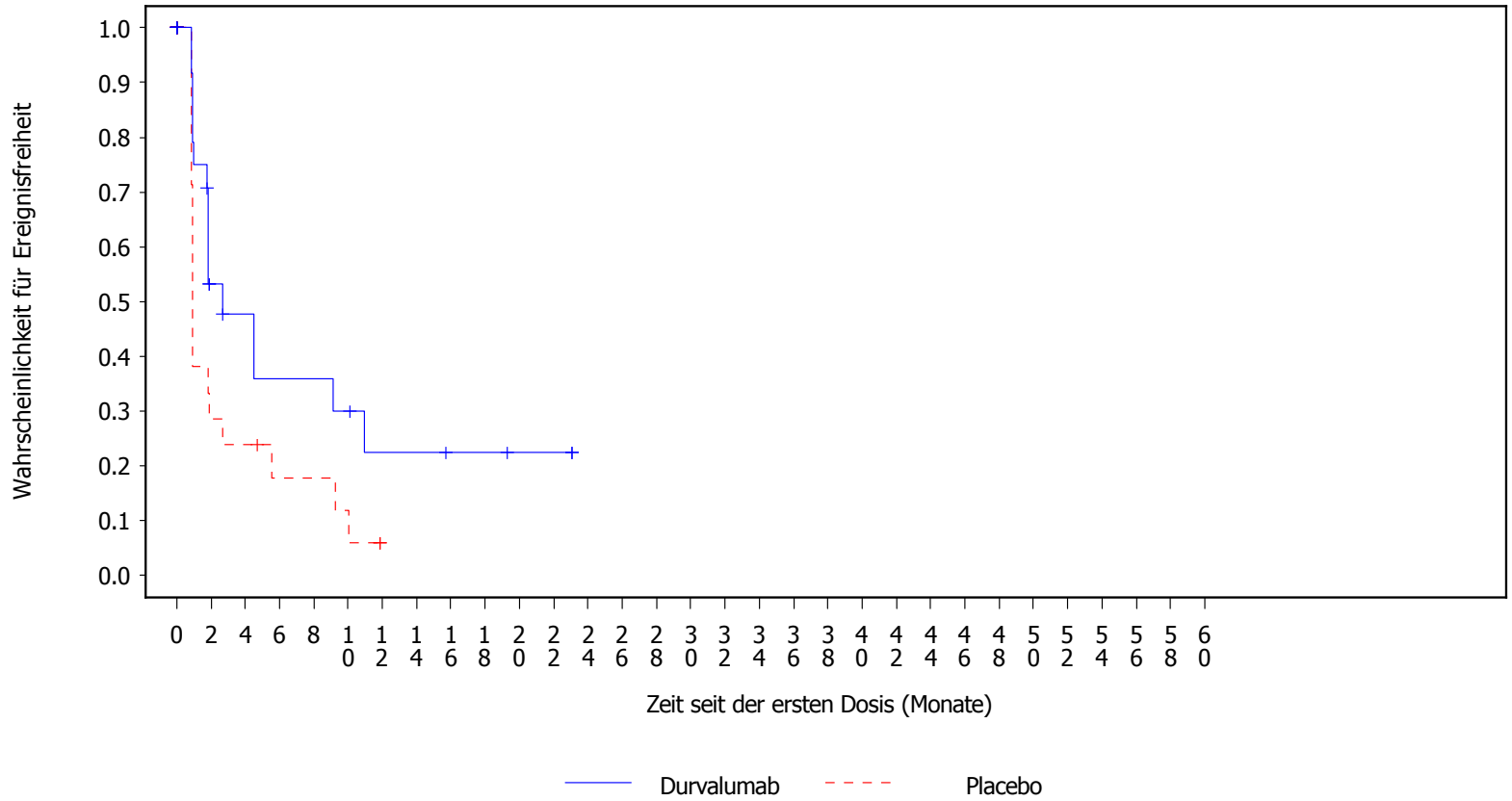
Figure 3.6.1.26 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue for Bestes Ansprechen auf cCRT - DEU=CR
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

31	10	8	6	6	5	3	3	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
34	6	5	3	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreak 07NOV2024:14:41

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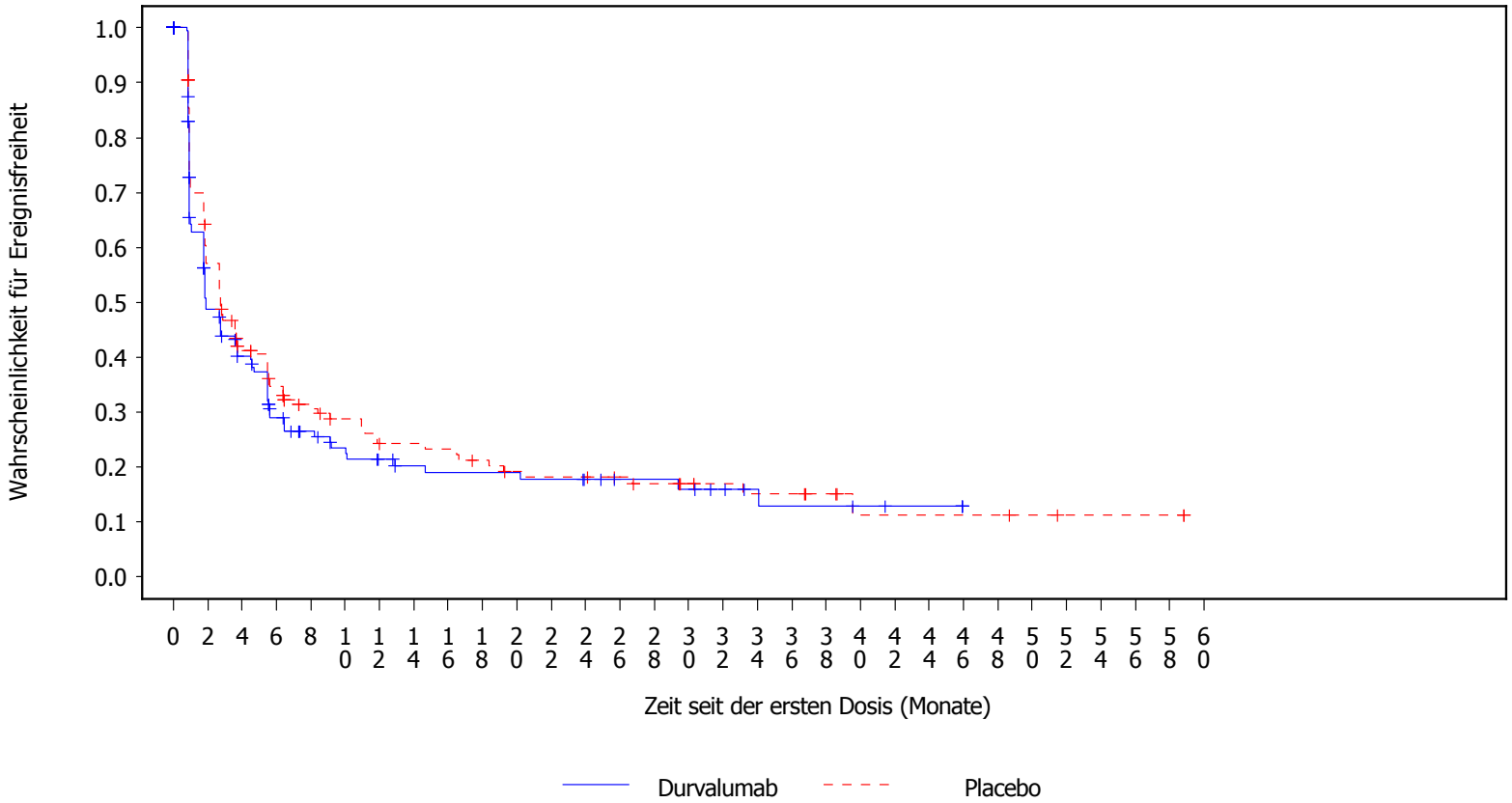
Figure 3.6.1.27 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue for Bestes Ansprechen auf cCRT - DEU=PR
Full Analysis Set, DCO 15JAN2024



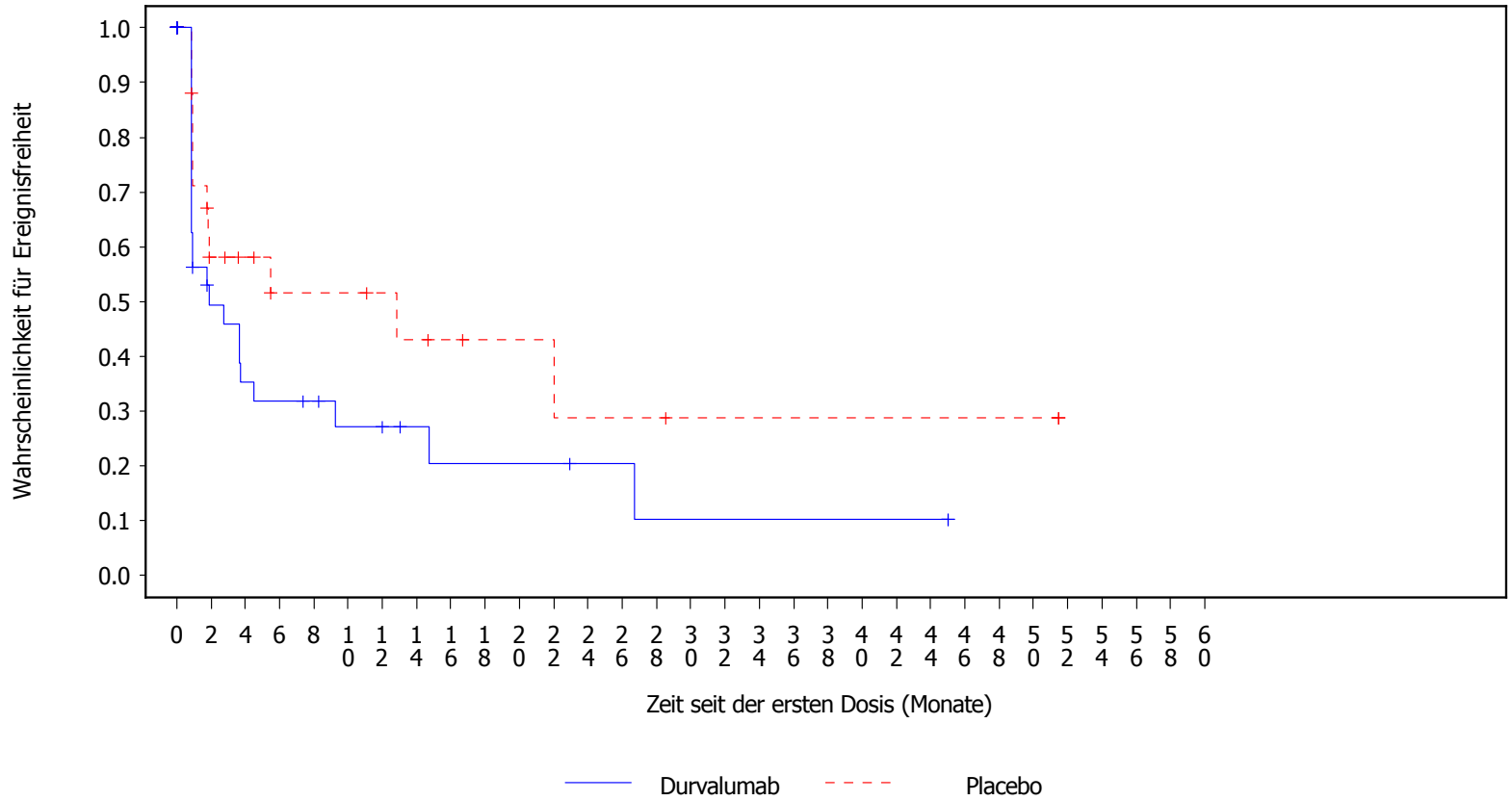
Anzahl an Patienten unter Risiko:

191	171	155	136	128	123	119	116	115	115	115	114	112	110	110	9	7	5	4	4	3	2	2	0	0	0	0	0	0	0	Durvalumab
200	188	158	146	136	131	126	125	124	121	118	117	117	115	113	11	9	8	8	6	3	3	3	3	3	2	1	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreal 07NOV2024:14:41

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.1.28 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Fatigue for Bestes Ansprechen auf cCRT - DEU=SD
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

42	14	10	9	8	6	5	4	3	3	3	3	2	2	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	Durvalumab
32	12	10	7	7	7	6	5	4	3	3	3	2	2	2	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpream 07NOV2024:14:41

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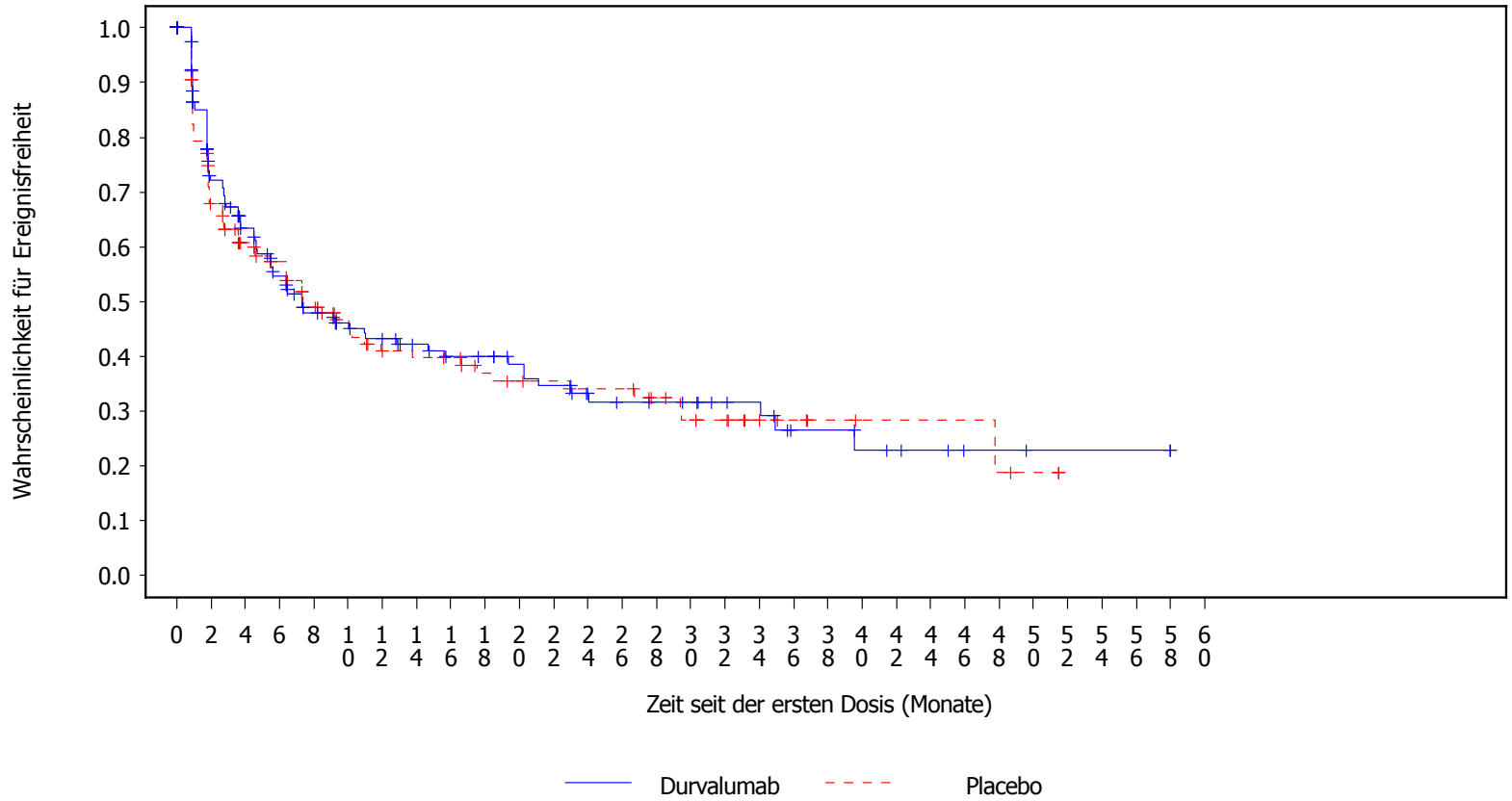
Figure 3.6.1.29 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust for Vorheriges Radiochemotherapieregime - DEU=Täglich
Full Analysis Set, DCO 15JAN2024



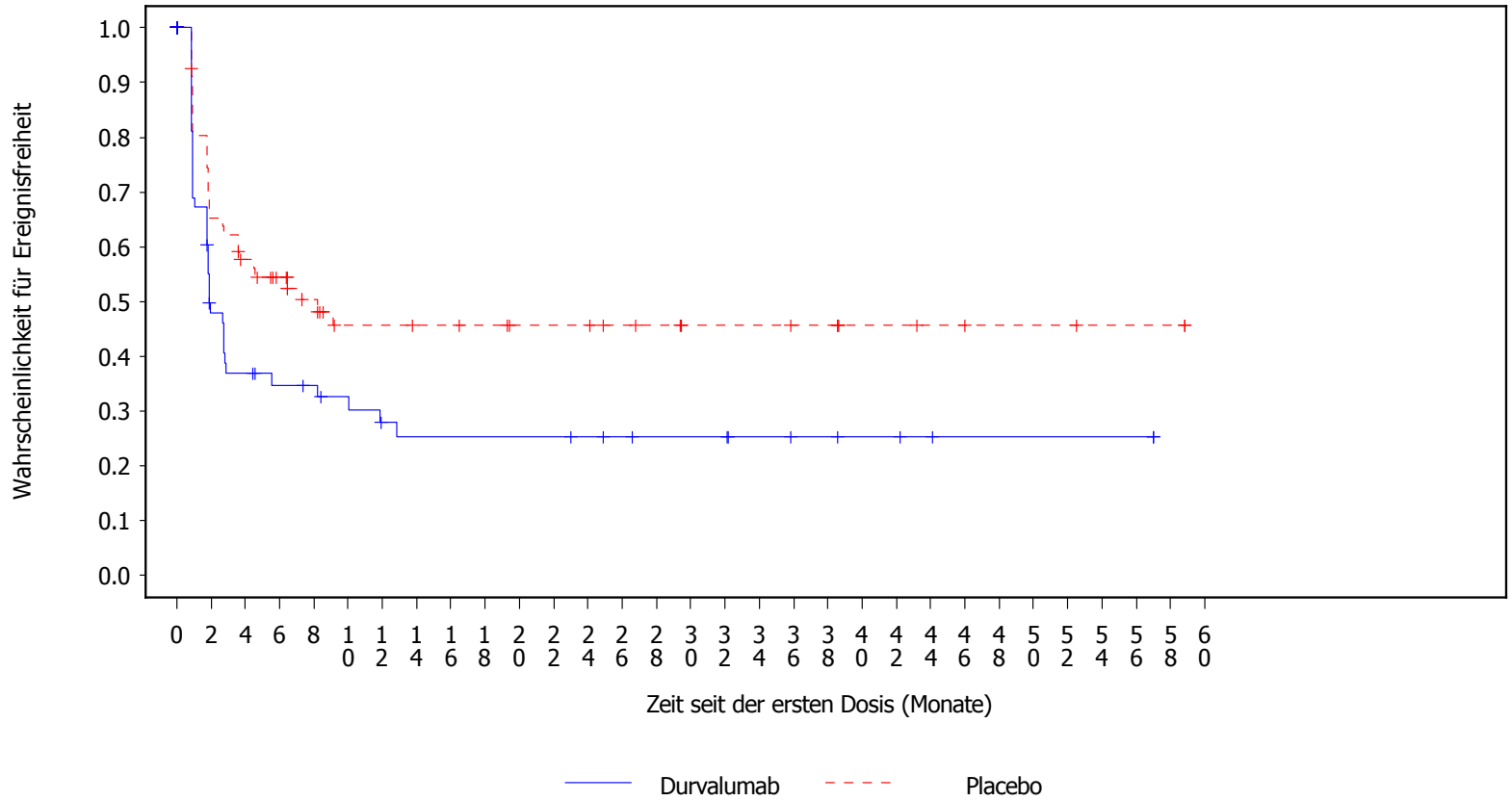
Anzahl an Patienten unter Risiko:

195	101	82	67	54	48	43	38	34	33	29	26	21	19	18	17	14	13	8	8	6	5	4	2	2	1	1	1	1	0	0	Durvalumab
187	88	71	63	50	41	34	32	31	26	24	23	21	21	17	14	12	8	6	4	3	3	3	3	2	1	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubprean 07NOV2024:14:41

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.1.30 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Appetitverlust for Vorheriges Radiochemotherapieregime - DEU=Zweimal täglich
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

69	26	20	17	16	14	11	10	10	10	10	10	9	8	7	7	7	5	4	4	3	3	2	1	1	1	1	1	1	0	0	Durvalumab
79	43	36	30	23	17	17	16	16	15	13	13	13	11	10	8	8	8	7	7	4	4	3	2	2	2	2	1	1	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreao 07NOV2024:14:41

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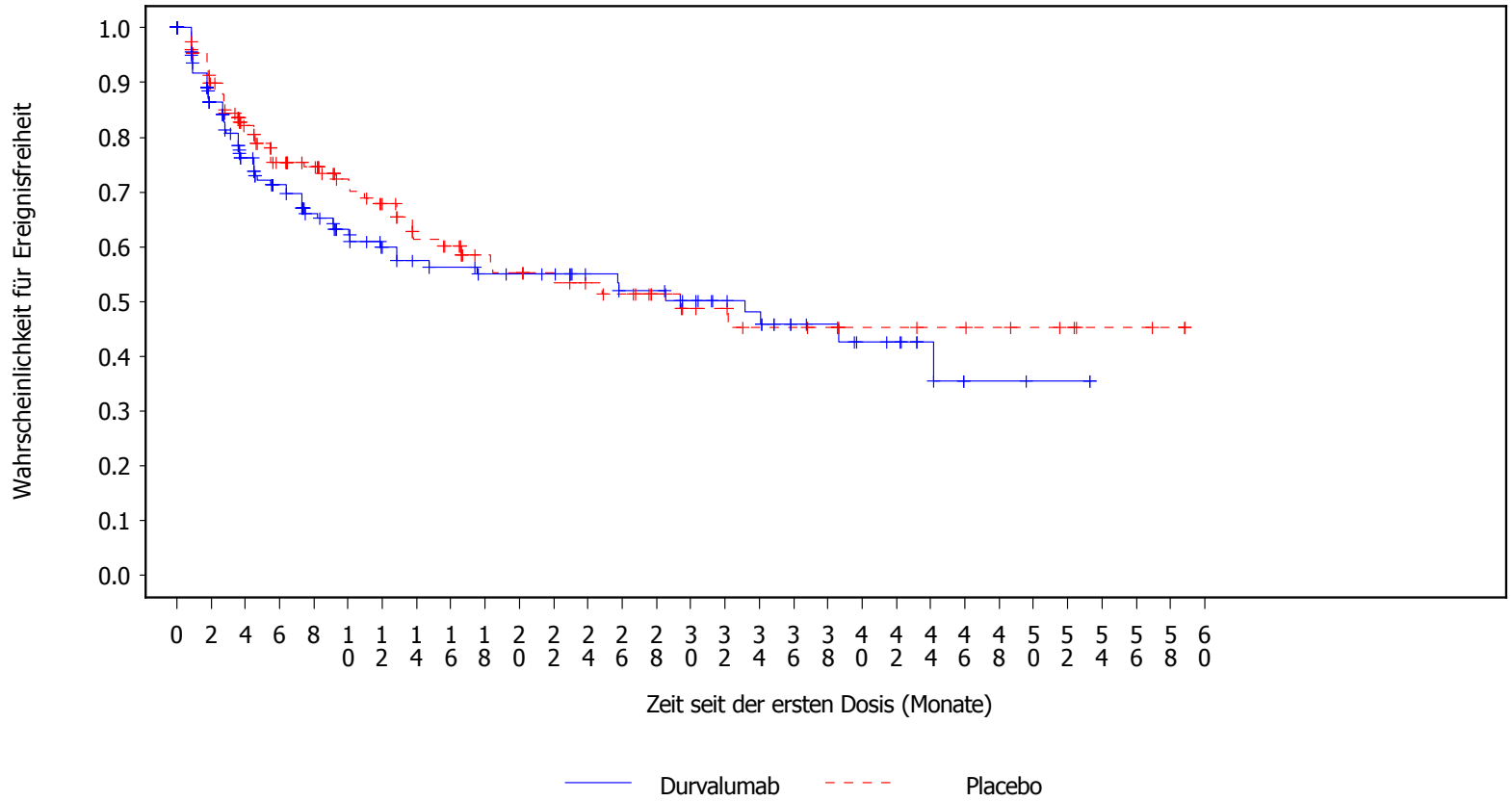
Figure 3.6.1.31 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö for Geschlecht - DEU=Männer
Full Analysis Set, DCO 15JAN2024



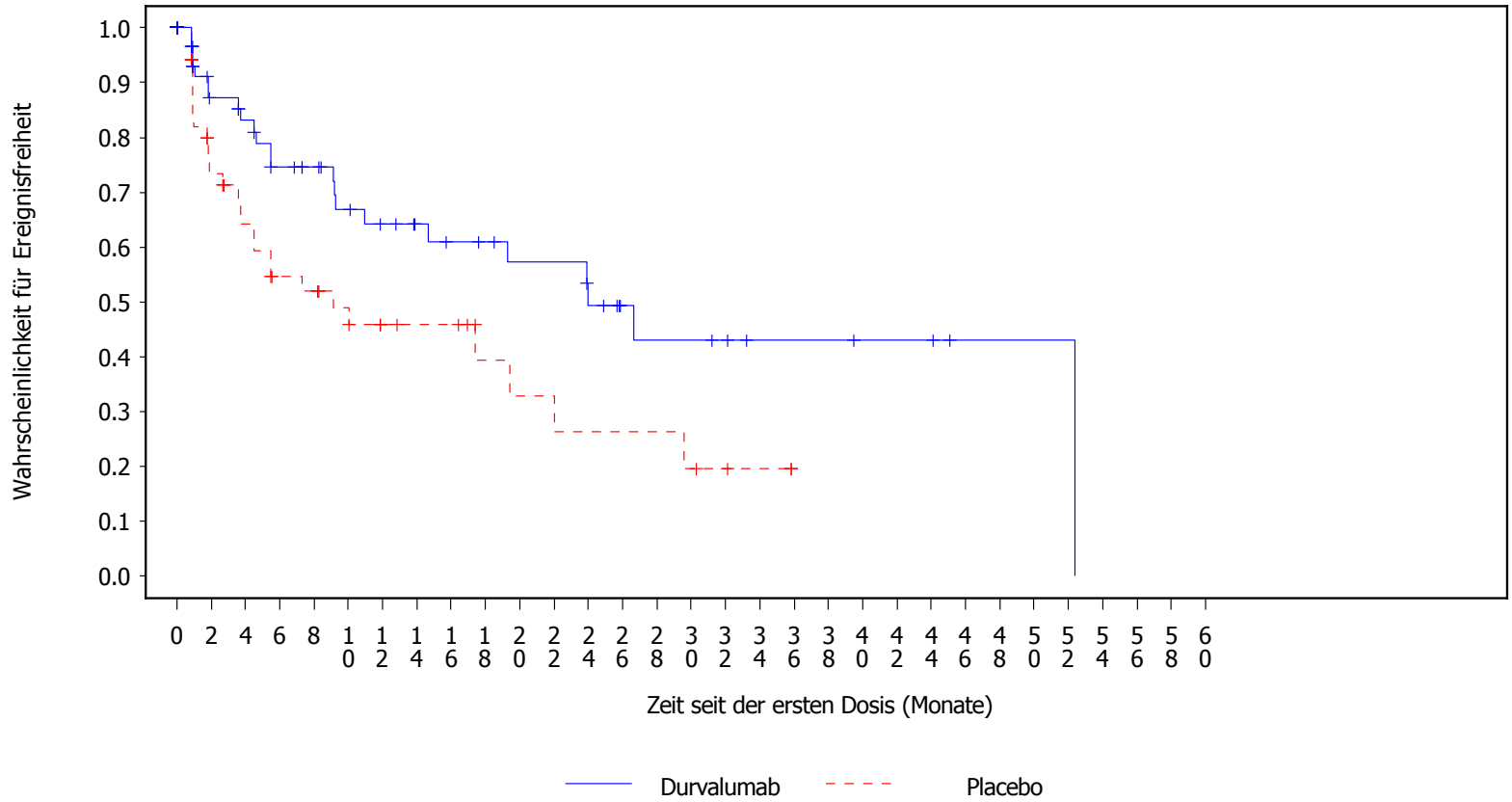
Anzahl an Patienten unter Risiko:

178	124	98	83	68	60	51	47	45	42	41	40	35	32	32	28	24	22	15	14	11	10	6	2	2	1	1	0	0	0	0	Durvalumab
188	129	104	87	76	64	57	46	43	35	33	30	27	25	20	16	15	12	12	11	8	8	7	7	6	5	4	2	2	1	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreap 07NOV2024:14:41

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.1.32 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Diarrhö for Geschlecht - DEU=Frauen
Full Analysis Set, DCO 15JAN2024



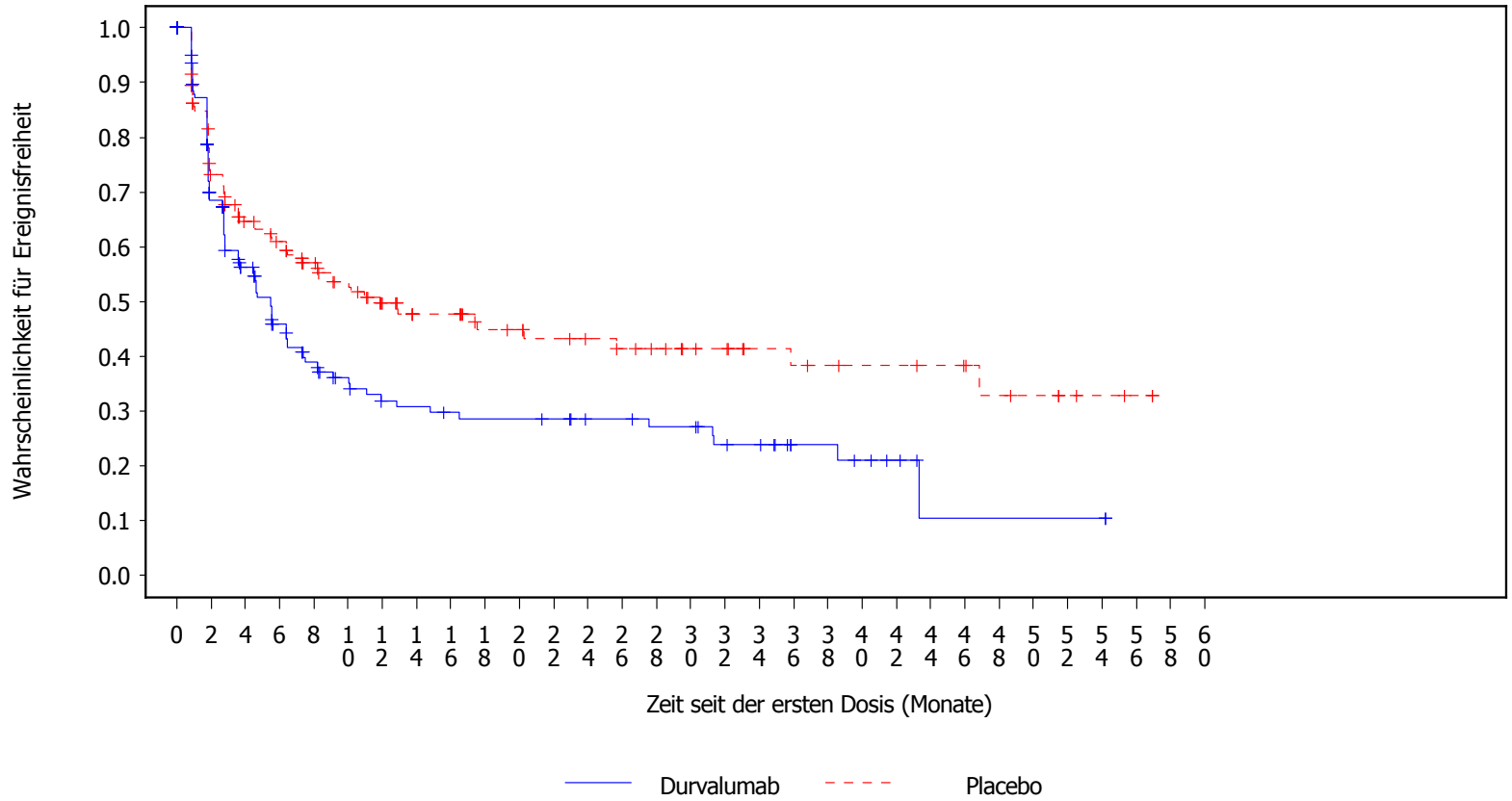
Anzahl an Patienten unter Risiko:

86	44	40	34	31	26	23	20	18	17	15	15	12	8	7	7	6	4	4	4	3	3	3	1	1	1	1	0	0	0	0	Durvalumab
78	34	27	21	20	16	11	10	10	6	5	5	4	4	4	3	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubpreaq 07NOV2024:14:41

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.1.33 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit for Geschlecht - DEU=Männer
Full Analysis Set, DCO 15JAN2024



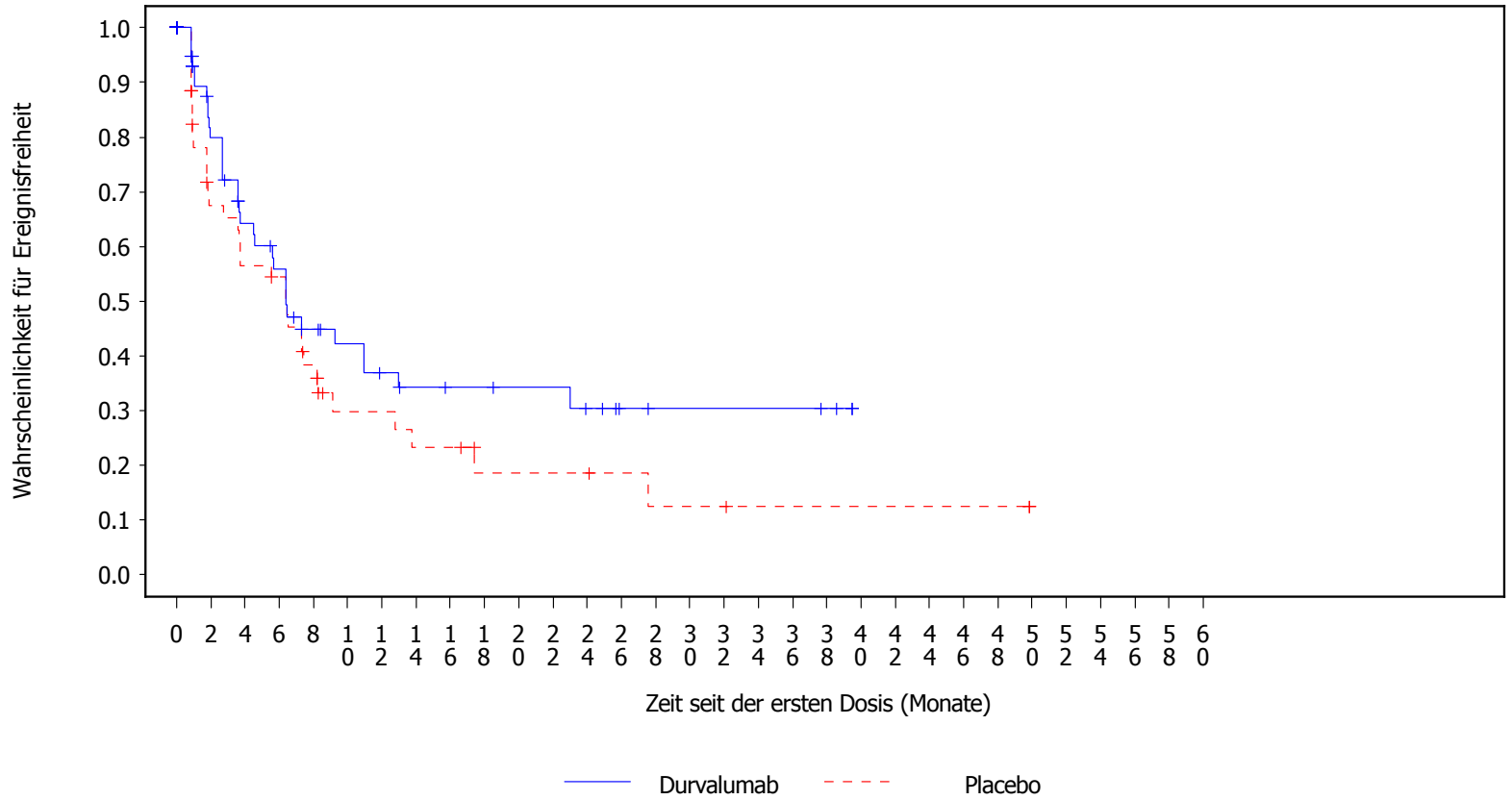
Anzahl an Patienten unter Risiko:

178	99	73	54	43	35	29	28	26	25	25	24	21	21	19	19	15	14	8	8	6	4	1	1	1	1	1	0	0	0	Durvalumab
188	105	87	79	68	59	49	39	39	31	30	27	25	23	21	18	17	13	12	11	10	10	9	8	6	5	3	2	1	0	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubpr.sas gttesubprear 07NOV2024:14:41

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.1.34 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-C30 Schlaflosigkeit for Geschlecht - DEU=Frauen
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

86	42	31	26	19	16	13	11	10	10	9	9	7	4	3	3	3	3	3	2	0	0	0	0	0	0	0	0	0	0	Durvalumab
78	31	26	24	16	9	9	7	7	4	4	4	4	3	2	2	2	1	1	1	1	1	1	1	1	0	0	0	0	0	Placebo

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Anhang 4-G6.3: EORTC QLQ-LC13

Nutzenbewertung nach AMNOG

Table 3.5.2.1 ADRIATIC: Summary of analysis of time to clinically meaningful deterioration in EORTC QLQ-LC13, symptom and single item scales
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe	264	184 (69,7)	1,1 [1,0; 1,4]	266	167 (62,8)	1,4 [0,9; 1,8]	1,16	[0,94; 1,43]	0,1766
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie	264	100 (37,9)	18,3 [12,8;33,2]	266	87 (32,7)	22,2 [12,8; NE]	1,08	[0,81; 1,44]	0,6323
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie	264	92 (34,8)	27,5 [15,7; NE]	266	84 (31,6)	31,3 [18,4; NE]	0,99	[0,73; 1,33]	0,9303
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe	264	60 (22,7)	NE [NE; NE]	266	47 (17,7)	NE [NE; NE]	1,13	[0,77; 1,67]	0,5270
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten	264	147 (55,7)	2,7 [1,6; 5,5]	266	128 (48,1)	4,6 [2,7; 9,1]	1,14	[0,90; 1,45]	0,2961
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie	264	127 (48,1)	6,5 [5,5;10,1]	266	129 (48,5)	6,5 [4,5;10,1]	0,89	[0,69; 1,14]	0,3564

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.5.2.1 ADRIATIC: Summary of analysis of time to clinically meaningful deterioration in EORTC QLQ-LC13, symptom and single item scales
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers	264	135 (51,1)	4,6 [3,6; 7,3]	266	136 (51,1)	2,8 [1,6; 6,4]	0,91	[0,72; 1,16]	0,4539
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter	264	125 (47,3)	8,3 [5,6;14,7]	266	143 (53,8)	4,5 [1,8; 6,4]	0,70	[0,55; 0,89]	0,0036*
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust	264	129 (48,9)	5,6 [2,8;11,0]	266	123 (46,2)	5,5 [1,7;11,0]	0,90	[0,70; 1,15]	0,4202
Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund	264	106 (40,2)	15,6 [8,3;29,4]	266	100 (37,6)	18,5 [8,2;30,3]	0,97	[0,74; 1,28]	0,8407

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Anhang 4-G6.3.1: EORTC QLQ-LC13 - Kaplan-Meier-Plot

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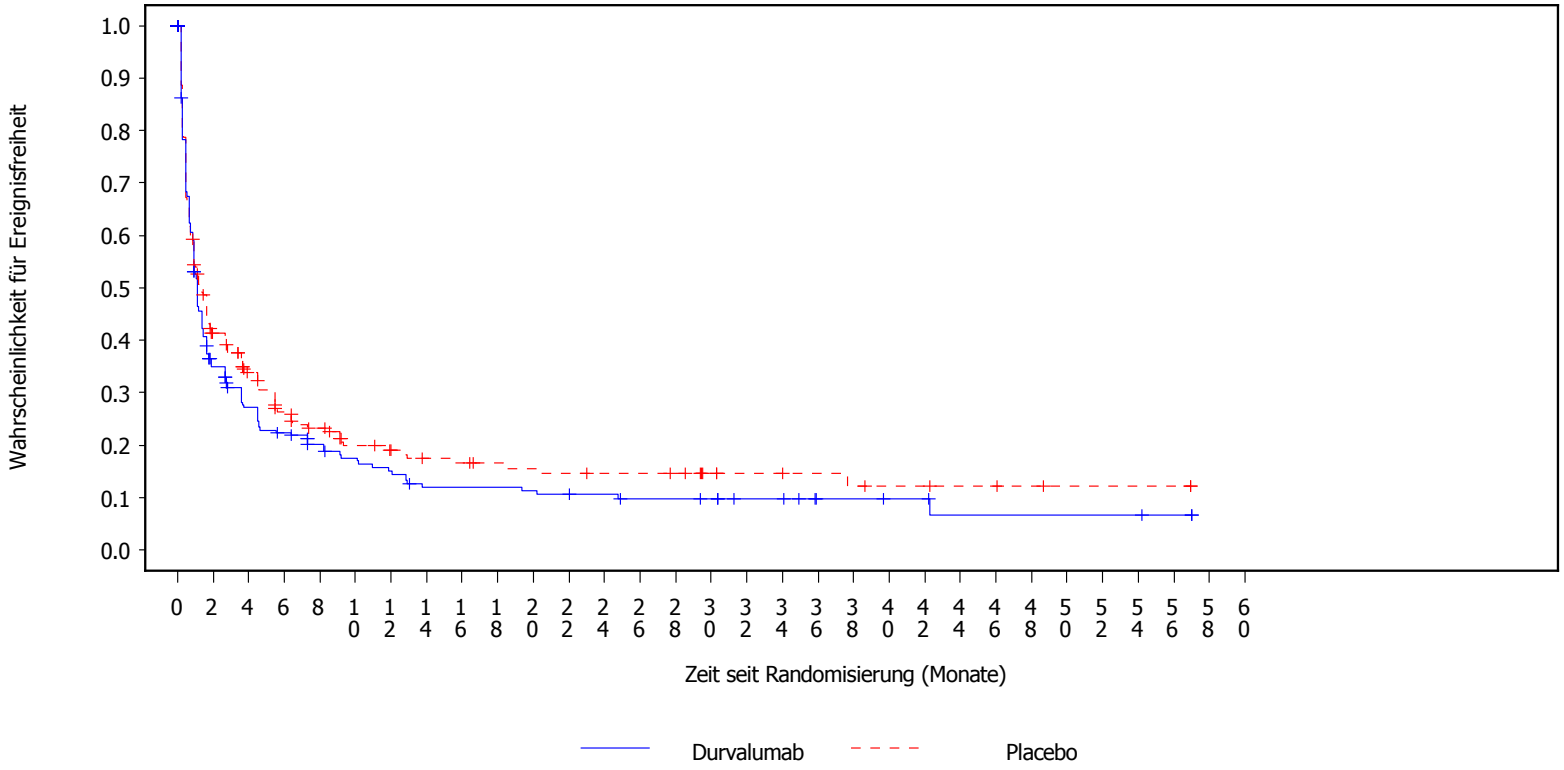
Figure 3.5.2.2 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

26470	51	41	33	28	24	18	18	18	17	16	15	13	13	12	9	9	5	5	4	4	2	2	2	2	2	1	0	0	Durvalumab
26681	60	44	36	27	24	20	19	17	16	15	14	14	13	9	7	7	6	5	4	4	3	3	2	1	1	1	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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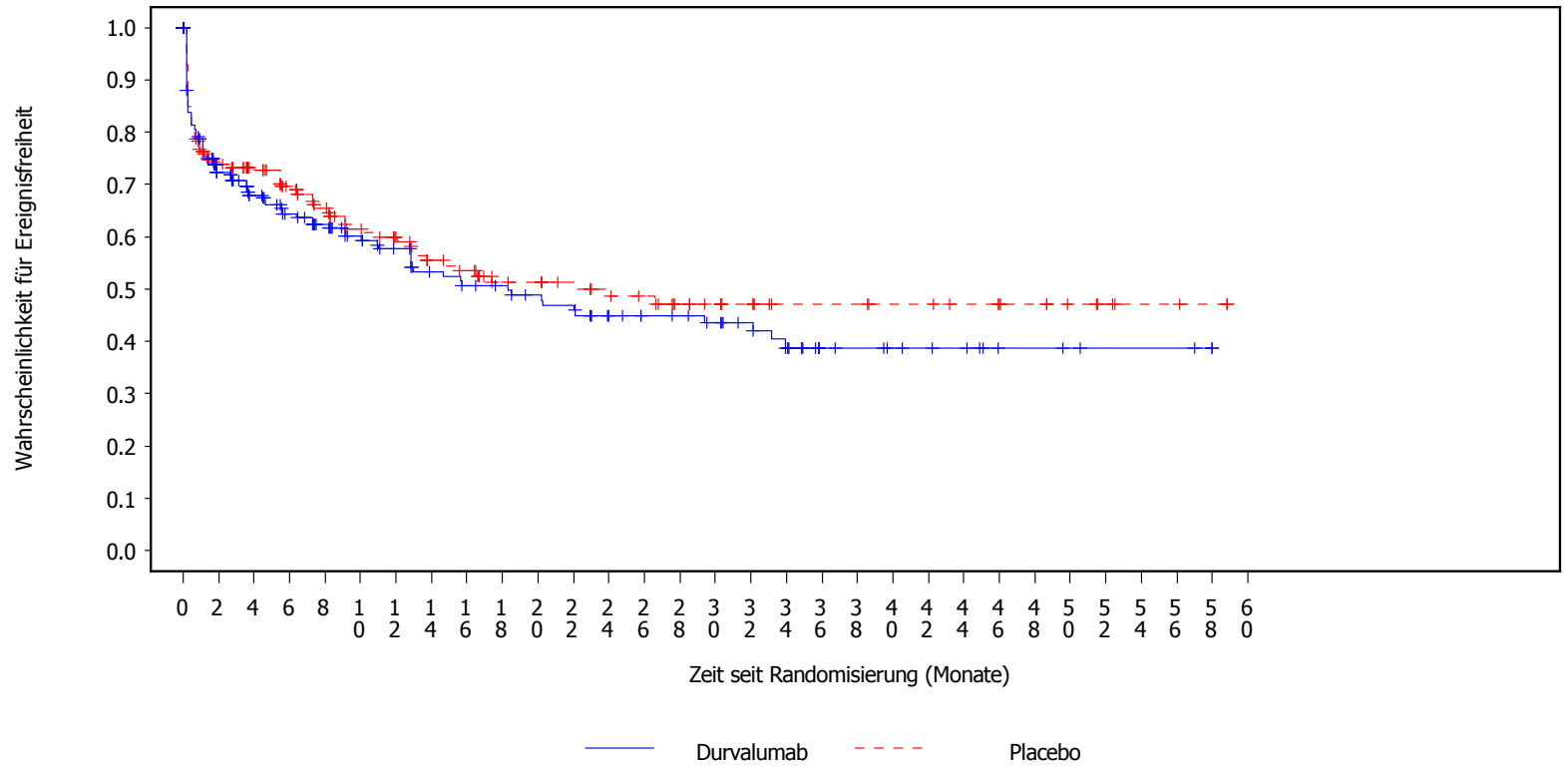
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.5.2.3 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	139	115	100	88	77	69	60	56	54	50	48	39	36	35	32	28	23	13	12	10	9	8	4	4	3	2	2	2	0	0	Durvalumab
266	141	123	105	90	77	69	58	54	44	43	39	35	33	27	24	21	16	16	16	14	14	12	10	9	6	4	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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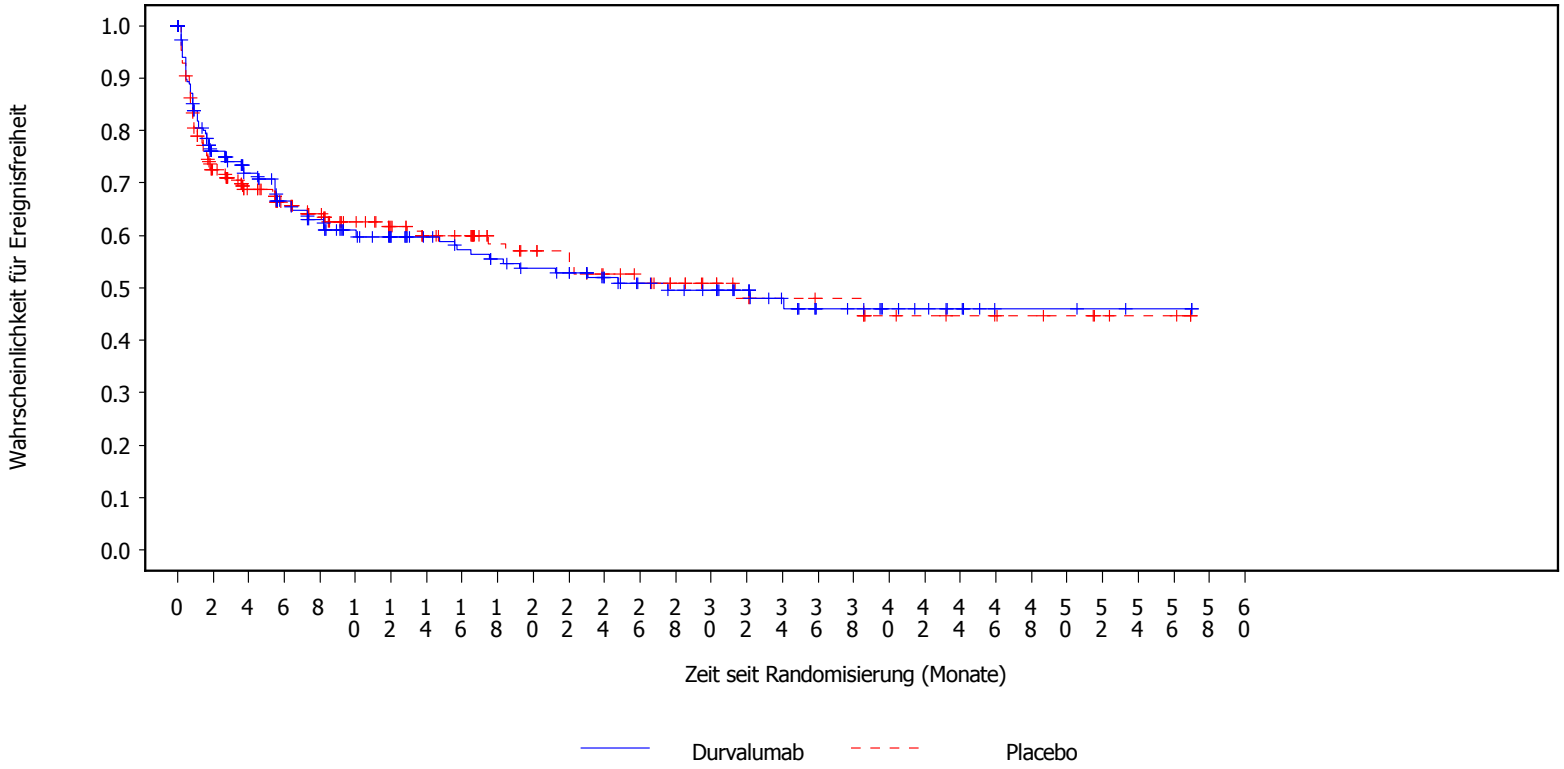
Figure 3.5.2.4 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	148	129	111	101	89	80	73	68	64	60	58	48	43	40	38	32	25	18	17	13	11	8	3	3	3	2	1	1	0	0	Durvalumab
266	141	115	100	87	75	67	58	55	43	40	38	32	29	25	21	17	15	14	14	10	9	8	7	6	5	3	2	2	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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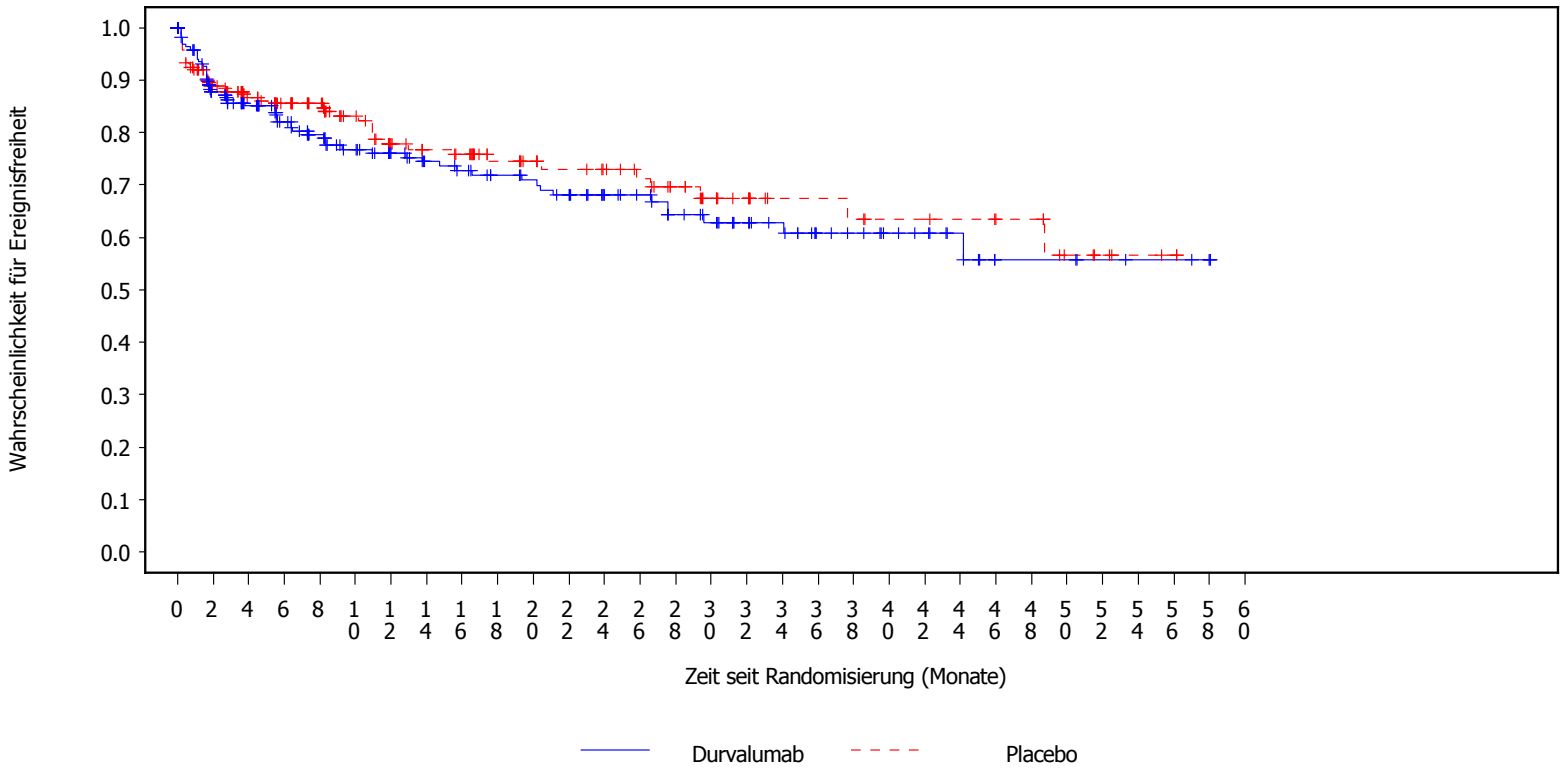
Figure 3.5.2.5 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	173	150	134	118	106	97	88	84	78	75	71	59	56	48	44	37	32	24	22	18	16	12	6	6	6	4	3	3	1	0	Durvalumab
266	171	147	130	116	96	80	73	70	58	53	49	46	42	36	29	24	17	17	16	14	14	13	11	11	6	4	2	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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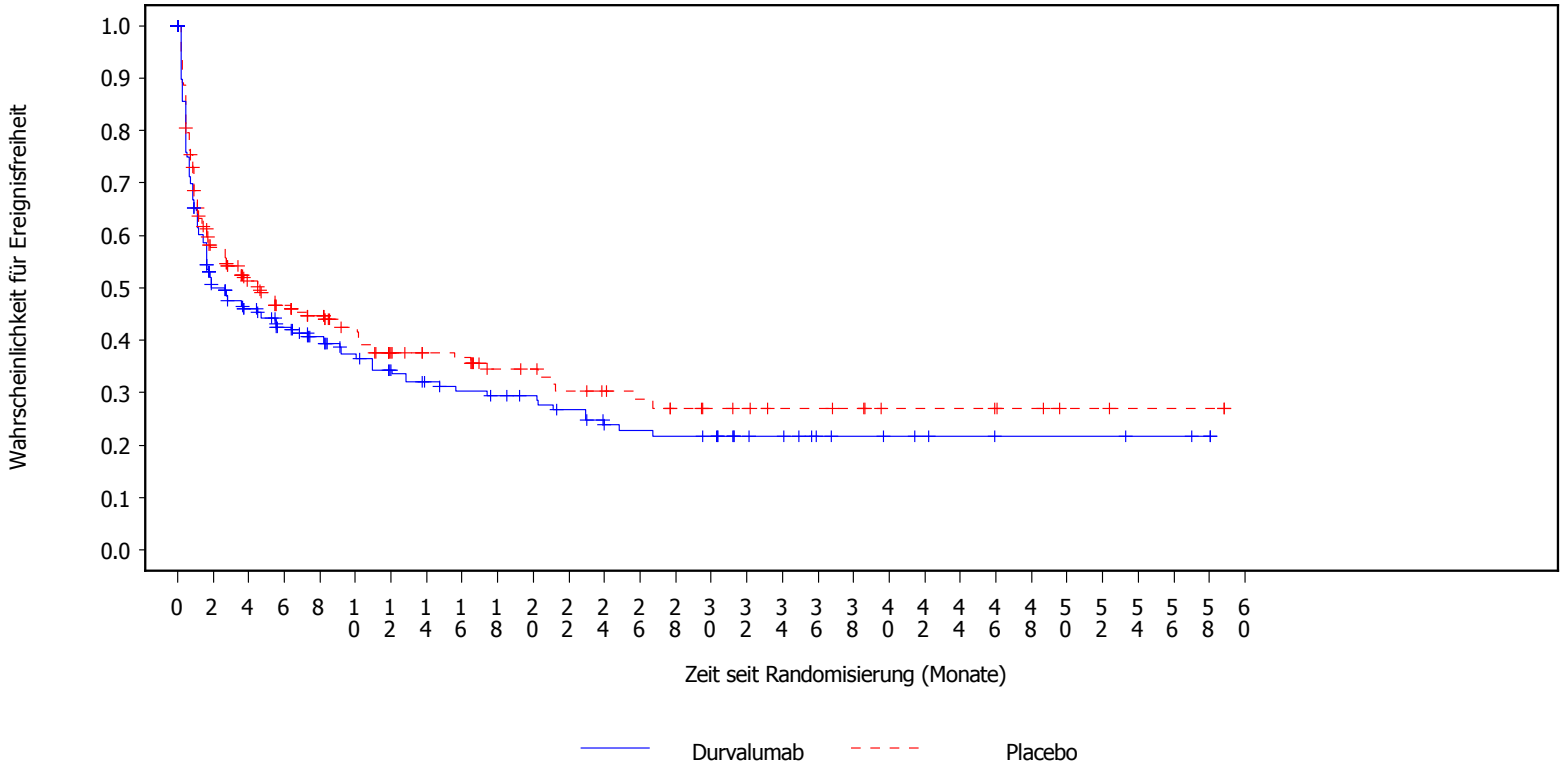
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.5.2.6 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	100	85	72	62	52	45	39	36	34	32	28	22	21	20	19	13	12	8	7	6	5	4	3	3	3	2	2	1	0	Durvalumab
266	112	89	75	65	54	42	37	36	27	26	22	20	18	15	13	12	10	10	9	6	6	6	5	4	2	2	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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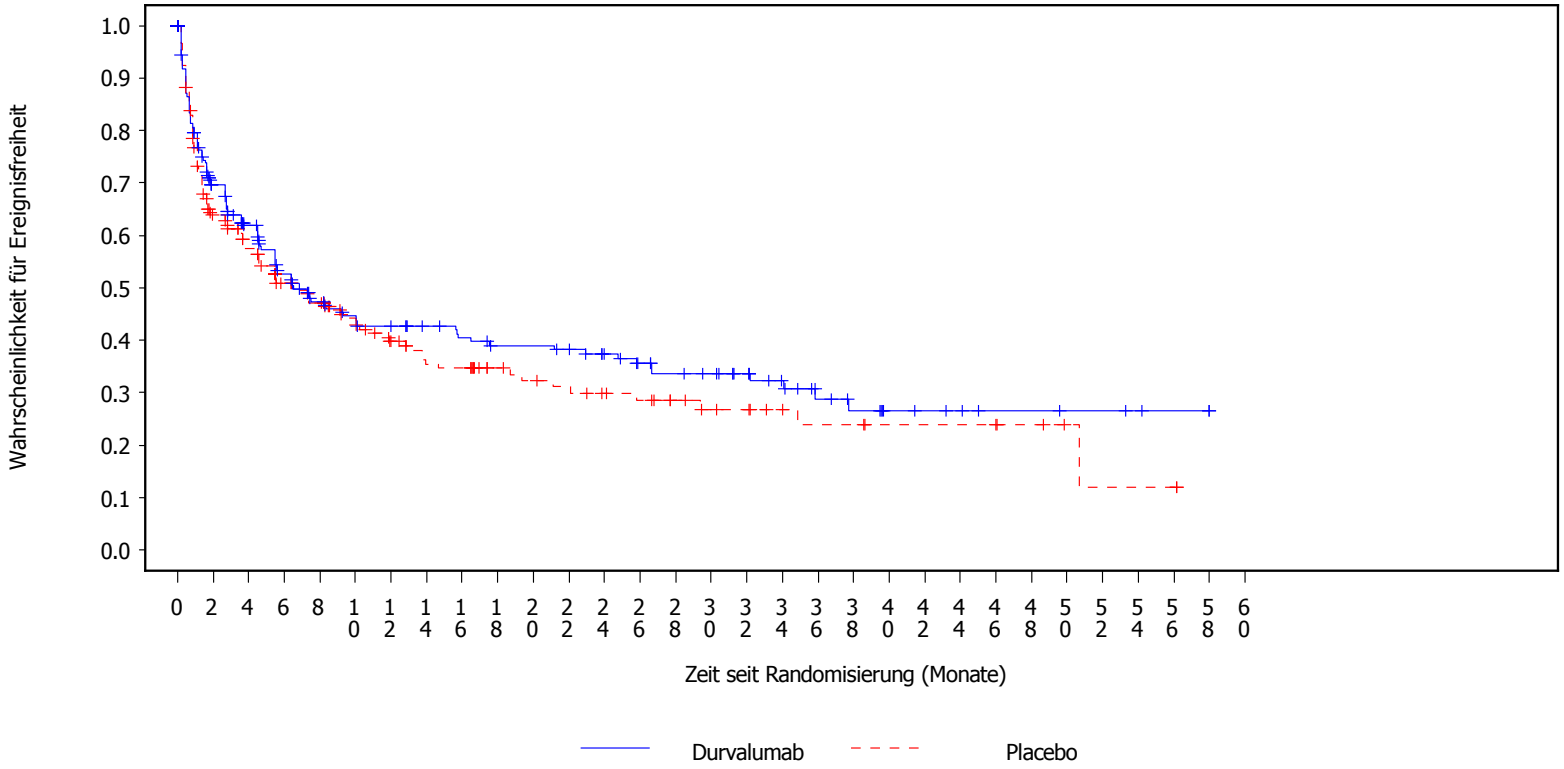
Figure 3.5.2.7 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	138	112	90	75	68	63	59	55	51	51	49	43	38	34	32	27	21	15	12	8	7	6	4	4	3	3	2	1	0	0	Durvalumab
266	125	106	85	75	61	50	41	40	31	28	26	23	21	17	14	13	10	8	8	6	6	6	5	4	2	1	1	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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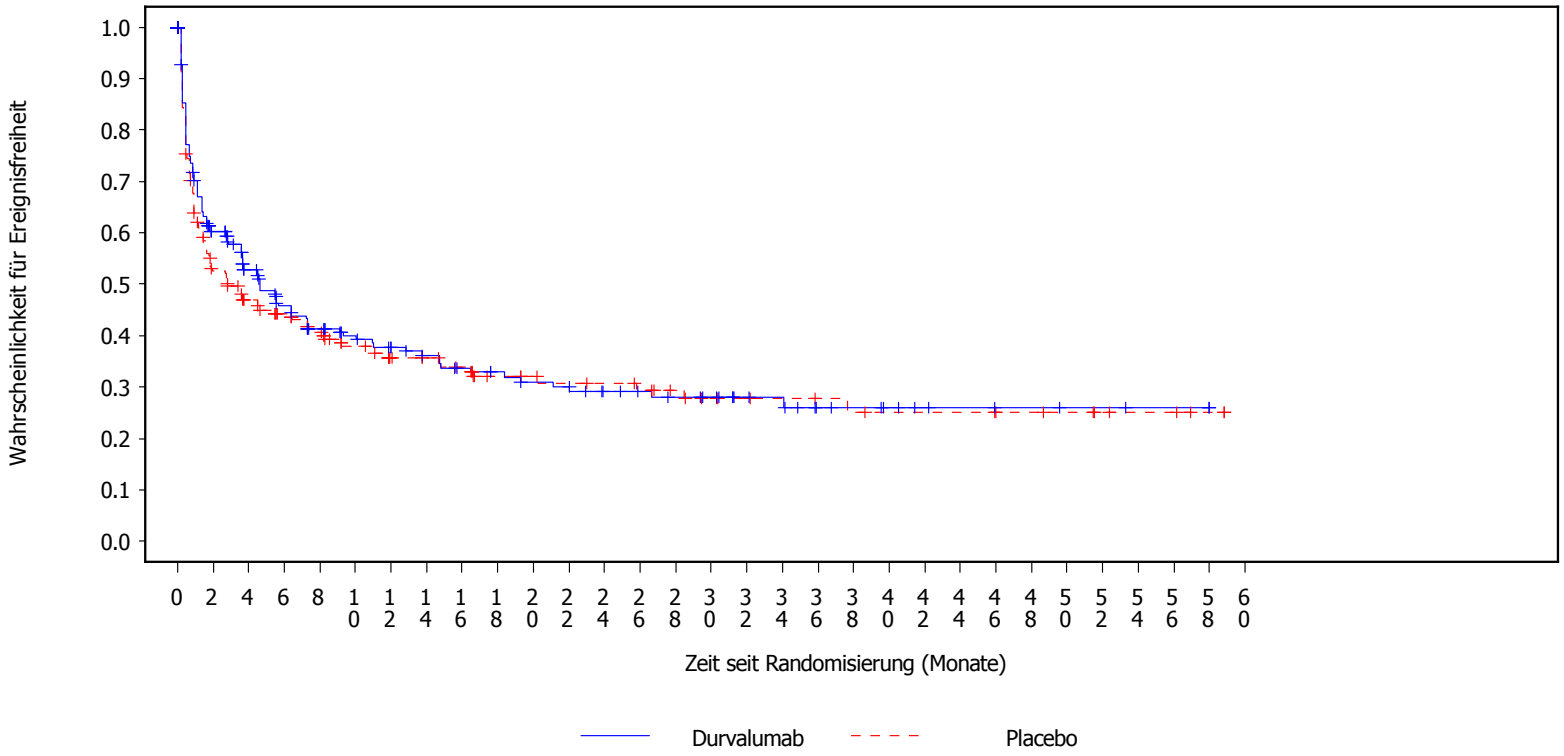
Figure 3.5.2.8 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	120	93	75	63	55	49	44	39	36	33	32	27	25	23	21	16	15	10	9	7	5	4	3	3	2	2	1	1	0	0	Durvalumab
266	105	87	76	65	54	44	41	37	28	26	24	23	21	18	15	13	12	11	10	9	9	9	7	7	6	4	3	3	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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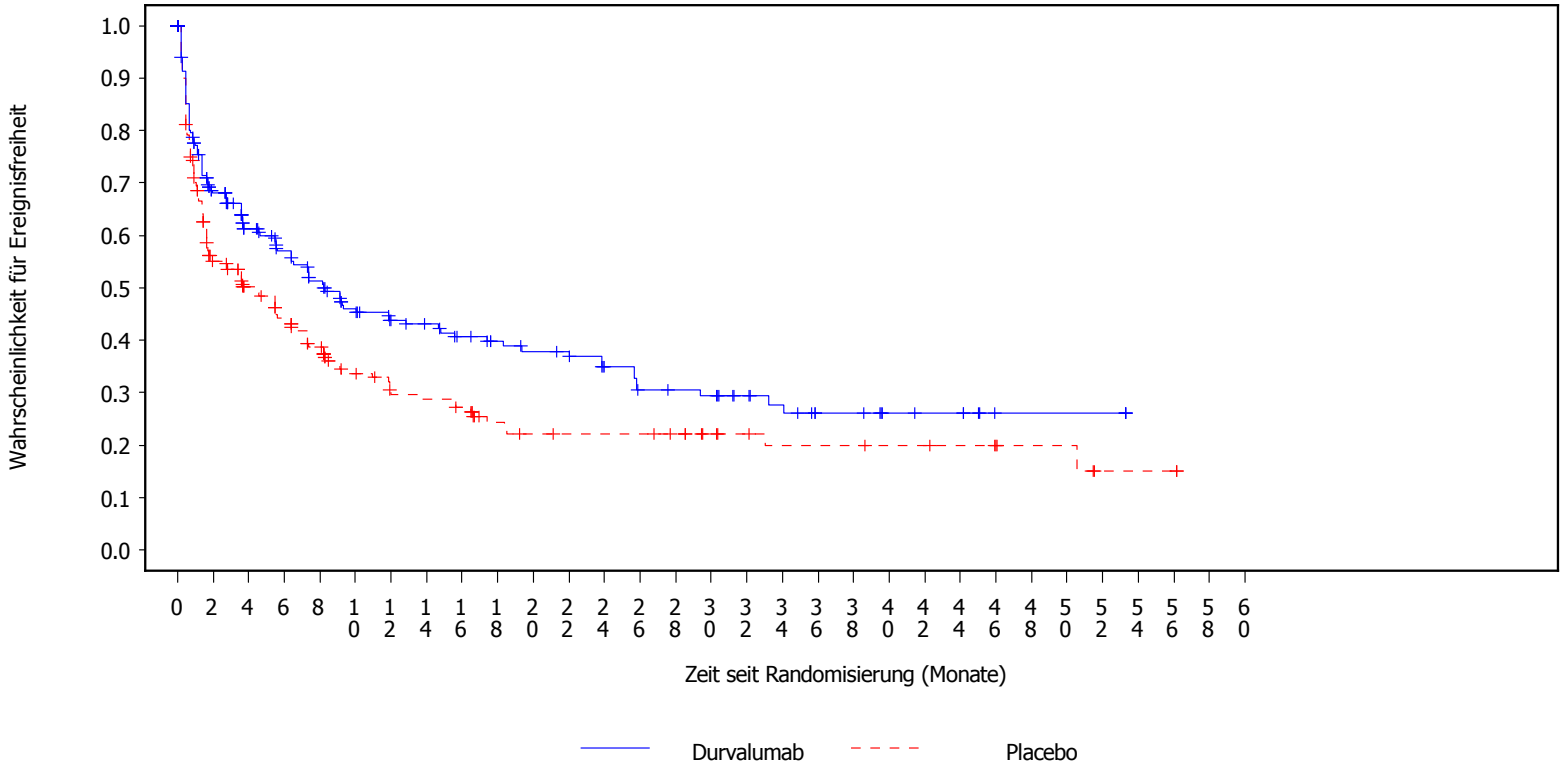
Figure 3.5.2.9 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	136	107	93	80	66	57	54	48	43	40	39	32	27	26	25	20	17	12	12	8	7	7	2	2	2	2	0	0	0	0	Durvalumab
266	105	87	74	60	44	36	35	32	23	20	19	19	19	17	13	11	9	9	9	8	8	7	5	4	4	1	1	1	0	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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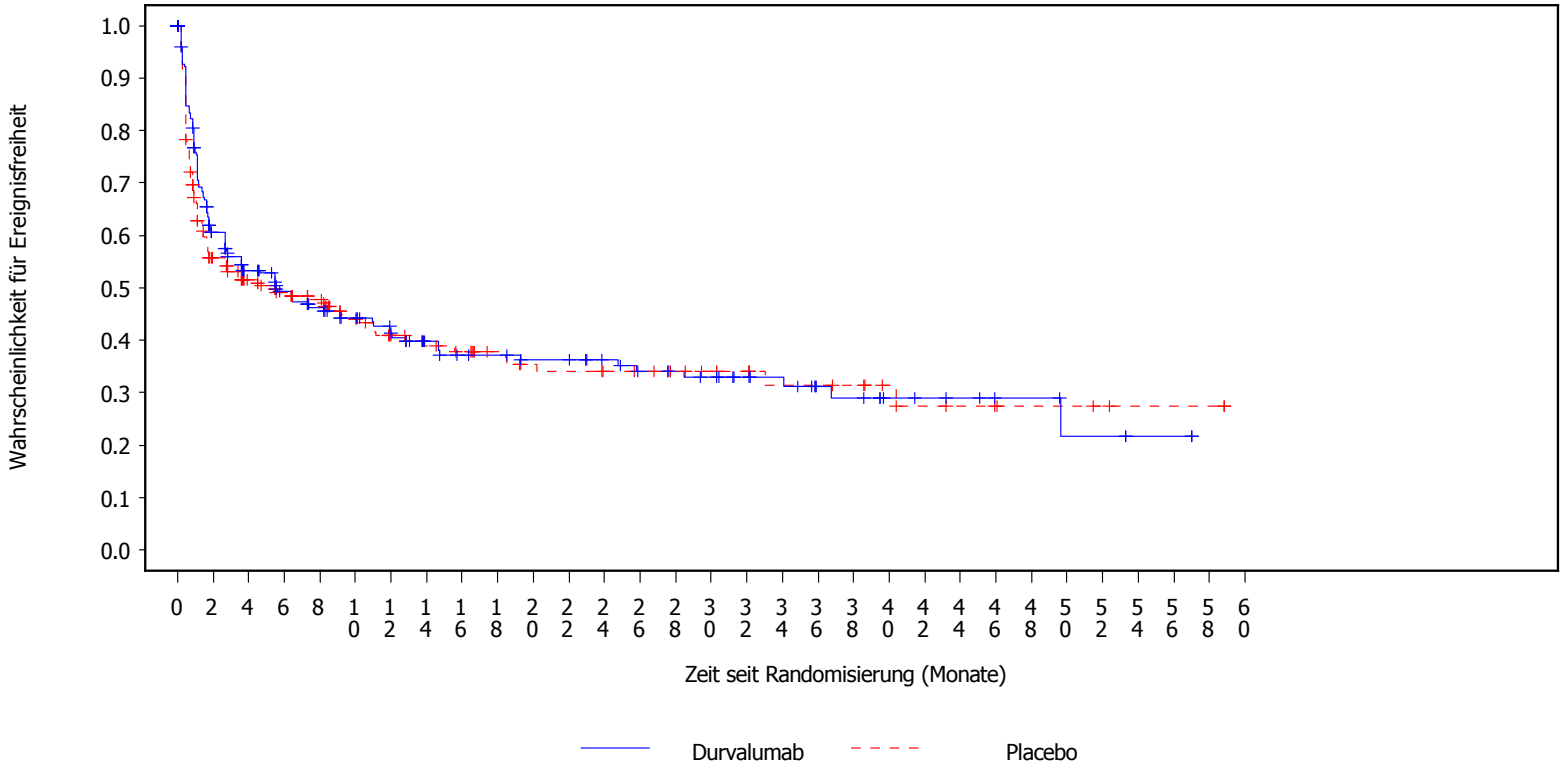
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.5.2.10 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	121	97	81	72	64	55	47	42	41	38	38	34	30	28	26	22	20	14	13	9	8	7	5	5	3	3	1	1	0	0	Durvalumab
266	107	89	79	70	56	46	39	36	31	27	26	24	23	20	18	16	12	12	11	8	6	5	4	3	3	2	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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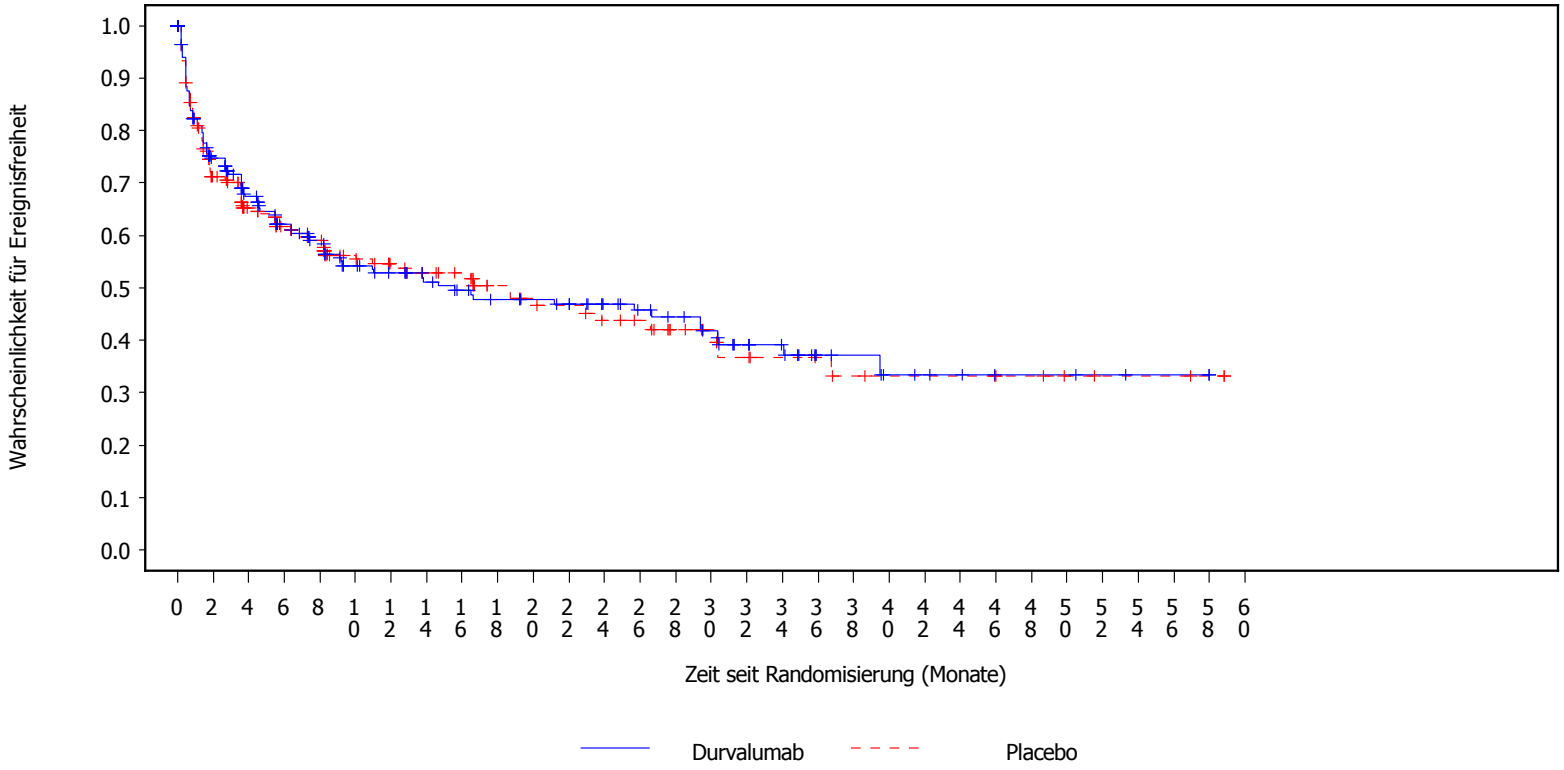
Figure 3.5.2.11 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	151	121	101	89	75	69	63	58	54	52	50	42	38	35	31	24	20	11	10	7	6	5	3	3	3	2	1	1	0	0	Durvalumab
266	139	114	99	86	70	59	52	49	39	35	33	29	27	21	17	13	11	10	8	7	7	7	5	5	3	2	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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Anhang 4-G6.3.2: EORTC QLQ-LC13 - Subgruppenanalysen

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Table 3.6.2.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	24 (66,7)	1,2 [0,7; 1,6]	37	24 (64,9)	0,6 [0,3; 3,6]	0,93	[0,53; 1,65]	0,8058
Stadium III	228	160 (70,2)	1,1 [0,9; 1,4]	229	143 (62,4)	1,4 [1,0; 1,9]	1,19	[0,95; 1,49]	0,1308
Interaktions p-Wert									0,4314
TNM Status (eCRF) - DEU									
Stadium I/II	33	22 (66,7)	1,3 [0,7; 2,7]	34	21 (61,8)	0,5 [0,3; 5,6]	0,91	[0,50; 1,66]	0,7555
Stadium III	231	162 (70,1)	1,1 [0,9; 1,4]	232	146 (62,9)	1,4 [1,0; 1,9]	1,19	[0,95; 1,49]	0,1263
Interaktions p-Wert									0,4091
Erhalt einer PCI (IVRS) - DEU									
Ja	142	100 (70,4)	1,1 [0,7; 1,4]	144	85 (59,0)	1,4 [0,9; 1,9]	1,05	[0,79; 1,41]	0,7405
Nein	122	84 (68,9)	1,1 [1,0; 1,6]	122	82 (67,2)	1,1 [0,7; 2,8]	1,29	[0,95; 1,75]	0,1070
Interaktions p-Wert									0,3469
Erhalt einer PCI (eCRF) - DEU									
Ja	142	100 (70,4)	1,1 [0,7; 1,4]	143	85 (59,4)	1,4 [0,9; 1,9]	1,05	[0,79; 1,41]	0,7405
Nein	122	84 (68,9)	1,1 [1,0; 1,6]	123	82 (66,7)	1,1 [0,7; 2,8]	1,29	[0,95; 1,75]	0,1070
Interaktions p-Wert									0,3469
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	27 (84,4)	1,1 [0,3; 1,4]	32	20 (62,5)	1,6 [0,7; 5,5]	2,12	[1,19; 3,84]	0,0107*
>=14 bis <28 Tage	79	53 (67,1)	1,4 [0,9; 2,7]	80	50 (62,5)	1,7 [0,7; 4,5]	1,26	[0,86; 1,86]	0,2391
>=28 Tage	153	104 (68,0)	1,1 [0,7; 1,6]	154	97 (63,0)	1,2 [0,7; 1,8]	0,95	[0,72; 1,26]	0,7295
Interaktions p-Wert									0,0434*
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	13 (81,3)	1,4 [0,5; 1,9]	24	17 (70,8)	1,2 [0,5; 7,3]	1,23	[0,59; 2,54]	0,5694
>=28 bis <56 Tage	104	67 (64,4)	1,1 [0,9; 2,8]	104	59 (56,7)	1,2 [0,7; 2,8]	1,11	[0,78; 1,58]	0,5604
>=56 bis <84 Tage	98	71 (72,4)	1,1 [0,7; 1,6]	76	50 (65,8)	1,6 [1,0; 2,7]	1,08	[0,75; 1,56]	0,6852
>=84 Tage	46	33 (71,7)	0,8 [0,5; 1,6]	62	41 (66,1)	0,9 [0,5; 3,6]	1,34	[0,84; 2,12]	0,2135
Interaktions p-Wert									0,8904
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	59 (64,8)	1,1 [1,0; 2,7]	88	56 (63,6)	1,7 [1,0; 3,6]	1,12	[0,77; 1,61]	0,5506
Cisplatin	173	125 (72,3)	1,0 [0,7; 1,4]	178	111 (62,4)	1,2 [0,7; 1,6]	1,17	[0,90; 1,51]	0,2385
Interaktions p-Wert									0,8527
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	130 (66,7)	1,1 [1,0; 1,6]	187	110 (58,8)	1,2 [0,7; 1,8]	1,14	[0,88; 1,47]	0,3244
Zweimal täglich	69	54 (78,3)	1,1 [0,7; 1,4]	79	57 (72,2)	1,4 [0,7; 2,8]	1,20	[0,82; 1,74]	0,3406
Interaktions p-Wert									0,8148
Bestes Ansprechen auf cCRT - DEU									
CR	31	20 (64,5)	1,2 [0,5; 4,5]	34	16 (47,1)	0,7 [0,5; 3,7]	0,98	[0,51; 1,92]	0,9511
PR	191	141 (73,8)	1,1 [0,9; 1,4]	200	133 (66,5)	1,2 [0,9; 1,7]	1,21	[0,95; 1,54]	0,1152
SD	42	23 (54,8)	1,4 [0,5; 3,6]	32	18 (56,3)	2,8 [0,7;11,9]	1,04	[0,56; 1,95]	0,9105
Interaktions p-Wert									0,7787
Geschlecht - DEU									
Männer	178	134 (75,3)	1,1 [1,0; 1,4]	188	121 (64,4)	1,4 [1,0; 2,7]	1,18	[0,92; 1,51]	0,1849
Frauen	86	50 (58,1)	0,9 [0,7; 1,8]	78	46 (59,0)	1,0 [0,5; 1,9]	1,07	[0,71; 1,59]	0,7577
Interaktions p-Wert									0,6671
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.2.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	116 (72,5)	1,1 [0,9; 1,4]	162	105 (64,8)	1,2 [0,7; 1,6]	1,03	[0,79; 1,34]	0,8201
>=65 Jahre	104	68 (65,4)	1,1 [0,9; 1,6]	104	62 (59,6)	2,7 [0,7; 5,5]	1,36	[0,96; 1,92]	0,0818
Interaktions p-Wert									0,2143
PD-L1-Status - DEU									
TC and IC <1%	78	59 (75,6)	1,0 [0,7; 1,4]	73	44 (60,3)	1,9 [1,2; 3,6]	1,49	[1,01; 2,21]	0,0444*
TC or IC >=1%	84	65 (77,4)	1,1 [0,7; 1,9]	98	66 (67,3)	1,0 [0,5; 1,6]	1,00	[0,71; 1,41]	0,9835
Interaktions p-Wert									0,1290
Raucherstatus - DEU									
Raucher	241	166 (68,9)	1,1 [1,0; 1,4]	240	148 (61,7)	1,4 [0,9; 2,7]	1,17	[0,94; 1,46]	0,1708
Nichtraucher	23	18 (78,3)	0,8 [0,3; 1,9]	26	19 (73,1)	1,2 [0,5; 1,8]	1,04	[0,54; 2,00]	0,8965
Interaktions p-Wert									0,7474
Abstammung - DEU									
Weiß	130	80 (61,5)	1,1 [0,9; 1,6]	137	76 (55,5)	1,6 [0,9; 2,7]	1,13	[0,83; 1,55]	0,4412
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	0,6 [0,5; NE]	NC	[NC]	NC
Asiatisch	131	104 (79,4)	1,1 [0,9; 1,4]	121	88 (72,7)	1,2 [0,7; 2,8]	1,18	[0,89; 1,57]	0,2465
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8373
Geographische Region - DEU									
Asien	129	104 (80,6)	1,1 [0,9; 1,4]	120	87 (72,5)	1,2 [0,7; 2,8]	1,18	[0,89; 1,58]	0,2428
Europa	94	63 (67,0)	1,1 [0,9; 2,7]	112	67 (59,8)	1,4 [0,7; 1,8]	1,02	[0,72; 1,44]	0,8929
Nordamerika	41	17 (41,5)	0,8 [0,3; 3,6]	34	13 (38,2)	3,2 [0,3; 8,4]	1,61	[0,79; 3,40]	0,1919
Interaktions p-Wert									0,5143
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	91 (68,4)	1,4 [0,9; 1,6]	131	83 (63,4)	1,6 [1,1; 3,6]	1,27	[0,94; 1,71]	0,1137
1	131	93 (71,0)	1,0 [0,8; 1,2]	135	84 (62,2)	0,9 [0,5; 1,8]	1,03	[0,76; 1,38]	0,8610
Interaktions p-Wert									0,3179

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	10 (27,8)	NE [NE; NE]	37	7 (18,9)	NE [NE; NE]	1,52	[0,58; 4,18]	0,3928
Stadium III	228	90 (39,5)	14,7 [10,1;32,1]	229	80 (34,9)	15,6 [10,1; NE]	1,09	[0,81; 1,48]	0,5704
Interaktions p-Wert									0,5197
TNM Status (eCRF) - DEU									
Stadium I/II	33	11 (33,3)	29,4 [7,3; NE]	34	7 (20,6)	NE [NE; NE]	1,57	[0,62; 4,27]	0,3452
Stadium III	231	89 (38,5)	15,6 [11,0;33,2]	232	80 (34,5)	16,5 [11,0; NE]	1,09	[0,81; 1,48]	0,5695
Interaktions p-Wert									0,4703
Erhalt einer PCI (IVRS) - DEU									
Ja	142	63 (44,4)	15,7 [3,7;29,4]	144	53 (36,8)	12,1 [1,4; NE]	1,01	[0,70; 1,46]	0,9628
Nein	122	37 (30,3)	22,1 [11,0; NE]	122	34 (27,9)	NE [NE; NE]	1,23	[0,77; 1,97]	0,3827
Interaktions p-Wert									0,5108
Erhalt einer PCI (eCRF) - DEU									
Ja	142	63 (44,4)	15,7 [3,7;29,4]	143	53 (37,1)	12,1 [1,4; NE]	1,01	[0,70; 1,46]	0,9628
Nein	122	37 (30,3)	22,1 [11,0; NE]	123	34 (27,6)	NE [NE; NE]	1,23	[0,77; 1,97]	0,3827
Interaktions p-Wert									0,5108
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	10 (31,3)	NE [NE; NE]	32	11 (34,4)	16,5 [7,3; NE]	0,85	[0,35; 2,02]	0,7097
>=14 bis <28 Tage	79	28 (35,4)	14,7 [9,1; NE]	80	24 (30,0)	22,2 [12,1; NE]	1,33	[0,77; 2,31]	0,3066
>=28 Tage	153	62 (40,5)	18,5 [6,4;32,1]	154	52 (33,8)	24,0 [9,2; NE]	1,09	[0,75; 1,58]	0,6465
Interaktions p-Wert									0,6714
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	4 (25,0)	NE [NE; NE]	24	7 (29,2)	17,4 [6,4; NE]	0,77	[0,20; 2,55]	0,6715
>=28 bis <56 Tage	104	31 (29,8)	32,1 [12,8; NE]	104	32 (30,8)	14,7 [7,4; NE]	0,88	[0,54; 1,45]	0,6122
>=56 bis <84 Tage	98	43 (43,9)	12,9 [4,5;22,1]	76	30 (39,5)	9,1 [3,7; NE]	0,99	[0,62; 1,59]	0,9593
>=84 Tage	46	22 (47,8)	9,1 [2,7;33,2]	62	18 (29,0)	NE [NE; NE]	2,01	[1,08; 3,80]	0,0277*
Interaktions p-Wert									0,1766
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	33 (36,3)	15,6 [8,2; NE]	88	28 (31,8)	26,6 [8,3; NE]	1,11	[0,67; 1,86]	0,6742
Cisplatin	173	67 (38,7)	20,2 [10,1;34,0]	178	59 (33,1)	22,2 [12,8; NE]	1,14	[0,80; 1,62]	0,4659
Interaktions p-Wert									0,9437
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	63 (32,3)	32,1 [12,8; NE]	187	53 (28,3)	NE [NE; NE]	1,05	[0,73; 1,51]	0,8065
Zweimal täglich	69	37 (53,6)	7,3 [1,8;20,2]	79	34 (43,0)	15,6 [5,5; NE]	1,41	[0,89; 2,26]	0,1463
Interaktions p-Wert									0,3214
Bestes Ansprechen auf cCRT - DEU									
CR	31	8 (25,8)	20,2 [12,8; NE]	34	5 (14,7)	NE [NE; NE]	1,43	[0,48; 4,74]	0,5250
PR	191	79 (41,4)	15,6 [7,3;32,1]	200	73 (36,5)	14,7 [9,2; NE]	1,13	[0,82; 1,55]	0,4670
SD	42	13 (31,0)	NE [NE; NE]	32	9 (28,1)	NE [NE; NE]	1,15	[0,50; 2,79]	0,7436
Interaktions p-Wert									0,9201
Geschlecht - DEU									
Männer	178	71 (39,9)	20,2 [11,0; NE]	188	67 (35,6)	22,2 [9,2; NE]	1,03	[0,73; 1,44]	0,8795
Frauen	86	29 (33,7)	14,7 [5,6;34,0]	78	20 (25,6)	NE [NE; NE]	1,49	[0,85; 2,68]	0,1632
Interaktions p-Wert									0,2623
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	69 (43,1)	12,8 [7,3;22,1]	162	58 (35,8)	15,6 [10,1; NE]	1,14	[0,81; 1,63]	0,4470
>=65 Jahre	104	31 (29,8)	34,0 [14,7; NE]	104	29 (27,9)	NE [NE; NE]	1,09	[0,65; 1,81]	0,7491
Interaktions p-Wert									0,8672
PD-L1-Status - DEU									
TC and IC <1%	78	30 (38,5)	22,1 [8,2; NE]	73	23 (31,5)	24,0 [12,8; NE]	1,24	[0,72; 2,15]	0,4410
TC or IC >=1%	84	40 (47,6)	14,7 [3,6;34,0]	98	38 (38,8)	15,6 [6,4; NE]	1,10	[0,70; 1,72]	0,6825
Interaktions p-Wert									0,7369
Raucherstatus - DEU									
Raucher	241	86 (35,7)	20,2 [12,8; NE]	240	76 (31,7)	26,6 [12,8; NE]	1,09	[0,80; 1,48]	0,5894
Nichtraucher	23	14 (60,9)	1,1 [0,3;29,4]	26	11 (42,3)	16,5 [0,7; NE]	1,59	[0,72; 3,58]	0,2480
Interaktions p-Wert									0,3800
Abstammung - DEU									
Weiß	130	41 (31,5)	18,5 [11,0; NE]	137	31 (22,6)	NE [NE; NE]	1,53	[0,96; 2,45]	0,0736
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	59 (45,0)	18,3 [9,1; NE]	121	55 (45,5)	12,8 [7,4;24,0]	0,89	[0,62; 1,29]	0,5401
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,0752
Geographische Region - DEU									
Asien	129	59 (45,7)	18,3 [9,1; NE]	120	55 (45,8)	12,8 [7,4;24,0]	0,89	[0,62; 1,29]	0,5366
Europa	94	36 (38,3)	15,6 [7,3;34,0]	112	30 (26,8)	NE [NE; NE]	1,51	[0,93; 2,47]	0,0943
Nordamerika	41	5 (12,2)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	2,45	[0,53; 17,10]	0,2605
Interaktions p-Wert									0,1416
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.2 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Alopezie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	47 (35,3)	22,1 [10,1; NE]	131	42 (32,1)	26,6 [13,7; NE]	1,12	[0,74; 1,71]	0,5869
1	131	53 (40,5)	12,8 [8,2;34,0]	135	45 (33,3)	14,7 [9,1; NE]	1,13	[0,76; 1,69]	0,5365
Interaktions p-Wert									0,9732

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	10 (27,8)	NE [NE; NE]	37	11 (29,7)	NE [NE; NE]	0,91	[0,38; 2,17]	0,8371
Stadium III	228	82 (36,0)	27,5 [15,6; NE]	229	73 (31,9)	31,3 [17,4; NE]	0,99	[0,72; 1,36]	0,9647
Interaktions p-Wert									0,8591
TNM Status (eCRF) - DEU									
Stadium I/II	33	9 (27,3)	NE [NE; NE]	34	10 (29,4)	NE [NE; NE]	0,87	[0,34; 2,15]	0,7569
Stadium III	231	83 (35,9)	24,8 [15,6; NE]	232	74 (31,9)	31,3 [17,4; NE]	1,00	[0,73; 1,37]	0,9967
Interaktions p-Wert									0,7712
Erhalt einer PCI (IVRS) - DEU									
Ja	142	49 (34,5)	32,2 [16,5; NE]	144	45 (31,3)	25,8 [8,2; NE]	0,84	[0,56; 1,26]	0,3939
Nein	122	43 (35,2)	18,3 [7,3; NE]	122	39 (32,0)	38,6 [17,4; NE]	1,18	[0,77; 1,83]	0,4469
Interaktions p-Wert									0,2548
Erhalt einer PCI (eCRF) - DEU									
Ja	142	49 (34,5)	32,2 [16,5; NE]	143	45 (31,5)	25,8 [8,2; NE]	0,84	[0,56; 1,26]	0,3939
Nein	122	43 (35,2)	18,3 [7,3; NE]	123	39 (31,7)	38,6 [17,4; NE]	1,18	[0,77; 1,83]	0,4469
Interaktions p-Wert									0,2548
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	8 (25,0)	NE [NE; NE]	32	9 (28,1)	38,6 [11,9; NE]	0,75	[0,28; 1,95]	0,5469
>=14 bis <28 Tage	79	34 (43,0)	10,1 [3,7; NE]	80	23 (28,8)	NE [NE; NE]	1,61	[0,96; 2,77]	0,0732
>=28 Tage	153	50 (32,7)	32,2 [14,8; NE]	154	52 (33,8)	22,3 [8,3; NE]	0,80	[0,54; 1,18]	0,2508
Interaktions p-Wert									0,0866
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	5 (31,3)	NE [NE; NE]	24	6 (25,0)	NE [NE; NE]	0,98	[0,28; 3,26]	0,9742
>=28 bis <56 Tage	104	34 (32,7)	23,1 [10,1; NE]	104	31 (29,8)	22,3 [13,7; NE]	0,97	[0,59; 1,58]	0,8971
>=56 bis <84 Tage	98	37 (37,8)	17,5 [6,4; NE]	76	25 (32,9)	38,6 [7,3; NE]	1,03	[0,63; 1,74]	0,8987
>=84 Tage	46	16 (34,8)	NE [NE; NE]	62	22 (35,5)	31,3 [5,5; NE]	0,89	[0,46; 1,69]	0,7260
Interaktions p-Wert									0,9885
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	28 (30,8)	34,1 [8,2; NE]	88	28 (31,8)	25,8 [8,2; NE]	0,86	[0,51; 1,45]	0,5666
Cisplatin	173	64 (37,0)	23,1 [10,1; NE]	178	56 (31,5)	31,3 [13,7; NE]	1,06	[0,74; 1,51]	0,7695
Interaktions p-Wert									0,5228
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	70 (35,9)	23,1 [10,1; NE]	187	54 (28,9)	31,3 [17,4; NE]	1,10	[0,78; 1,58]	0,5847
Zweimal täglich	69	22 (31,9)	NE [NE; NE]	79	30 (38,0)	25,8 [7,3; NE]	0,75	[0,43; 1,29]	0,2944
Interaktions p-Wert									0,2388
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	15,6 [1,2; NE]	34	7 (20,6)	NE [NE; NE]	1,89	[0,78; 5,04]	0,1633
PR	191	65 (34,0)	NE [NE; NE]	200	68 (34,0)	22,3 [17,4; NE]	0,90	[0,64; 1,26]	0,5288
SD	42	14 (33,3)	32,2 [7,3; NE]	32	9 (28,1)	28,6 [12,9; NE]	1,02	[0,45; 2,45]	0,9628
Interaktions p-Wert									0,3111
Geschlecht - DEU									
Männer	178	69 (38,8)	27,5 [14,8; NE]	188	54 (28,7)	NE [NE; NE]	1,22	[0,86; 1,75]	0,2703
Frauen	86	23 (26,7)	NE [NE; NE]	78	30 (38,5)	7,3 [1,8;31,3]	0,58	[0,33; 0,99]	0,0477*
Interaktions p-Wert									0,0237*
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	61 (38,1)	18,3 [10,1; NE]	162	51 (31,5)	38,6 [11,9; NE]	1,06	[0,73; 1,55]	0,7446
>=65 Jahre	104	31 (29,8)	34,1 [19,3; NE]	104	33 (31,7)	31,3 [17,4; NE]	0,86	[0,53; 1,41]	0,5565
Interaktions p-Wert									0,5055
PD-L1-Status - DEU									
TC and IC <1%	78	28 (35,9)	34,1 [8,2; NE]	73	20 (27,4)	NE [NE; NE]	1,19	[0,67; 2,14]	0,5489
TC or IC >=1%	84	34 (40,5)	23,1 [7,3; NE]	98	34 (34,7)	25,8 [11,9; NE]	1,03	[0,64; 1,66]	0,8957
Interaktions p-Wert									0,7065
Raucherstatus - DEU									
Raucher	241	88 (36,5)	23,1 [10,1; NE]	240	78 (32,5)	25,8 [17,4; NE]	1,03	[0,76; 1,40]	0,8582
Nichtraucher	23	4 (17,4)	NE [NE; NE]	26	6 (23,1)	NE [NE; NE]	0,54	[0,14; 1,88]	0,3295
Interaktions p-Wert									0,3222
Abstammung - DEU									
Weiß	130	42 (32,3)	16,5 [6,5; NE]	137	46 (33,6)	18,4 [5,5;31,3]	0,89	[0,58; 1,35]	0,5740
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	50 (38,2)	34,1 [18,3; NE]	121	38 (31,4)	NE [NE; NE]	1,08	[0,71; 1,66]	0,7182
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5141
Geographische Region - DEU									
Asien	129	50 (38,8)	34,1 [18,3; NE]	120	37 (30,8)	NE [NE; NE]	1,11	[0,73; 1,71]	0,6280
Europa	94	35 (37,2)	15,7 [6,5; NE]	112	39 (34,8)	22,0 [5,5; NE]	0,94	[0,59; 1,48]	0,7824
Nordamerika	41	7 (17,1)	NE [NE; NE]	34	8 (23,5)	17,4 [0,9; NE]	0,76	[0,27; 2,13]	0,6024
Interaktions p-Wert									0,7473
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.3 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	41 (30,8)	NE [NE; NE]	131	32 (24,4)	NE [NE; NE]	1,26	[0,79; 2,01]	0,3315
1	131	51 (38,9)	19,3 [7,3; NE]	135	52 (38,5)	12,9 [3,6;31,3]	0,80	[0,54; 1,18]	0,2556
Interaktions p-Wert									0,1398

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	6 (16,7)	NE [NE; NE]	37	7 (18,9)	48,8 [25,8; NE]	1,11	[0,36; 3,36]	0,8455
Stadium III	228	54 (23,7)	NE [NE; NE]	229	40 (17,5)	NE [NE; NE]	1,16	[0,77; 1,76]	0,4664
Interaktions p-Wert									0,9422
TNM Status (eCRF) - DEU									
Stadium I/II	33	5 (15,2)	NE [NE; NE]	34	7 (20,6)	48,8 [25,8; NE]	0,85	[0,25; 2,68]	0,7868
Stadium III	231	55 (23,8)	NE [NE; NE]	232	40 (17,2)	NE [NE; NE]	1,21	[0,80; 1,83]	0,3661
Interaktions p-Wert									0,5766
Erhalt einer PCI (IVRS) - DEU									
Ja	142	38 (26,8)	NE [NE; NE]	144	25 (17,4)	NE [NE; NE]	1,31	[0,79; 2,19]	0,2958
Nein	122	22 (18,0)	NE [NE; NE]	122	22 (18,0)	NE [NE; NE]	0,98	[0,54; 1,78]	0,9430
Interaktions p-Wert									0,4659
Erhalt einer PCI (eCRF) - DEU									
Ja	142	38 (26,8)	NE [NE; NE]	143	25 (17,5)	NE [NE; NE]	1,31	[0,79; 2,19]	0,2958
Nein	122	22 (18,0)	NE [NE; NE]	123	22 (17,9)	NE [NE; NE]	0,98	[0,54; 1,78]	0,9430
Interaktions p-Wert									0,4659
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	5 (15,6)	NE [NE; NE]	32	5 (15,6)	NE [NE; NE]	0,70	[0,19; 2,54]	0,5800
>=14 bis <28 Tage	79	19 (24,1)	NE [NE; NE]	80	14 (17,5)	NE [NE; NE]	1,34	[0,68; 2,73]	0,4026
>=28 Tage	153	36 (23,5)	NE [NE; NE]	154	28 (18,2)	NE [NE; NE]	1,19	[0,73; 1,97]	0,4862
Interaktions p-Wert									0,6726
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	5 (31,3)	34,1 [5,5; NE]	24	4 (16,7)	NE [NE; NE]	1,51	[0,40; 6,10]	0,5405
>=28 bis <56 Tage	104	18 (17,3)	NE [NE; NE]	104	19 (18,3)	NE [NE; NE]	0,78	[0,41; 1,50]	0,4606
>=56 bis <84 Tage	98	23 (23,5)	44,2 [27,5; NE]	76	14 (18,4)	NE [NE; NE]	0,98	[0,51; 1,96]	0,9592
>=84 Tage	46	14 (30,4)	NE [NE; NE]	62	10 (16,1)	NE [NE; NE]	2,45	[1,09; 5,69]	0,0294*
Interaktions p-Wert									0,1646
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	19 (20,9)	NE [NE; NE]	88	16 (18,2)	NE [NE; NE]	0,95	[0,49; 1,88]	0,8872
Cisplatin	173	41 (23,7)	NE [NE; NE]	178	31 (17,4)	NE [NE; NE]	1,28	[0,81; 2,06]	0,2915
Interaktions p-Wert									0,4732
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	43 (22,1)	NE [NE; NE]	187	31 (16,6)	NE [NE; NE]	1,13	[0,71; 1,80]	0,6162
Zweimal täglich	69	17 (24,6)	NE [NE; NE]	79	16 (20,3)	48,8 [29,4; NE]	1,25	[0,63; 2,49]	0,5290
Interaktions p-Wert									0,8093
Bestes Ansprechen auf cCRT - DEU									
CR	31	6 (19,4)	NE [NE; NE]	34	5 (14,7)	48,8 [15,6; NE]	1,07	[0,32; 3,72]	0,9089
PR	191	39 (20,4)	NE [NE; NE]	200	37 (18,5)	NE [NE; NE]	0,99	[0,63; 1,56]	0,9752
SD	42	15 (35,7)	29,6 [5,5; NE]	32	5 (15,6)	NE [NE; NE]	2,30	[0,89; 7,07]	0,0880
Interaktions p-Wert									0,3004
Geschlecht - DEU									
Männer	178	48 (27,0)	NE [NE; NE]	188	37 (19,7)	NE [NE; NE]	1,23	[0,80; 1,91]	0,3362
Frauen	86	12 (14,0)	NE [NE; NE]	78	10 (12,8)	NE [NE; NE]	0,98	[0,42; 2,32]	0,9619
Interaktions p-Wert									0,6328
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	42 (26,3)	NE [NE; NE]	162	32 (19,8)	NE [NE; NE]	1,16	[0,73; 1,85]	0,5268
>=65 Jahre	104	18 (17,3)	NE [NE; NE]	104	15 (14,4)	NE [NE; NE]	1,15	[0,58; 2,31]	0,6960
Interaktions p-Wert									0,9775
PD-L1-Status - DEU									
TC and IC <1%	78	21 (26,9)	NE [NE; NE]	73	12 (16,4)	NE [NE; NE]	1,46	[0,73; 3,06]	0,2917
TC or IC >=1%	84	19 (22,6)	NE [NE; NE]	98	24 (24,5)	48,8 [25,8; NE]	0,80	[0,43; 1,45]	0,4597
Interaktions p-Wert									0,2002
Raucherstatus - DEU									
Raucher	241	50 (20,7)	NE [NE; NE]	240	41 (17,1)	NE [NE; NE]	1,12	[0,74; 1,70]	0,5969
Nichtraucher	23	10 (43,5)	8,3 [1,6; NE]	26	6 (23,1)	NE [NE; NE]	1,45	[0,54; 4,27]	0,4689
Interaktions p-Wert									0,6408
Abstammung - DEU									
Weiß	130	21 (16,2)	NE [NE; NE]	137	17 (12,4)	NE [NE; NE]	1,22	[0,65; 2,35]	0,5381
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	39 (29,8)	44,2 [29,6; NE]	121	29 (24,0)	48,8 [29,4; NE]	1,12	[0,70; 1,83]	0,6370
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8357
Geographische Region - DEU									
Asien	129	39 (30,2)	44,2 [29,6; NE]	120	29 (24,2)	48,8 [29,4; NE]	1,12	[0,69; 1,82]	0,6529
Europa	94	18 (19,1)	NE [NE; NE]	112	17 (15,2)	NE [NE; NE]	1,06	[0,54; 2,07]	0,8631
Nordamerika	41	3 (7,3)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	3,39	[0,43; 68,49]	0,2535
Interaktions p-Wert									0,5827
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.4 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Hämoptoe
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	30 (22,6)	NE [NE; NE]	131	25 (19,1)	NE [NE; NE]	1,14	[0,67; 1,95]	0,6339
1	131	30 (22,9)	44,2 [29,6; NE]	135	22 (16,3)	NE [NE; NE]	1,20	[0,69; 2,10]	0,5239
Interaktions p-Wert									0,8993

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	17 (47,2)	1,7 [0,8; NE]	37	17 (45,9)	3,6 [0,5; NE]	0,98	[0,50; 1,94]	0,9648
Stadium III	228	130 (57,0)	2,8 [1,6; 5,5]	229	111 (48,5)	4,6 [2,7; 9,1]	1,20	[0,93; 1,54]	0,1657
Interaktions p-Wert									0,5967
TNM Status (eCRF) - DEU									
Stadium I/II	33	16 (48,5)	1,7 [0,8; NE]	34	16 (47,1)	3,6 [0,5;21,1]	0,90	[0,45; 1,81]	0,7644
Stadium III	231	131 (56,7)	2,8 [1,6; 5,5]	232	112 (48,3)	4,6 [2,7; 9,1]	1,21	[0,94; 1,56]	0,1399
Interaktions p-Wert									0,4324
Erhalt einer PCI (IVRS) - DEU									
Ja	142	87 (61,3)	1,8 [1,2; 3,6]	144	70 (48,6)	3,6 [1,4; 9,1]	1,11	[0,81; 1,52]	0,5232
Nein	122	60 (49,2)	5,5 [1,6;12,8]	122	58 (47,5)	5,5 [2,7;20,3]	1,21	[0,84; 1,74]	0,2970
Interaktions p-Wert									0,7137
Erhalt einer PCI (eCRF) - DEU									
Ja	142	87 (61,3)	1,8 [1,2; 3,6]	143	70 (49,0)	3,6 [1,4; 9,1]	1,11	[0,81; 1,52]	0,5232
Nein	122	60 (49,2)	5,5 [1,6;12,8]	123	58 (47,2)	5,5 [2,7;20,3]	1,21	[0,84; 1,74]	0,2970
Interaktions p-Wert									0,7137
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	22 (68,8)	1,4 [0,5; 3,7]	32	15 (46,9)	4,6 [1,6; NE]	2,03	[1,06; 3,99]	0,0326*
>=14 bis <28 Tage	79	43 (54,4)	5,5 [1,9;11,0]	80	38 (47,5)	7,3 [2,7;20,3]	1,13	[0,73; 1,76]	0,5701
>=28 Tage	153	82 (53,6)	1,6 [1,1; 8,2]	154	75 (48,7)	3,6 [1,4;10,2]	1,05	[0,77; 1,44]	0,7579
Interaktions p-Wert									0,1991
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	10 (62,5)	1,0 [0,3;22,9]	24	11 (45,8)	4,7 [1,1; NE]	1,91	[0,79; 4,52]	0,1452
>=28 bis <56 Tage	104	48 (46,2)	6,5 [1,9;12,8]	104	51 (49,0)	2,8 [1,1; 6,5]	0,81	[0,55; 1,20]	0,2978
>=56 bis <84 Tage	98	61 (62,2)	1,9 [1,6; 8,2]	76	35 (46,1)	4,6 [1,4;16,5]	1,27	[0,84; 1,94]	0,2544
>=84 Tage	46	28 (60,9)	0,8 [0,5; 1,4]	62	31 (50,0)	10,2 [1,1;21,3]	1,71	[1,02; 2,85]	0,0417*
Interaktions p-Wert									0,0797
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	50 (54,9)	3,6 [1,1; 9,2]	88	40 (45,5)	5,5 [3,6;15,6]	1,36	[0,90; 2,08]	0,1420
Cisplatin	173	97 (56,1)	1,9 [1,6; 5,6]	178	88 (49,4)	2,8 [1,2;10,2]	1,08	[0,81; 1,44]	0,6070
Interaktions p-Wert									0,3626
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	102 (52,3)	3,7 [1,8; 9,2]	187	85 (45,5)	4,7 [1,8;11,0]	1,06	[0,80; 1,42]	0,6897
Zweimal täglich	69	45 (65,2)	1,2 [0,9; 1,6]	79	43 (54,4)	3,7 [1,6;10,2]	1,50	[0,99; 2,29]	0,0564
Interaktions p-Wert									0,1780
Bestes Ansprechen auf cCRT - DEU									
CR	31	19 (61,3)	1,8 [0,6; 9,2]	34	14 (41,2)	1,2 [0,7; 3,6]	1,05	[0,53; 2,14]	0,8802
PR	191	108 (56,5)	2,7 [1,4; 6,5]	200	99 (49,5)	5,5 [2,7;10,2]	1,20	[0,92; 1,58]	0,1812
SD	42	20 (47,6)	2,8 [0,7;22,9]	32	15 (46,9)	9,1 [0,9;25,7]	1,00	[0,51; 1,99]	0,9974
Interaktions p-Wert									0,8482
Geschlecht - DEU									
Männer	178	101 (56,7)	2,8 [1,6; 8,2]	188	89 (47,3)	7,3 [3,7;11,0]	1,21	[0,91; 1,61]	0,1898
Frauen	86	46 (53,5)	1,6 [0,7; 6,5]	78	39 (50,0)	1,1 [0,9; 3,6]	1,02	[0,66; 1,57]	0,9331
Interaktions p-Wert									0,5118
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	92 (57,5)	1,9 [1,4; 8,2]	162	84 (51,9)	2,7 [1,1; 5,5]	0,98	[0,73; 1,32]	0,8783
>=65 Jahre	104	55 (52,9)	2,8 [1,1; 7,3]	104	44 (42,3)	10,1 [4,5;16,5]	1,55	[1,05; 2,32]	0,0284*
Interaktions p-Wert									0,0652
PD-L1-Status - DEU									
TC and IC <1%	78	50 (64,1)	1,5 [0,9; 4,7]	73	29 (39,7)	20,3 [2,8; NE]	1,95	[1,24; 3,12]	0,0035*
TC or IC >=1%	84	52 (61,9)	3,6 [1,1;11,0]	98	50 (51,0)	5,5 [1,6;11,0]	1,16	[0,79; 1,72]	0,4478
Interaktions p-Wert									0,0894
Raucherstatus - DEU									
Raucher	241	131 (54,4)	2,8 [1,6; 6,5]	240	114 (47,5)	5,5 [2,7;10,1]	1,15	[0,89; 1,48]	0,2793
Nichtraucher	23	16 (69,6)	1,1 [0,3; 6,4]	26	14 (53,8)	2,8 [0,5;10,2]	1,40	[0,68; 2,92]	0,3542
Interaktions p-Wert									0,6049
Abstammung - DEU									
Weiß	130	67 (51,5)	1,9 [1,1; 8,2]	137	61 (44,5)	3,6 [1,4; 8,3]	1,17	[0,83; 1,66]	0,3802
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	0,9 [0,7; NE]	NC	[NC]	NC
Asiatisch	131	80 (61,1)	2,8 [1,6; 7,3]	121	64 (52,9)	6,5 [2,7;16,5]	1,20	[0,86; 1,67]	0,2815
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9185
Geographische Region - DEU									
Asien	129	80 (62,0)	2,8 [1,6; 7,3]	120	64 (53,3)	6,5 [1,8;16,5]	1,19	[0,86; 1,66]	0,2990
Europa	94	54 (57,4)	2,8 [1,2;10,1]	112	57 (50,9)	2,8 [1,2; 5,5]	1,03	[0,71; 1,49]	0,8838
Nordamerika	41	13 (31,7)	0,8 [0,5;17,4]	34	7 (20,6)	NE [NE; NE]	2,23	[0,92; 5,95]	0,0779
Interaktions p-Wert									0,2908
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.2.5 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Husten
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	75 (56,4)	1,6 [1,1; 4,5]	131	67 (51,1)	3,6 [1,2; 9,1]	1,16	[0,83; 1,61]	0,3915
1	131	72 (55,0)	5,6 [1,6;11,0]	135	61 (45,2)	6,4 [2,7;16,5]	1,18	[0,84; 1,67]	0,3340
Interaktions p-Wert									0,9220

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	13 (36,1)	15,7 [5,5;35,8]	37	15 (40,5)	25,8 [1,6; NE]	0,86	[0,40; 1,82]	0,6982
Stadium III	228	114 (50,0)	6,4 [4,5;10,1]	229	114 (49,8)	5,5 [3,7;10,1]	0,89	[0,68; 1,15]	0,3604
Interaktions p-Wert									0,9503
TNM Status (eCRF) - DEU									
Stadium I/II	33	12 (36,4)	15,7 [5,5; NE]	34	15 (44,1)	25,8 [1,1; NE]	0,71	[0,33; 1,52]	0,3765
Stadium III	231	115 (49,8)	6,4 [4,5; 9,3]	232	114 (49,1)	6,4 [3,7;10,1]	0,91	[0,70; 1,18]	0,4855
Interaktions p-Wert									0,5428
Erhalt einer PCI (IVRS) - DEU									
Ja	142	74 (52,1)	6,5 [4,5;15,7]	144	67 (46,5)	5,5 [1,6;11,0]	0,80	[0,57; 1,11]	0,1857
Nein	122	53 (43,4)	7,4 [4,5;26,6]	122	62 (50,8)	9,2 [4,6;13,0]	0,99	[0,68; 1,42]	0,9389
Interaktions p-Wert									0,4055
Erhalt einer PCI (eCRF) - DEU									
Ja	142	74 (52,1)	6,5 [4,5;15,7]	143	67 (46,9)	5,5 [1,6;11,0]	0,80	[0,57; 1,11]	0,1857
Nein	122	53 (43,4)	7,4 [4,5;26,6]	123	62 (50,4)	9,2 [4,6;13,0]	0,99	[0,68; 1,42]	0,9389
Interaktions p-Wert									0,4055
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	15 (46,9)	10,1 [3,6; NE]	32	16 (50,0)	9,1 [2,7; NE]	0,86	[0,42; 1,74]	0,6694
>=14 bis <28 Tage	79	40 (50,6)	7,3 [3,6;15,7]	80	38 (47,5)	10,2 [4,6;13,8]	1,22	[0,78; 1,91]	0,3779
>=28 Tage	153	72 (47,1)	5,6 [3,7;24,8]	154	75 (48,7)	4,6 [1,6; 9,2]	0,75	[0,54; 1,03]	0,0788
Interaktions p-Wert									0,2162

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	9 (56,3)	16,5 [1,4; NE]	24	12 (50,0)	9,3 [1,8; NE]	0,93	[0,38; 2,20]	0,8704
>=28 bis <56 Tage	104	45 (43,3)	6,5 [4,5;26,6]	104	42 (40,4)	10,1 [4,6;18,7]	0,97	[0,64; 1,49]	0,9019
>=56 bis <84 Tage	98	47 (48,0)	7,4 [5,5;26,6]	76	43 (56,6)	3,7 [1,4; 5,6]	0,62	[0,41; 0,94]	0,0243*
>=84 Tage	46	26 (56,5)	2,8 [1,4; 9,3]	62	32 (51,6)	6,5 [1,6;22,1]	1,27	[0,75; 2,12]	0,3760
Interaktions p-Wert									0,1830
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	6,4 [4,5;16,5]	88	46 (52,3)	3,6 [1,1; 8,3]	0,75	[0,49; 1,13]	0,1675
Cisplatin	173	83 (48,0)	7,3 [4,7;24,8]	178	83 (46,6)	9,1 [4,6;13,7]	0,96	[0,71; 1,30]	0,8007
Interaktions p-Wert									0,3346
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	92 (47,2)	6,5 [4,6;10,1]	187	84 (44,9)	7,3 [4,5;11,9]	0,94	[0,70; 1,26]	0,6712
Zweimal täglich	69	35 (50,7)	6,5 [2,8;26,6]	79	45 (57,0)	6,5 [2,8;13,0]	0,78	[0,50; 1,22]	0,2779
Interaktions p-Wert									0,5067
Bestes Ansprechen auf cCRT - DEU									
CR	31	16 (51,6)	2,8 [0,9;15,7]	34	13 (38,2)	5,5 [1,2; NE]	1,18	[0,57; 2,49]	0,6626
PR	191	94 (49,2)	7,3 [4,6;15,6]	200	101 (50,5)	6,5 [4,5;11,0]	0,90	[0,68; 1,19]	0,4528
SD	42	17 (40,5)	8,3 [4,5; NE]	32	15 (46,9)	7,4 [0,9;25,8]	0,67	[0,33; 1,35]	0,2557
Interaktions p-Wert									0,5430
Geschlecht - DEU									
Männer	178	90 (50,6)	7,5 [5,6;21,2]	188	94 (50,0)	7,4 [4,6;11,9]	0,86	[0,64; 1,15]	0,3118
Frauen	86	37 (43,0)	4,5 [1,6;16,5]	78	35 (44,9)	3,7 [1,4;13,9]	0,96	[0,60; 1,53]	0,8661

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,6936
Altersgruppe - DEU									
<65 Jahre	160	79 (49,4)	6,5 [4,5;21,2]	162	84 (51,9)	5,5 [2,7; 9,1]	0,76	[0,56; 1,04]	0,0832
>=65 Jahre	104	48 (46,2)	6,5 [4,5;15,6]	104	45 (43,3)	10,1 [4,5;22,1]	1,15	[0,76; 1,72]	0,5127
Interaktions p-Wert									0,1167
PD-L1-Status - DEU									
TC and IC <1%	78	37 (47,4)	15,7 [5,5;34,1]	73	31 (42,5)	12,8 [4,6;34,9]	0,97	[0,60; 1,58]	0,9150
TC or IC >=1%	84	52 (61,9)	4,6 [2,7; 7,4]	98	54 (55,1)	5,6 [1,6;13,7]	1,01	[0,69; 1,47]	0,9773
Interaktions p-Wert									0,9195
Raucherstatus - DEU									
Raucher	241	117 (48,5)	6,4 [4,6;10,1]	240	120 (50,0)	6,4 [4,5;10,1]	0,87	[0,68; 1,13]	0,2943
Nichtraucher	23	10 (43,5)	21,2 [1,6; NE]	26	9 (34,6)	NE [NE; NE]	1,08	[0,44; 2,72]	0,8656
Interaktions p-Wert									0,6533
Abstammung - DEU									
Weiß	130	57 (43,8)	5,6 [2,7;10,1]	137	60 (43,8)	5,5 [1,6;10,1]	0,90	[0,62; 1,29]	0,5598
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	2,5 [0,5; NE]	NC	[NC]	NC
Asiatisch	131	70 (53,4)	7,4 [5,5;25,8]	121	66 (54,5)	8,3 [4,6;13,8]	0,91	[0,65; 1,27]	0,5785
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9605
Geographische Region - DEU									
Asien	129	70 (54,3)	7,4 [5,5;25,8]	120	65 (54,2)	9,1 [4,6;14,7]	0,92	[0,66; 1,29]	0,6264
Europa	94	47 (50,0)	5,6 [2,7;10,1]	112	54 (48,2)	3,6 [1,4;10,1]	0,81	[0,54; 1,19]	0,2827

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.6 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Periphere Neuropathie
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	10 (24,4)	2,8 [0,7; NE]	34	10 (29,4)	6,5 [1,3; NE]	1,20	[0,49; 2,93]	0,6797
Interaktions p-Wert									0,6949
ECOG-Status zu Baseline - DEU									
0	133	64 (48,1)	5,5 [3,6;15,8]	131	69 (52,7)	5,5 [3,6;10,2]	0,86	[0,61; 1,20]	0,3715
1	131	63 (48,1)	7,3 [5,5;17,5]	135	60 (44,4)	8,3 [3,7;13,7]	0,92	[0,65; 1,32]	0,6657
Interaktions p-Wert									0,7583

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	13 (36,1)	13,7 [1,4; NE]	37	12 (32,4)	NE [NE; NE]	1,26	[0,57; 2,81]	0,5587
Stadium III	228	122 (53,5)	4,5 [2,8; 6,4]	229	124 (54,1)	1,9 [1,4; 4,5]	0,88	[0,69; 1,13]	0,3291
Interaktions p-Wert									0,3938
TNM Status (eCRF) - DEU									
Stadium I/II	33	14 (42,4)	13,7 [1,1; NE]	34	11 (32,4)	NE [NE; NE]	1,43	[0,65; 3,23]	0,3716
Stadium III	231	121 (52,4)	4,6 [2,9; 6,4]	232	125 (53,9)	1,9 [1,4; 4,5]	0,88	[0,68; 1,13]	0,3086
Interaktions p-Wert									0,2461
Erhalt einer PCI (IVRS) - DEU									
Ja	142	77 (54,2)	4,7 [2,8;11,0]	144	71 (49,3)	2,7 [1,1; 6,4]	0,89	[0,64; 1,23]	0,4706
Nein	122	58 (47,5)	4,6 [1,6; 7,3]	122	65 (53,3)	4,6 [1,4; 8,3]	0,97	[0,68; 1,39]	0,8819
Interaktions p-Wert									0,7066
Erhalt einer PCI (eCRF) - DEU									
Ja	142	77 (54,2)	4,7 [2,8;11,0]	143	71 (49,7)	2,7 [1,1; 6,4]	0,89	[0,64; 1,23]	0,4706
Nein	122	58 (47,5)	4,6 [1,6; 7,3]	123	65 (52,8)	4,6 [1,4; 8,3]	0,97	[0,68; 1,39]	0,8819
Interaktions p-Wert									0,7066
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	18 (56,3)	4,6 [1,1;34,1]	32	15 (46,9)	8,3 [1,2; NE]	1,18	[0,60; 2,39]	0,6267
>=14 bis <28 Tage	79	37 (46,8)	6,4 [1,1;19,3]	80	42 (52,5)	3,6 [1,1; 9,1]	0,93	[0,60; 1,45]	0,7525
>=28 Tage	153	80 (52,3)	4,7 [2,8; 7,3]	154	79 (51,3)	1,9 [1,4; 4,5]	0,88	[0,64; 1,20]	0,4060
Interaktions p-Wert									0,7332

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	11 (68,8)	2,4 [0,5;34,1]	24	12 (50,0)	7,3 [0,7; NE]	1,40	[0,61; 3,20]	0,4219
>=28 bis <56 Tage	104	47 (45,2)	6,4 [2,7;16,5]	104	53 (51,0)	2,8 [0,9; 6,4]	0,72	[0,49; 1,07]	0,1037
>=56 bis <84 Tage	98	52 (53,1)	3,7 [1,9; 7,3]	76	37 (48,7)	2,8 [1,4;14,8]	1,03	[0,68; 1,58]	0,8870
>=84 Tage	46	25 (54,3)	4,6 [1,4; 9,3]	62	34 (54,8)	3,6 [1,1;16,6]	1,03	[0,61; 1,72]	0,9154
Interaktions p-Wert									0,4036
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	5,5 [1,9;14,8]	88	45 (51,1)	2,8 [1,4; 8,3]	0,86	[0,57; 1,30]	0,4738
Cisplatin	173	91 (52,6)	4,6 [2,8; 7,3]	178	91 (51,1)	3,6 [1,4; 7,3]	0,97	[0,72; 1,29]	0,8163
Interaktions p-Wert									0,6498
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	95 (48,7)	5,5 [3,6; 9,3]	187	89 (47,6)	2,8 [1,6; 8,2]	0,92	[0,69; 1,23]	0,5730
Zweimal täglich	69	40 (58,0)	3,6 [1,4;11,0]	79	47 (59,5)	3,6 [1,0; 7,4]	0,96	[0,63; 1,47]	0,8583
Interaktions p-Wert									0,8636
Bestes Ansprechen auf cCRT - DEU									
CR	31	14 (45,2)	12,8 [1,4;26,7]	34	12 (35,3)	16,5 [0,9; NE]	1,04	[0,48; 2,28]	0,9262
PR	191	101 (52,9)	4,5 [2,8; 7,3]	200	107 (53,5)	2,8 [1,6; 5,5]	0,92	[0,70; 1,20]	0,5324
SD	42	20 (47,6)	5,5 [0,7;14,8]	32	17 (53,1)	6,4 [0,5;16,6]	0,92	[0,48; 1,78]	0,8062
Interaktions p-Wert									0,9572
Geschlecht - DEU									
Männer	178	98 (55,1)	4,6 [2,7; 7,3]	188	95 (50,5)	4,5 [1,8; 9,2]	1,02	[0,77; 1,36]	0,8795
Frauen	86	37 (43,0)	6,4 [2,8;14,8]	78	41 (52,6)	1,5 [0,9; 3,6]	0,71	[0,46; 1,11]	0,1383

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,1826
Altersgruppe - DEU									
<65 Jahre	160	90 (56,3)	3,6 [1,6; 6,4]	162	85 (52,5)	1,9 [1,1; 6,4]	0,97	[0,72; 1,30]	0,8302
>=65 Jahre	104	45 (43,3)	9,3 [3,7;18,4]	104	51 (49,0)	4,5 [1,6;11,0]	0,86	[0,57; 1,28]	0,4441
Interaktions p-Wert									0,6260
PD-L1-Status - DEU									
TC and IC <1%	78	41 (52,6)	4,5 [1,4;11,0]	73	39 (53,4)	2,8 [0,9;16,5]	0,90	[0,58; 1,40]	0,6396
TC or IC >=1%	84	47 (56,0)	5,6 [2,8;11,0]	98	57 (58,2)	1,8 [0,7; 6,4]	0,79	[0,53; 1,16]	0,2256
Interaktions p-Wert									0,6542
Raucherstatus - DEU									
Raucher	241	120 (49,8)	5,5 [3,6; 7,3]	240	121 (50,4)	3,6 [1,6; 7,4]	0,92	[0,72; 1,19]	0,5295
Nichtraucher	23	15 (65,2)	1,6 [0,7;12,8]	26	15 (57,7)	1,6 [0,3; 7,3]	1,01	[0,49; 2,08]	0,9804
Interaktions p-Wert									0,8161
Abstammung - DEU									
Weiß	130	57 (43,8)	5,6 [2,8;12,8]	137	69 (50,4)	1,8 [1,0; 3,6]	0,75	[0,53; 1,06]	0,1052
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	78 (59,5)	4,6 [1,9; 7,3]	121	65 (53,7)	4,6 [1,8;14,8]	1,11	[0,80; 1,54]	0,5409
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,1097
Geographische Region - DEU									
Asien	129	78 (60,5)	4,6 [1,9; 7,3]	120	66 (55,0)	4,6 [1,6;14,8]	1,08	[0,78; 1,50]	0,6440
Europa	94	48 (51,1)	5,6 [1,4;10,1]	112	60 (53,6)	1,8 [0,9; 5,5]	0,79	[0,54; 1,15]	0,2120

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.7 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen an anderen Stellen des Körpers
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	9 (22,0)	14,8 [0,5; NE]	34	10 (29,4)	2,8 [1,1; NE]	0,81	[0,32; 2,01]	0,6443
Interaktions p-Wert									0,4370
ECOG-Status zu Baseline - DEU									
0	133	66 (49,6)	4,7 [1,4;13,7]	131	76 (58,0)	1,9 [1,4; 5,5]	0,88	[0,63; 1,23]	0,4565
1	131	69 (52,7)	4,6 [2,8; 7,3]	135	60 (44,4)	4,6 [1,1;14,8]	0,99	[0,70; 1,40]	0,9535
Interaktions p-Wert									0,6377

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	14 (38,9)	19,4 [7,4;25,8]	37	16 (43,2)	9,1 [1,7; NE]	0,93	[0,45; 1,92]	0,8513
Stadium III	228	111 (48,7)	7,4 [5,5;12,0]	229	127 (55,5)	3,6 [1,6; 5,5]	0,68	[0,53; 0,88]	0,0037*
Interaktions p-Wert									0,4272
TNM Status (eCRF) - DEU									
Stadium I/II	33	15 (45,5)	11,9 [3,6;25,8]	34	15 (44,1)	9,1 [1,7; NE]	1,01	[0,49; 2,07]	0,9882
Stadium III	231	110 (47,6)	8,2 [5,5;12,8]	232	128 (55,2)	3,6 [1,6; 5,6]	0,68	[0,53; 0,88]	0,0035*
Interaktions p-Wert									0,3208
Erhalt einer PCI (IVRS) - DEU									
Ja	142	75 (52,8)	8,2 [4,6;14,8]	144	75 (52,1)	3,6 [1,6; 6,4]	0,70	[0,50; 0,96]	0,0279*
Nein	122	50 (41,0)	9,1 [4,6;25,7]	122	68 (55,7)	5,5 [1,6; 8,2]	0,74	[0,51; 1,06]	0,0997
Interaktions p-Wert									0,8202
Erhalt einer PCI (eCRF) - DEU									
Ja	142	75 (52,8)	8,2 [4,6;14,8]	143	75 (52,4)	3,6 [1,6; 6,4]	0,70	[0,50; 0,96]	0,0279*
Nein	122	50 (41,0)	9,1 [4,6;25,7]	123	68 (55,3)	5,5 [1,6; 8,2]	0,74	[0,51; 1,06]	0,0997
Interaktions p-Wert									0,8202
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	14 (43,8)	15,6 [3,6;34,1]	32	18 (56,3)	7,3 [1,0; 9,1]	0,64	[0,31; 1,28]	0,2074
>=14 bis <28 Tage	79	36 (45,6)	7,4 [3,6;25,8]	80	41 (51,3)	6,4 [1,2;15,6]	0,82	[0,52; 1,28]	0,3706
>=28 Tage	153	75 (49,0)	8,3 [3,7;14,8]	154	84 (54,5)	3,6 [1,6; 5,5]	0,69	[0,50; 0,94]	0,0202*
Interaktions p-Wert									0,7891

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	10 (62,5)	6,4 [1,1;34,1]	24	14 (58,3)	7,3 [1,2;15,6]	0,97	[0,42; 2,17]	0,9398
>=28 bis <56 Tage	104	39 (37,5)	25,7 [7,3;33,2]	104	50 (48,1)	3,6 [1,4; 8,3]	0,54	[0,35; 0,82]	0,0040*
>=56 bis <84 Tage	98	53 (54,1)	6,4 [3,6; 9,2]	76	43 (56,6)	1,9 [1,2; 7,3]	0,74	[0,50; 1,11]	0,1472
>=84 Tage	46	23 (50,0)	9,3 [1,4;17,4]	62	36 (58,1)	5,5 [1,6;11,9]	0,87	[0,51; 1,47]	0,6140
Interaktions p-Wert									0,4225
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	47 (51,6)	5,5 [1,9;14,7]	88	48 (54,5)	3,6 [1,4; 8,2]	0,79	[0,53; 1,19]	0,2550
Cisplatin	173	78 (45,1)	9,2 [7,4;18,3]	178	95 (53,4)	4,6 [1,6; 7,3]	0,68	[0,51; 0,92]	0,0127*
Interaktions p-Wert									0,5706
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	88 (45,1)	7,4 [5,5;14,8]	187	94 (50,3)	5,5 [1,7; 7,3]	0,72	[0,54; 0,97]	0,0280*
Zweimal täglich	69	37 (53,6)	9,2 [1,8;19,4]	79	49 (62,0)	2,8 [1,4; 6,4]	0,73	[0,47; 1,11]	0,1449
Interaktions p-Wert									0,9683
Bestes Ansprechen auf cCRT - DEU									
CR	31	15 (48,4)	3,6 [1,0; NE]	34	13 (38,2)	1,4 [1,1;11,9]	0,98	[0,47; 2,10]	0,9615
PR	191	92 (48,2)	9,1 [6,4;15,6]	200	120 (60,0)	3,6 [1,6; 5,5]	0,63	[0,48; 0,82]	0,0008*
SD	42	18 (42,9)	8,3 [1,8; NE]	32	10 (31,3)	17,4 [8,2; NE]	1,49	[0,70; 3,36]	0,3034
Interaktions p-Wert									0,0737
Geschlecht - DEU									
Männer	178	92 (51,7)	8,2 [5,6;12,8]	188	102 (54,3)	5,5 [1,9; 8,3]	0,81	[0,61; 1,07]	0,1387
Frauen	86	33 (38,4)	11,9 [3,6;23,9]	78	41 (52,6)	1,8 [0,9; 4,5]	0,52	[0,32; 0,82]	0,0049*

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,1044
Altersgruppe - DEU									
<65 Jahre	160	81 (50,6)	7,4 [3,7;18,3]	162	87 (53,7)	1,8 [1,4; 5,5]	0,68	[0,50; 0,92]	0,0118*
>=65 Jahre	104	44 (42,3)	9,1 [5,6;17,4]	104	56 (53,8)	7,3 [3,6;11,9]	0,77	[0,52; 1,14]	0,1962
Interaktions p-Wert									0,6057
PD-L1-Status - DEU									
TC and IC <1%	78	39 (50,0)	9,1 [3,7;25,7]	73	33 (45,2)	7,3 [3,6;18,4]	0,98	[0,62; 1,57]	0,9358
TC or IC >=1%	84	42 (50,0)	9,2 [5,6;25,7]	98	60 (61,2)	3,6 [1,1; 5,5]	0,59	[0,39; 0,87]	0,0075*
Interaktions p-Wert									0,0961
Raucherstatus - DEU									
Raucher	241	115 (47,7)	8,2 [5,5;12,8]	240	128 (53,3)	4,5 [1,7; 6,4]	0,76	[0,59; 0,98]	0,0341*
Nichtraucher	23	10 (43,5)	22,0 [1,4; NE]	26	15 (57,7)	5,6 [0,9; 8,2]	0,43	[0,19; 0,95]	0,0368*
Interaktions p-Wert									0,1774
Abstammung - DEU									
Weiß	130	52 (40,0)	8,2 [5,5;18,3]	137	66 (48,2)	3,6 [1,6; 7,3]	0,69	[0,48; 0,998]	0,0489*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	3,0 [0,5; NE]	NC	[NC]	NC
Asiatisch	131	73 (55,7)	9,1 [4,6;19,4]	121	74 (61,2)	5,6 [1,6; 9,1]	0,76	[0,55; 1,05]	0,0928
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7306
Geographische Region - DEU									
Asien	129	73 (56,6)	9,1 [4,6;19,4]	120	74 (61,7)	5,5 [1,6; 9,1]	0,75	[0,54; 1,04]	0,0831
Europa	94	46 (48,9)	7,4 [3,6;12,8]	112	57 (50,9)	3,6 [1,6; 7,3]	0,79	[0,53; 1,17]	0,2376

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.8 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen im Arm oder in der Schulter
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	6 (14,6)	NE [NE; NE]	34	12 (35,3)	1,7 [0,9; NE]	0,33	[0,11; 0,84]	0,0199*
Interaktions p-Wert									0,2264
ECOG-Status zu Baseline - DEU									
0	133	57 (42,9)	9,3 [5,6;22,0]	131	72 (55,0)	3,6 [1,6; 6,4]	0,66	[0,46; 0,93]	0,0190*
1	131	68 (51,9)	7,3 [3,6;11,9]	135	71 (52,6)	5,5 [1,6; 9,1]	0,78	[0,56; 1,09]	0,1431
Interaktions p-Wert									0,4985

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	17 (47,2)	6,4 [1,1;25,8]	37	18 (48,6)	6,0 [1,0;40,4]	0,96	[0,49; 1,87]	0,9040
Stadium III	228	112 (49,1)	5,5 [2,7;11,0]	229	105 (45,9)	5,5 [1,7;11,0]	0,93	[0,71; 1,21]	0,5892
Interaktions p-Wert									0,9287
TNM Status (eCRF) - DEU									
Stadium I/II	33	16 (48,5)	6,4 [1,1;25,8]	34	16 (47,1)	9,2 [1,0;40,4]	0,98	[0,49; 1,97]	0,9541
Stadium III	231	113 (48,9)	5,5 [2,7;11,0]	232	107 (46,1)	5,5 [1,7;11,0]	0,93	[0,71; 1,21]	0,5726
Interaktions p-Wert									0,8827
Erhalt einer PCI (IVRS) - DEU									
Ja	142	78 (54,9)	3,6 [1,8; 8,2]	144	68 (47,2)	2,7 [1,4; 9,2]	0,87	[0,63; 1,21]	0,4033
Nein	122	51 (41,8)	11,0 [3,6;34,1]	122	55 (45,1)	11,1 [1,8; NE]	0,97	[0,66; 1,42]	0,8807
Interaktions p-Wert									0,6675
Erhalt einer PCI (eCRF) - DEU									
Ja	142	78 (54,9)	3,6 [1,8; 8,2]	143	68 (47,6)	2,7 [1,4; 9,2]	0,87	[0,63; 1,21]	0,4033
Nein	122	51 (41,8)	11,0 [3,6;34,1]	123	55 (44,7)	11,1 [1,8; NE]	0,97	[0,66; 1,42]	0,8807
Interaktions p-Wert									0,6675
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	14 (43,8)	19,3 [2,8; NE]	32	11 (34,4)	NE [NE; NE]	1,09	[0,50; 2,46]	0,8298
>=14 bis <28 Tage	79	35 (44,3)	11,0 [1,8; NE]	80	42 (52,5)	2,7 [1,1;12,8]	0,77	[0,49; 1,20]	0,2488
>=28 Tage	153	80 (52,3)	3,6 [1,8; 7,3]	154	70 (45,5)	4,6 [1,4;11,0]	1,01	[0,73; 1,39]	0,9620
Interaktions p-Wert									0,5785

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	11 (68,8)	2,4 [0,2;34,1]	24	11 (45,8)	13,8 [1,1; NE]	1,83	[0,78; 4,27]	0,1617
>=28 bis <56 Tage	104	43 (41,3)	11,0 [5,6;24,8]	104	45 (43,3)	2,8 [1,4;15,6]	0,76	[0,50; 1,16]	0,2073
>=56 bis <84 Tage	98	54 (55,1)	2,7 [1,6; 6,4]	76	34 (44,7)	8,3 [1,1; NE]	1,11	[0,73; 1,72]	0,6348
>=84 Tage	46	21 (45,7)	7,4 [1,2; NE]	62	33 (53,2)	4,6 [0,7;11,1]	0,75	[0,43; 1,28]	0,2947
Interaktions p-Wert									0,2062
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	46 (50,5)	3,6 [1,6;12,0]	88	43 (48,9)	2,7 [1,4; 7,4]	0,99	[0,65; 1,51]	0,9657
Cisplatin	173	83 (48,0)	6,4 [2,8;14,7]	178	80 (44,9)	9,1 [1,6;12,8]	0,91	[0,67; 1,23]	0,5328
Interaktions p-Wert									0,7367
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	91 (46,7)	6,4 [3,6;12,8]	187	83 (44,4)	5,5 [1,6;11,1]	0,90	[0,67; 1,21]	0,4694
Zweimal täglich	69	38 (55,1)	2,8 [1,6;12,1]	79	40 (50,6)	8,3 [1,4;18,5]	1,03	[0,66; 1,60]	0,9107
Interaktions p-Wert									0,6198
Bestes Ansprechen auf cCRT - DEU									
CR	31	13 (41,9)	9,1 [0,7; NE]	34	12 (35,3)	9,2 [1,1; NE]	0,92	[0,42; 2,04]	0,8301
PR	191	99 (51,8)	5,5 [2,7;11,0]	200	99 (49,5)	3,6 [1,6; 9,2]	0,93	[0,70; 1,23]	0,6089
SD	42	17 (40,5)	6,4 [1,6; NE]	32	12 (37,5)	15,6 [0,9; NE]	1,02	[0,49; 2,19]	0,9621
Interaktions p-Wert									0,9733
Geschlecht - DEU									
Männer	178	99 (55,6)	5,5 [2,7; 9,1]	188	87 (46,3)	9,1 [2,8;13,8]	1,11	[0,84; 1,49]	0,4602
Frauen	86	30 (34,9)	14,8 [2,8; NE]	78	36 (46,2)	1,4 [0,9; 5,5]	0,56	[0,34; 0,91]	0,0187*

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,0164*
Altersgruppe - DEU									
<65 Jahre	160	81 (50,6)	5,5 [2,7;14,7]	162	76 (46,9)	1,8 [1,1; 9,2]	0,87	[0,63; 1,19]	0,3758
>=65 Jahre	104	48 (46,2)	6,4 [2,7;12,1]	104	47 (45,2)	8,3 [2,7;15,6]	1,04	[0,69; 1,56]	0,8491
Interaktions p-Wert									0,4873
PD-L1-Status - DEU									
TC and IC <1%	78	41 (52,6)	2,7 [1,1;34,1]	73	32 (43,8)	9,1 [1,1; NE]	1,13	[0,71; 1,80]	0,6158
TC or IC >=1%	84	43 (51,2)	9,1 [2,7;25,8]	98	45 (45,9)	7,4 [1,4;40,4]	0,94	[0,62; 1,44]	0,7907
Interaktions p-Wert									0,5829
Raucherstatus - DEU									
Raucher	241	116 (48,1)	6,4 [3,6;12,0]	240	112 (46,7)	4,6 [1,6;11,0]	0,90	[0,69; 1,17]	0,4186
Nichtraucher	23	13 (56,5)	1,6 [1,0; NE]	26	11 (42,3)	5,5 [0,5; NE]	1,36	[0,61; 3,10]	0,4491
Interaktions p-Wert									0,3322
Abstammung - DEU									
Weiß	130	60 (46,2)	5,5 [2,7;11,0]	137	61 (44,5)	2,7 [1,1;10,1]	0,91	[0,64; 1,30]	0,5974
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	69 (52,7)	6,4 [1,9;25,8]	121	60 (49,6)	9,1 [2,7;18,5]	0,97	[0,68; 1,37]	0,8503
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8046
Geographische Region - DEU									
Asien	129	69 (53,5)	6,4 [1,9;25,8]	120	60 (50,0)	9,1 [2,7;18,5]	0,96	[0,68; 1,36]	0,8232
Europa	94	48 (51,1)	5,5 [2,7;11,0]	112	54 (48,2)	1,7 [1,1; 8,3]	0,86	[0,58; 1,27]	0,4487

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.9 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Nordamerika	41	12 (29,3)	9,1 [0,9;14,8]	34	9 (26,5)	12,8 [0,7; NE]	1,25	[0,53; 3,07]	0,6086
Interaktions p-Wert									0,7257
ECOG-Status zu Baseline - DEU									
0	133	57 (42,9)	12,0 [2,8;28,5]	131	66 (50,4)	3,6 [1,6;11,1]	0,75	[0,53; 1,07]	0,1141
1	131	72 (55,0)	4,6 [1,8; 8,2]	135	57 (42,2)	7,4 [1,4;18,5]	1,15	[0,81; 1,64]	0,4255
Interaktions p-Wert									0,0916

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.2.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	14 (38,9)	7,4 [2,8; NE]	37	15 (40,5)	12,8 [3,6; NE]	1,17	[0,56; 2,44]	0,6707
Stadium III	228	92 (40,4)	16,5 [9,1;30,4]	229	85 (37,1)	18,5 [8,2;30,3]	0,95	[0,71; 1,28]	0,7470
Interaktions p-Wert									0,6067
TNM Status (eCRF) - DEU									
Stadium I/II	33	13 (39,4)	7,4 [2,8; NE]	34	14 (41,2)	10,1 [3,6; NE]	1,06	[0,49; 2,27]	0,8767
Stadium III	231	93 (40,3)	16,5 [9,1;30,4]	232	86 (37,1)	18,7 [8,2;30,4]	0,97	[0,72; 1,30]	0,8327
Interaktions p-Wert									0,8250
Erhalt einer PCI (IVRS) - DEU									
Ja	142	62 (43,7)	16,5 [6,4;29,4]	144	55 (38,2)	12,8 [5,5;26,6]	0,89	[0,62; 1,29]	0,5361
Nein	122	44 (36,1)	13,8 [8,2;34,1]	122	45 (36,9)	23,9 [8,2; NE]	1,08	[0,71; 1,63]	0,7293
Interaktions p-Wert									0,5039
Erhalt einer PCI (eCRF) - DEU									
Ja	142	62 (43,7)	16,5 [6,4;29,4]	143	55 (38,5)	12,8 [5,5;26,6]	0,89	[0,62; 1,29]	0,5361
Nein	122	44 (36,1)	13,8 [8,2;34,1]	123	45 (36,6)	23,9 [8,2; NE]	1,08	[0,71; 1,63]	0,7293
Interaktions p-Wert									0,5039
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	9 (28,1)	34,1 [8,3; NE]	32	9 (28,1)	NE [NE; NE]	0,75	[0,29; 1,92]	0,5426
>=14 bis <28 Tage	79	32 (40,5)	9,2 [3,6; NE]	80	26 (32,5)	NE [NE; NE]	1,46	[0,87; 2,47]	0,1493
>=28 Tage	153	65 (42,5)	13,8 [7,4;29,4]	154	65 (42,2)	11,0 [5,5;20,2]	0,84	[0,60; 1,19]	0,3363
Interaktions p-Wert									0,1883
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	6 (37,5)	34,1 [5,5; NE]	24	7 (29,2)	NE [NE; NE]	0,94	[0,30; 2,85]	0,9183
>=28 bis <56 Tage	104	30 (28,8)	30,5 [13,8; NE]	104	36 (34,6)	18,7 [6,4; NE]	0,70	[0,43; 1,13]	0,1442
>=56 bis <84 Tage	98	45 (45,9)	8,2 [3,7;29,4]	76	29 (38,2)	10,1 [4,6; NE]	1,09	[0,69; 1,76]	0,7160
>=84 Tage	46	25 (54,3)	8,2 [1,1;14,7]	62	28 (45,2)	16,5 [3,6;36,7]	1,42	[0,82; 2,44]	0,2040
Interaktions p-Wert									0,2739
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	40 (44,0)	8,3 [3,6;29,4]	88	38 (43,2)	7,3 [3,5;26,6]	0,97	[0,62; 1,52]	0,9003
Cisplatin	173	66 (38,2)	16,6 [9,1; NE]	178	62 (34,8)	20,2 [11,0;36,7]	0,98	[0,69; 1,39]	0,9201
Interaktions p-Wert									0,9704
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	71 (36,4)	25,7 [9,2;34,1]	187	61 (32,6)	20,2 [10,1; NE]	1,00	[0,71; 1,41]	0,9809
Zweimal täglich	69	35 (50,7)	8,2 [3,6;39,5]	79	39 (49,4)	8,3 [3,6;26,6]	1,00	[0,63; 1,57]	0,9838
Interaktions p-Wert									0,9985
Bestes Ansprechen auf cCRT - DEU									
CR	31	12 (38,7)	25,7 [2,7; NE]	34	11 (32,4)	7,3 [2,8; NE]	0,77	[0,34; 1,76]	0,5235
PR	191	74 (38,7)	15,6 [8,2; NE]	200	78 (39,0)	18,5 [8,2;36,7]	0,93	[0,68; 1,28]	0,6574
SD	42	20 (47,6)	9,2 [1,2;29,4]	32	11 (34,4)	26,6 [3,6; NE]	1,42	[0,69; 3,08]	0,3422
Interaktions p-Wert									0,4834
Geschlecht - DEU									
Männer	178	77 (43,3)	15,6 [8,3;34,1]	188	71 (37,8)	22,9 [8,2; NE]	1,02	[0,74; 1,41]	0,8963
Frauen	86	29 (33,7)	13,8 [5,5; NE]	78	29 (37,2)	16,6 [3,5;30,3]	0,87	[0,52; 1,47]	0,6045
Interaktions p-Wert									0,6110
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Nutzenbewertung nach AMNOG

Table 3.6.2.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	67 (41,9)	16,5 [6,4;39,5]	162	64 (39,5)	16,5 [6,4;36,7]	0,89	[0,63; 1,26]	0,5173
>=65 Jahre	104	39 (37,5)	14,7 [7,3;34,1]	104	36 (34,6)	18,5 [7,3; NE]	1,14	[0,72; 1,79]	0,5779
Interaktions p-Wert									0,4037
PD-L1-Status - DEU									
TC and IC <1%	78	33 (42,3)	16,5 [8,2; NE]	73	26 (35,6)	36,7 [7,3; NE]	1,06	[0,64; 1,79]	0,8144
TC or IC >=1%	84	34 (40,5)	21,2 [8,3; NE]	98	37 (37,8)	18,7 [8,2; NE]	0,95	[0,59; 1,51]	0,8281
Interaktions p-Wert									0,7491
Raucherstatus - DEU									
Raucher	241	96 (39,8)	15,6 [8,2;30,4]	240	92 (38,3)	16,6 [8,2;26,6]	0,96	[0,72; 1,28]	0,7703
Nichtraucher	23	10 (43,5)	13,8 [1,4; NE]	26	8 (30,8)	NE [NE; NE]	1,22	[0,48; 3,19]	0,6781
Interaktions p-Wert									0,6291
Abstammung - DEU									
Weiß	130	43 (33,1)	16,6 [7,4; NE]	137	44 (32,1)	18,5 [7,3;30,3]	0,95	[0,63; 1,46]	0,8270
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	63 (48,1)	13,8 [5,5;34,1]	121	55 (45,5)	12,8 [5,6;36,7]	0,98	[0,68; 1,41]	0,9092
Andere	2	0	NE [NE; NE]	5	1 (20,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9272
Geographische Region - DEU									
Asien	129	63 (48,8)	13,8 [5,5;34,1]	120	54 (45,0)	12,8 [5,6;36,7]	1,00	[0,69; 1,44]	0,9877
Europa	94	33 (35,1)	29,4 [11,0; NE]	112	39 (34,8)	20,2 [6,4; NE]	0,85	[0,53; 1,35]	0,4946
Nordamerika	41	10 (24,4)	7,4 [2,7; NE]	34	7 (20,6)	16,6 [3,5; NE]	1,48	[0,57; 4,07]	0,4233
Interaktions p-Wert									0,5847
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.2.10 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EORTC QLQ-LC13 Wunder Mund
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	52 (39,1)	13,8 [6,4; NE]	131	50 (38,2)	22,9 [8,2;36,7]	1,02	[0,69; 1,51]	0,9229
1	131	54 (41,2)	16,6 [8,2;29,4]	135	50 (37,0)	16,6 [4,5;30,3]	0,93	[0,64; 1,38]	0,7293
Interaktions p-Wert									0,7547

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Anhang 4-G6.3.3: EORTC QLQ-LC13 - Subgruppenanalysen Kaplan-Meier-Plot

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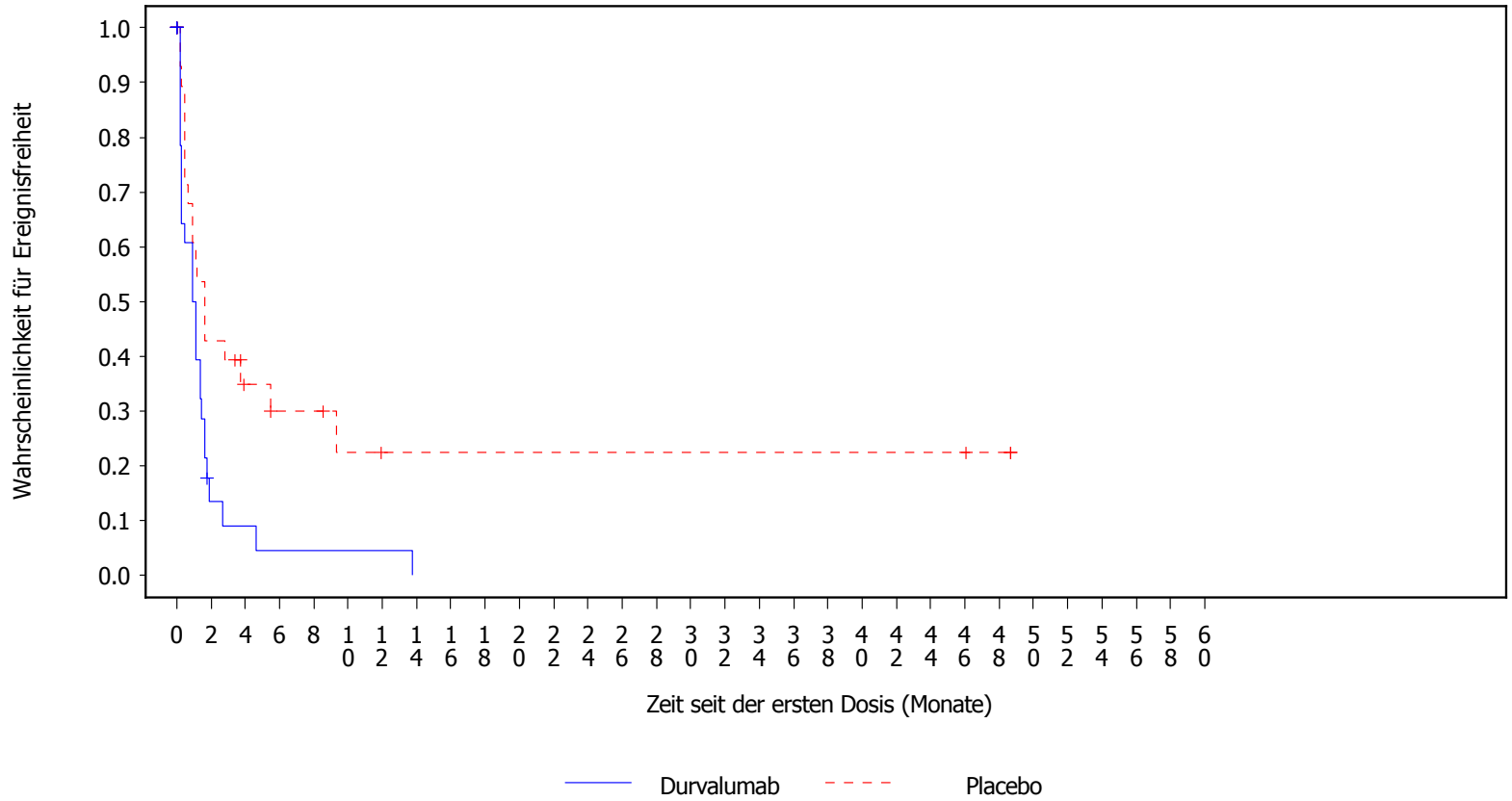
Figure 3.6.2.11 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe for Zeit vom Ende der cCRT bis Randomisierung - DEU=<14 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

32	3	2	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
32	12	7	5	5	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	0	0	0	0	0	Placebo

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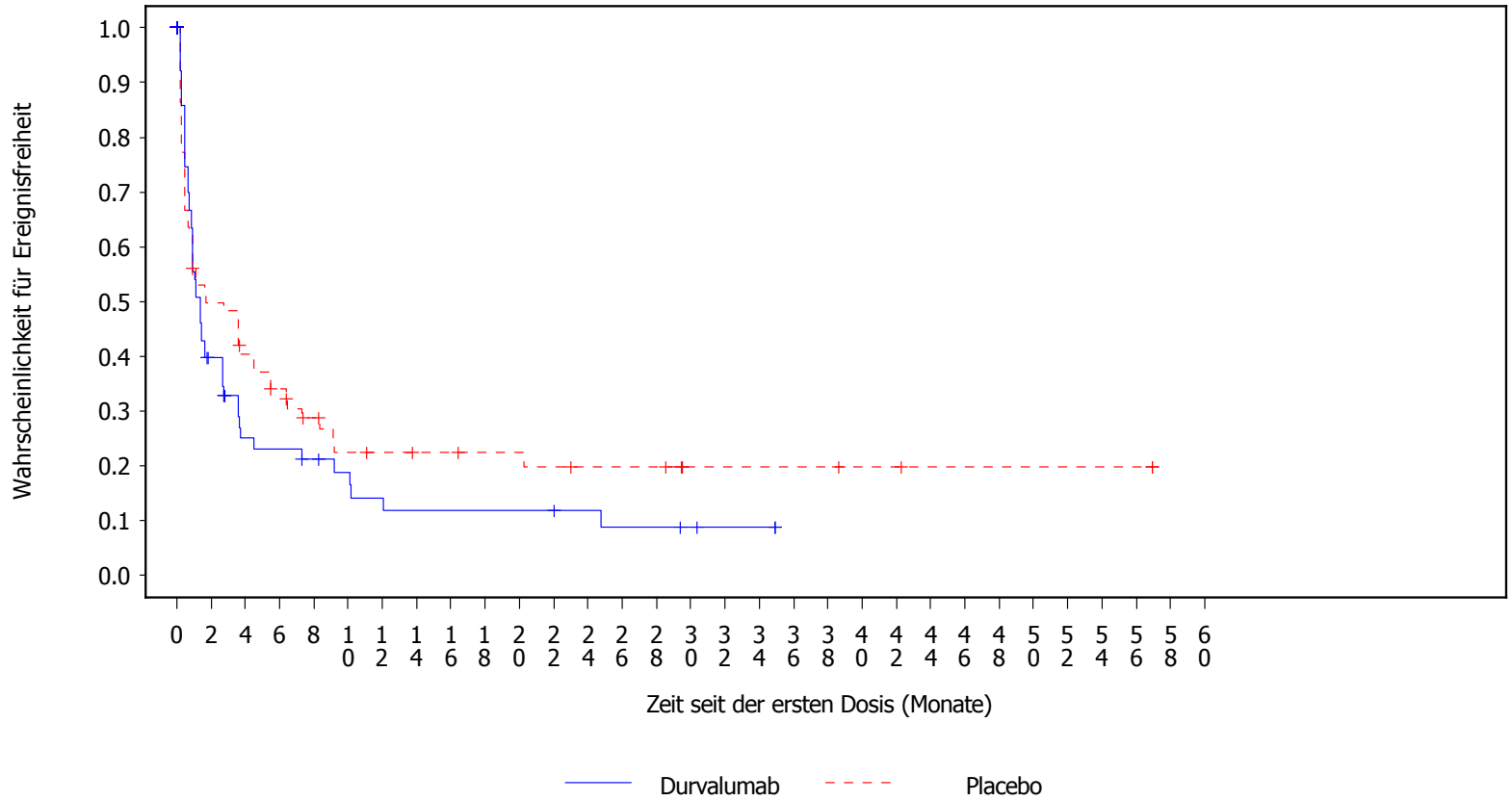
Figure 3.6.2.12 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe for Zeit vom Ende der cCRT bis Randomisierung - DEU=>=14 bis <28 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

79	23	13	12	10	8	6	5	5	5	5	5	4	3	3	2	1	1	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
80	32	25	20	15	11	10	9	9	8	8	7	6	6	6	3	3	3	3	2	2	1	1	1	1	1	1	0	0	Placebo

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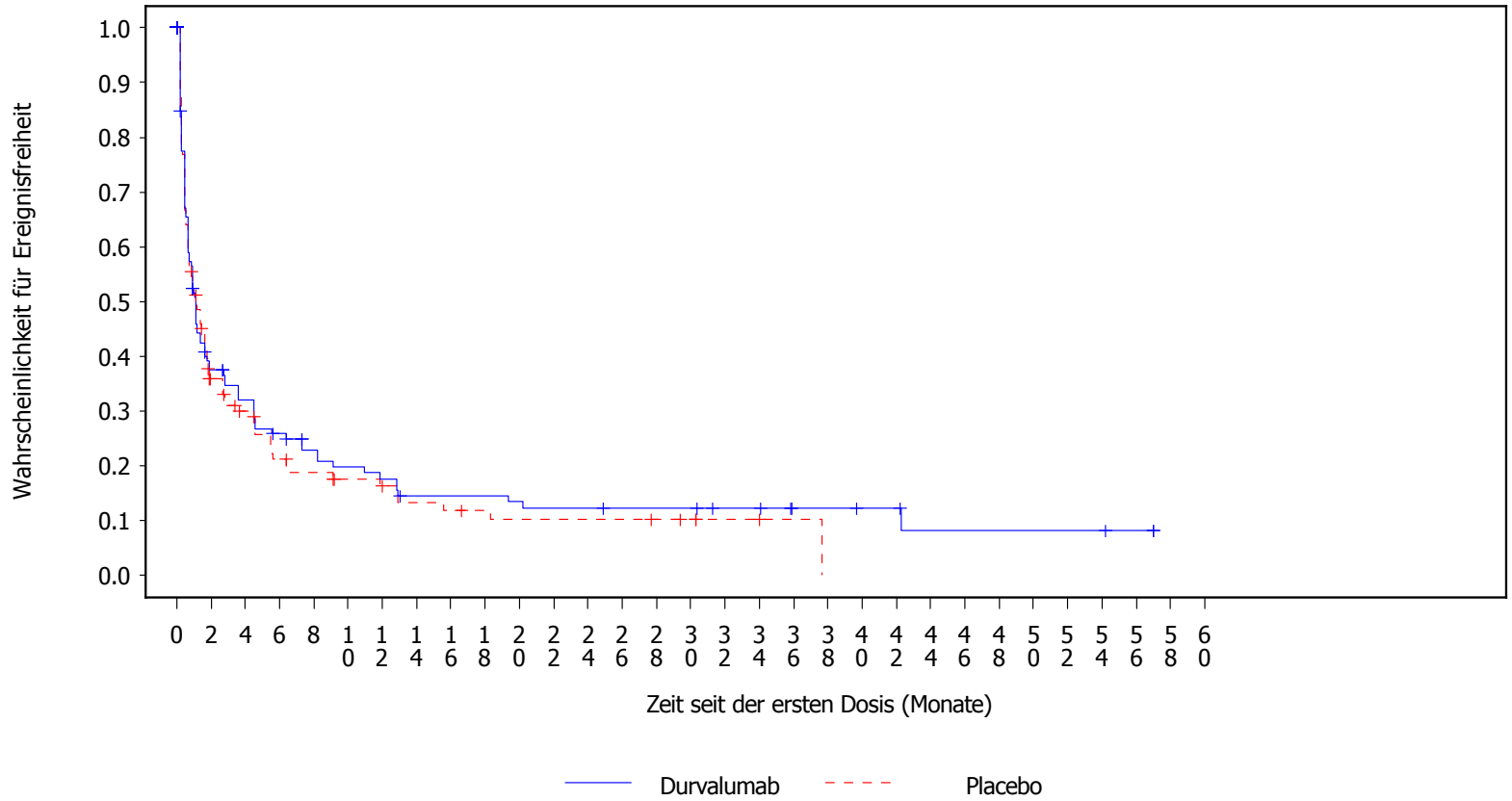
Figure 3.6.2.13 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dyspnoe for Zeit vom Ende der cCRT bis Randomisierung - DEU=>=28 Tage
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

153	44	36	28	22	19	17	13	13	13	12	11	11	10	10	10	8	8	5	5	4	4	2	2	2	2	2	2	1	0	0	Durvalumab
154	37	28	19	16	13	12	9	8	7	6	6	6	6	5	4	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	Placebo

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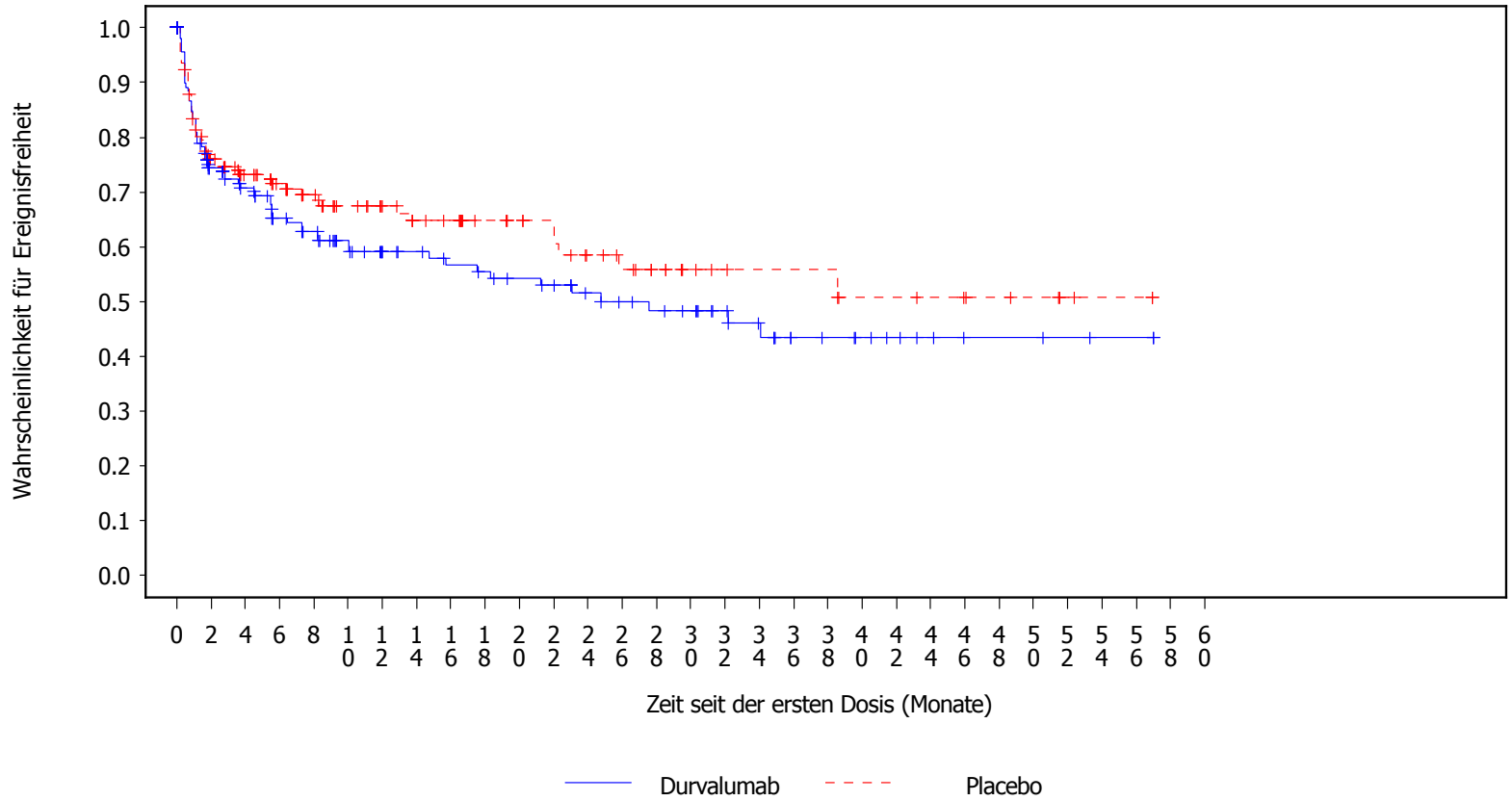
Figure 3.6.2.14 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie for Geschlecht - DEU=Männer
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

178	107	94	79	73	63	54	51	47	45	42	40	34	31	29	27	22	18	12	11	9	7	5	3	3	3	2	1	1	0	0	Durvalumab
188	110	90	78	67	57	52	45	43	35	33	31	25	22	18	14	12	11	11	11	8	8	7	6	5	4	2	1	1	0	0	Placebo

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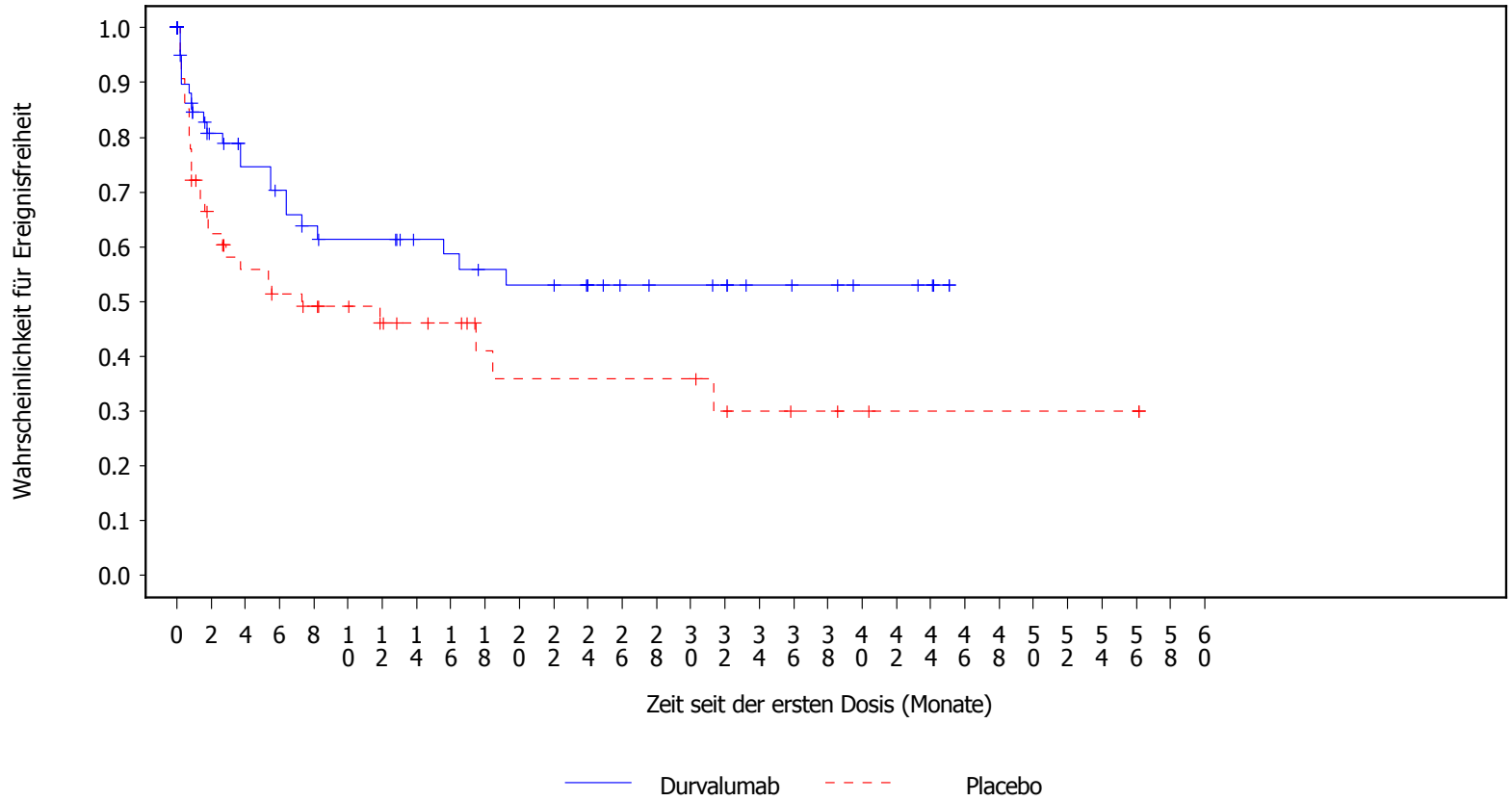
Figure 3.6.2.15 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Dysphagie for Geschlecht - DEU=Frauen
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

86	41	35	32	28	26	26	22	21	19	18	18	14	12	11	11	10	7	6	6	4	4	3	0	0	0	0	0	0	0	Durvalumab
78	31	25	22	20	18	15	13	12	8	7	7	7	7	7	7	5	4	3	3	2	1	1	1	1	1	1	1	0	0	Placebo

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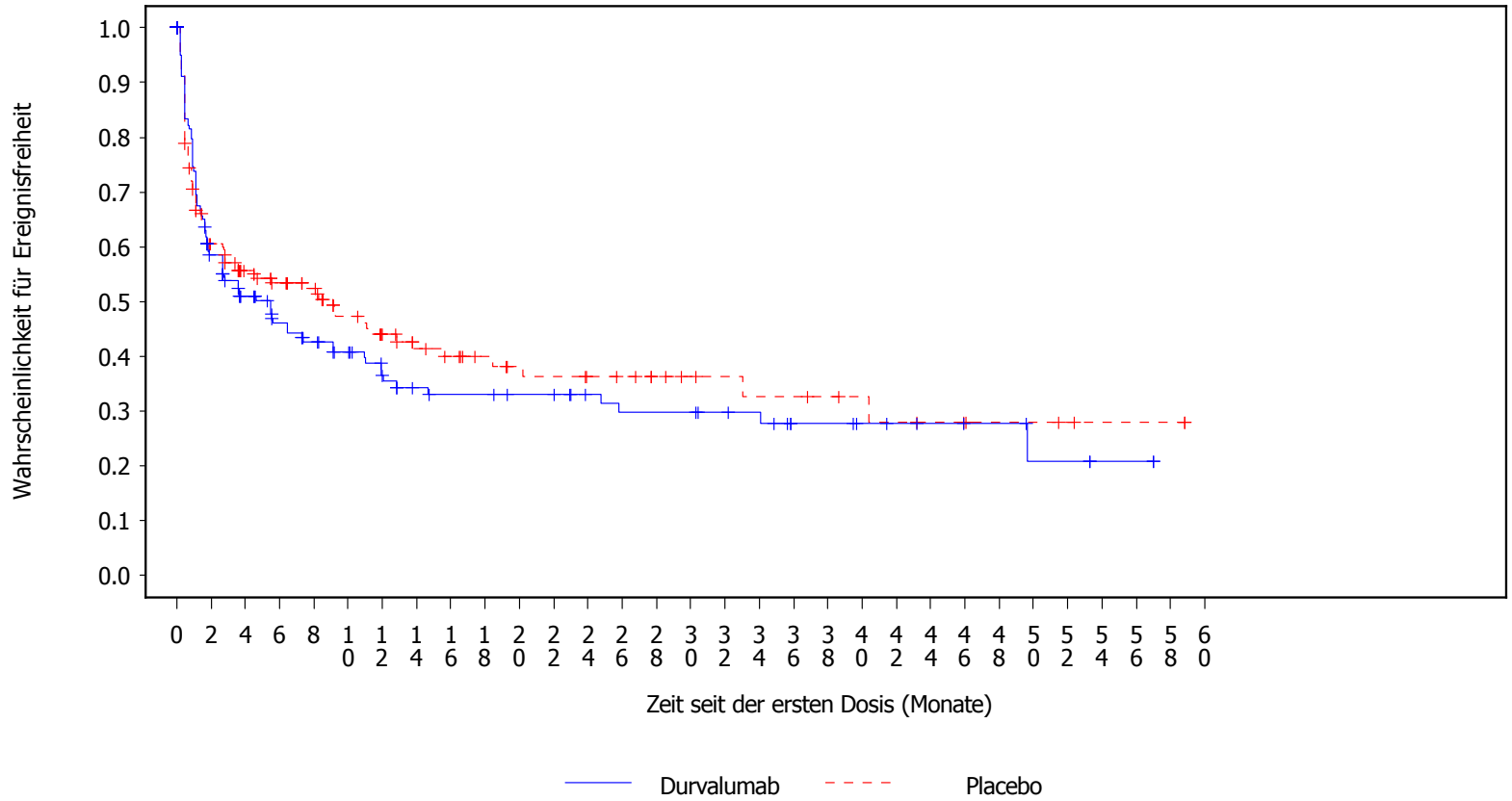
Figure 3.6.2.16 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust for Geschlecht - DEU=Männer
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

1787	68	55	48	42	33	28	26	26	24	24	20	18	18	18	16	15	10	10	8	7	6	5	5	3	3	1	1	0	0	Durvalumab
1888	72	63	55	44	37	30	27	23	20	19	17	16	13	11	10	9	9	8	7	6	5	4	3	3	2	1	1	1	0	Placebo

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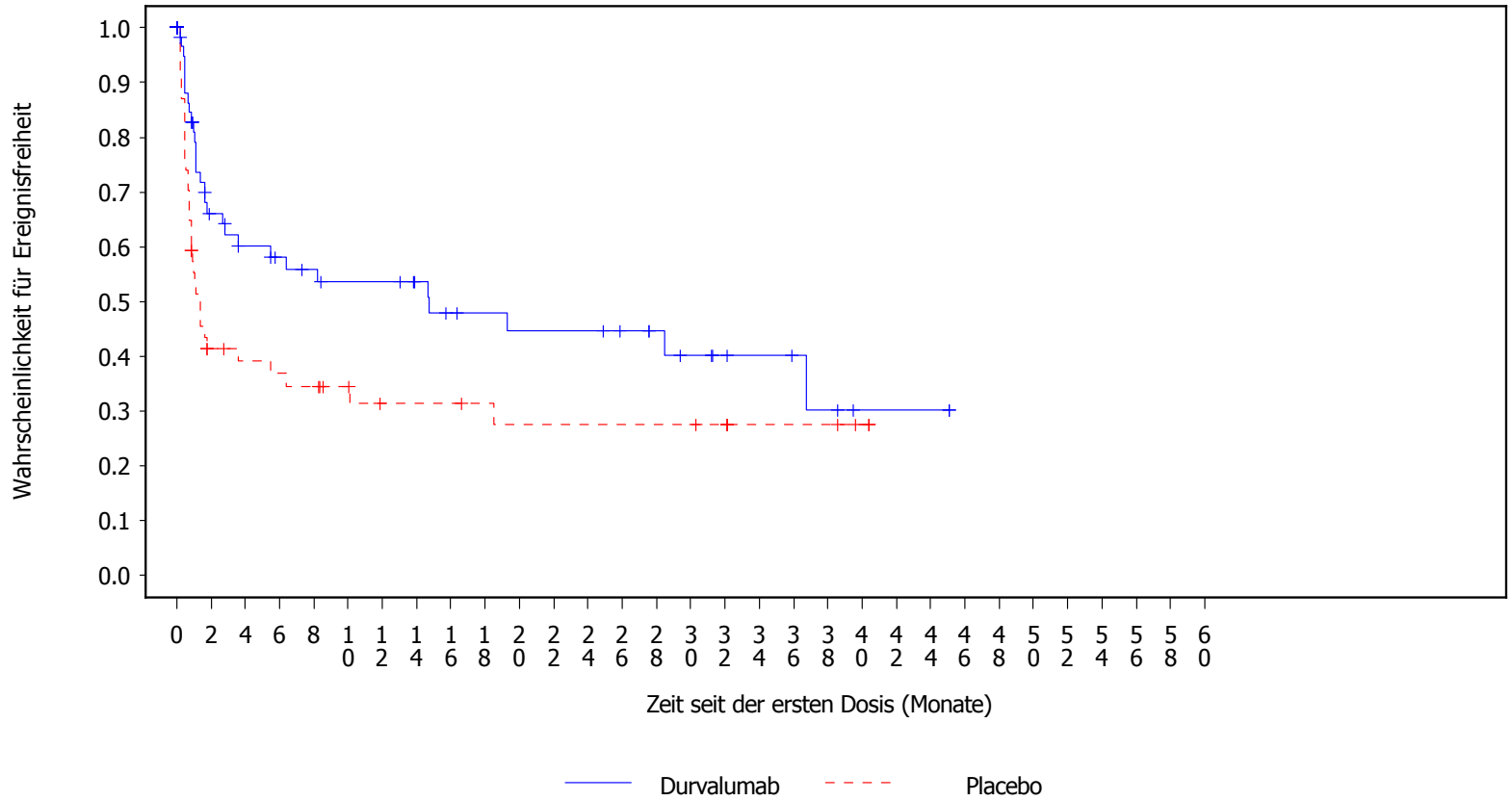
Figure 3.6.2.17 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung EORTC QLQ-LC13 Schmerzen in der Brust for Geschlecht - DEU=Frauen
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

86	34	29	26	24	22	22	19	16	15	14	14	14	12	10	8	6	5	4	3	1	1	1	0	0	0	0	0	0	0	Durvalumab
78	19	17	16	15	12	9	9	9	8	7	7	7	7	7	7	6	3	3	3	1	0	0	0	0	0	0	0	0	0	Placebo

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Anhang 4-G6.4: EQ-5D VAS

Nutzenbewertung nach AMNOG

Table 3.5.3.1 ADRIATIC: Summary of analysis of time to deterioration in EQ-5D VAS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung EQ-5D VAS	264	111 (42,0)	11,0 [9,1;16,5]	266	90 (33,8)	18,3 [7,4;31,2]	1,17	[0,88; 1,55]	0,2945

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Anhang 4-G6.4.1: EQ-5D VAS - Kaplan-Meier-Plot

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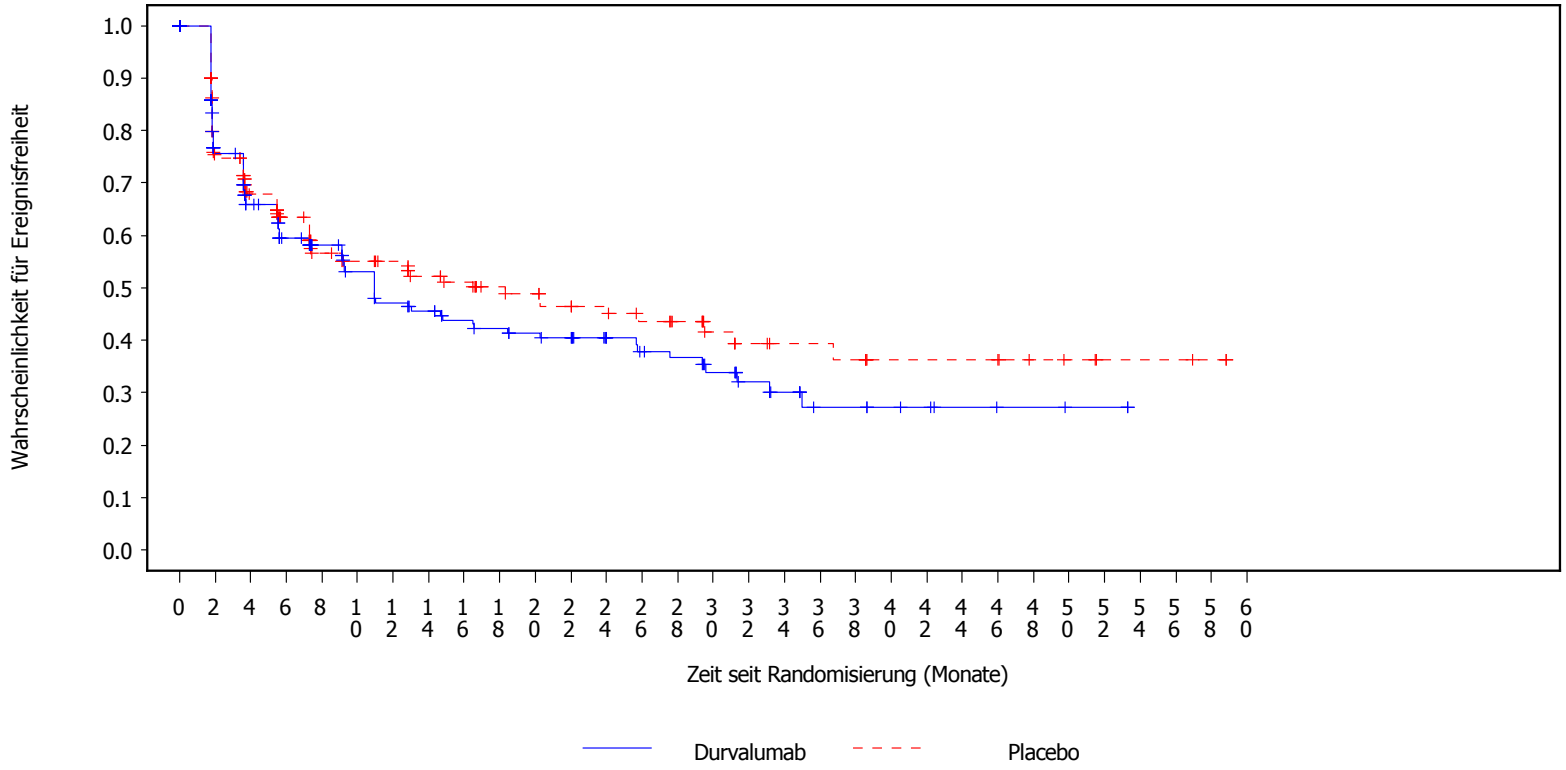
Figure 3.5.3.2 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung EQ-5D VAS
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	143	116	97	83	71	62	57	51	48	45	43	33	30	28	23	17	14	8	8	6	5	3	2	2	1	1	0	0	0	0	Durvalumab
266	134	109	90	69	64	61	53	49	43	41	37	33	30	26	19	15	13	13	12	8	8	8	7	5	4	2	2	2	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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Anhang 4-G6.4.2: EQ-5D VAS - Subgruppenanalysen

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Table 3.6.3.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EQ-5D VAS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	12 (33,3)	14,8 [3,6; NE]	37	9 (24,3)	31,2 [5,5; NE]	1,66	[0,70; 4,07]	0,2474
Stadium III	228	99 (43,4)	11,0 [9,1;18,4]	229	81 (35,4)	12,9 [7,3;25,8]	1,10	[0,82; 1,47]	0,5403
Interaktions p-Wert									0,3704
TNM Status (eCRF) - DEU									
Stadium I/II	33	10 (30,3)	14,8 [5,5; NE]	34	9 (26,5)	31,2 [3,6; NE]	1,23	[0,50; 3,10]	0,6491
Stadium III	231	101 (43,7)	11,0 [7,3;16,5]	232	81 (34,9)	14,7 [7,3;29,5]	1,14	[0,85; 1,53]	0,3720
Interaktions p-Wert									0,8750
Erhalt einer PCI (IVRS) - DEU									
Ja	142	58 (40,8)	18,4 [9,1;31,3]	144	49 (34,0)	12,8 [7,3;36,7]	0,94	[0,64; 1,38]	0,7613
Nein	122	53 (43,4)	9,2 [5,5;11,0]	122	41 (33,6)	20,3 [7,3; NE]	1,47	[0,98; 2,22]	0,0629
Interaktions p-Wert									0,1187
Erhalt einer PCI (eCRF) - DEU									
Ja	142	58 (40,8)	18,4 [9,1;31,3]	143	49 (34,3)	12,8 [7,3;36,7]	0,94	[0,64; 1,38]	0,7613
Nein	122	53 (43,4)	9,2 [5,5;11,0]	123	41 (33,3)	20,3 [7,3; NE]	1,47	[0,98; 2,22]	0,0629
Interaktions p-Wert									0,1187
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	16 (50,0)	5,6 [3,6;18,4]	32	15 (46,9)	5,5 [1,8; NE]	1,11	[0,55; 2,27]	0,7685
>=14 bis <28 Tage	79	35 (44,3)	9,2 [5,5;25,8]	80	21 (26,3)	31,2 [9,1; NE]	1,75	[1,03; 3,05]	0,0395*
>=28 Tage	153	60 (39,2)	13,0 [9,2;31,3]	154	54 (35,1)	12,9 [7,3;29,5]	0,96	[0,67; 1,39]	0,8412
Interaktions p-Wert									0,1956
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.3.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EQ-5D VAS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	10 (62,5)	4,5 [1,8;25,8]	24	9 (37,5)	18,3 [3,7; NE]	1,85	[0,74; 4,65]	0,1829
>=28 bis <56 Tage	104	40 (38,5)	14,7 [10,9;29,6]	104	32 (30,8)	20,2 [3,7; NE]	0,93	[0,58; 1,49]	0,7563
>=56 bis <84 Tage	98	43 (43,9)	9,2 [5,5;18,4]	76	22 (28,9)	23,9 [7,4; NE]	1,55	[0,94; 2,64]	0,0885
>=84 Tage	46	18 (39,1)	11,0 [3,6; NE]	62	27 (43,5)	9,1 [3,7;36,7]	1,02	[0,55; 1,84]	0,9445
Interaktions p-Wert									0,3501
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	39 (42,9)	10,9 [5,5;25,7]	88	34 (38,6)	7,4 [5,5;29,5]	1,01	[0,64; 1,60]	0,9789
Cisplatin	173	72 (41,6)	11,0 [9,1;25,8]	178	56 (31,5)	23,9 [9,1; NE]	1,25	[0,88; 1,77]	0,2163
Interaktions p-Wert									0,4693
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	79 (40,5)	11,0 [9,2;25,7]	187	56 (29,9)	20,2 [7,4; NE]	1,17	[0,83; 1,65]	0,3789
Zweimal täglich	69	32 (46,4)	9,1 [3,6;31,3]	79	34 (43,0)	9,1 [7,3;36,7]	1,16	[0,72; 1,89]	0,5374
Interaktions p-Wert									0,9975
Bestes Ansprechen auf cCRT - DEU									
CR	31	14 (45,2)	11,0 [1,9;29,4]	34	10 (29,4)	9,1 [1,8; NE]	1,16	[0,52; 2,69]	0,7203
PR	191	78 (40,8)	11,0 [5,6;25,8]	200	71 (35,5)	20,2 [7,4;36,7]	1,17	[0,84; 1,61]	0,3507
SD	42	19 (45,2)	16,5 [3,7;29,6]	32	9 (28,1)	7,4 [1,8; NE]	0,99	[0,46; 2,29]	0,9759
Interaktions p-Wert									0,9312
Geschlecht - DEU									
Männer	178	80 (44,9)	11,0 [9,1;25,7]	188	61 (32,4)	23,9 [12,8; NE]	1,29	[0,93; 1,81]	0,1332
Frauen	86	31 (36,0)	9,1 [5,5;29,4]	78	29 (37,2)	5,5 [2,0;12,8]	0,86	[0,52; 1,43]	0,5620
Interaktions p-Wert									0,1920
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.3.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EQ-5D VAS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	70 (43,8)	11,0 [7,3;16,5]	162	53 (32,7)	20,2 [7,3; NE]	1,15	[0,80; 1,65]	0,4514
>=65 Jahre	104	41 (39,4)	11,0 [5,6;29,6]	104	37 (35,6)	18,3 [7,3; NE]	1,17	[0,75; 1,84]	0,4773
Interaktions p-Wert									0,9337
PD-L1-Status - DEU									
TC and IC <1%	78	37 (47,4)	11,0 [5,5;25,8]	73	33 (45,2)	7,3 [3,8;23,9]	0,95	[0,59; 1,53]	0,8276
TC or IC >=1%	84	43 (51,2)	7,3 [3,7;14,8]	98	27 (27,6)	NE [NE; NE]	1,77	[1,10; 2,89]	0,0188*
Interaktions p-Wert									0,0699
Raucherstatus - DEU									
Raucher	241	100 (41,5)	11,0 [9,1;18,4]	240	81 (33,8)	18,3 [7,4;31,2]	1,17	[0,88; 1,58]	0,2828
Nichtraucher	23	11 (47,8)	14,8 [2,0;29,6]	26	9 (34,6)	7,3 [1,8; NE]	1,00	[0,41; 2,49]	0,9970
Interaktions p-Wert									0,7387
Abstammung - DEU									
Weiß	130	55 (42,3)	9,1 [3,6;11,0]	137	43 (31,4)	14,7 [5,5; NE]	1,40	[0,94; 2,09]	0,0998
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	2 (66,7)	12,8 [1,8; NE]	NC	[NC]	NC
Asiatisch	131	56 (42,7)	16,5 [9,2;33,1]	121	44 (36,4)	29,5 [7,4; NE]	1,04	[0,70; 1,56]	0,8349
Andere	2	0	NE [NE; NE]	5	1 (20,0)	3,6 [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,3090
Geographische Region - DEU									
Asien	129	56 (43,4)	16,5 [9,2;33,1]	120	43 (35,8)	29,5 [7,3; NE]	1,06	[0,71; 1,58]	0,7806
Europa	94	50 (53,2)	5,6 [3,6;11,0]	112	38 (33,9)	12,8 [5,5; NE]	1,54	[1,01; 2,37]	0,0431*
Nordamerika	41	5 (12,2)	NE [NE; NE]	34	9 (26,5)	12,9 [1,9; NE]	0,57	[0,17; 1,64]	0,2989
Interaktions p-Wert									0,1613
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Nutzenbewertung nach AMNOG

Table 3.6.3.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung EQ-5D VAS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	57 (42,9)	11,0 [5,5;25,8]	131	46 (35,1)	14,7 [7,3; NE]	1,25	[0,85; 1,85]	0,2659
1	131	54 (41,2)	11,0 [7,3;25,7]	135	44 (32,6)	16,5 [7,3; NE]	1,07	[0,72; 1,60]	0,7454
Interaktions p-Wert									0,5873

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Anhang 4-G6.5: PGIS

Nutzenbewertung nach AMNOG

Table 3.5.4.1 ADRIATIC: Summary of analysis of time to deterioration in PGIS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Zeit bis zur Verschlechterung PGIS	264	132 (50,0)	3,7 [1,9; 7,3]	266	127 (47,7)	5,5 [3,6; 5,5]	1,09	[0,85; 1,39]	0,5688

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] Estimated from Cox proportional hazards model stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Efron method for handling ties. 95% CI from profile likelihood estimation.[c] Determined using log-rank test stratified by IVRS TNM Stage (I/II vs. III) and IVRS Receipt of PCI (Yes vs. No). Hazard ratio <1 favours durva *p<0.05.
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Anhang 4-G6.5.1: PGIS - Kaplan-Meier-Plot

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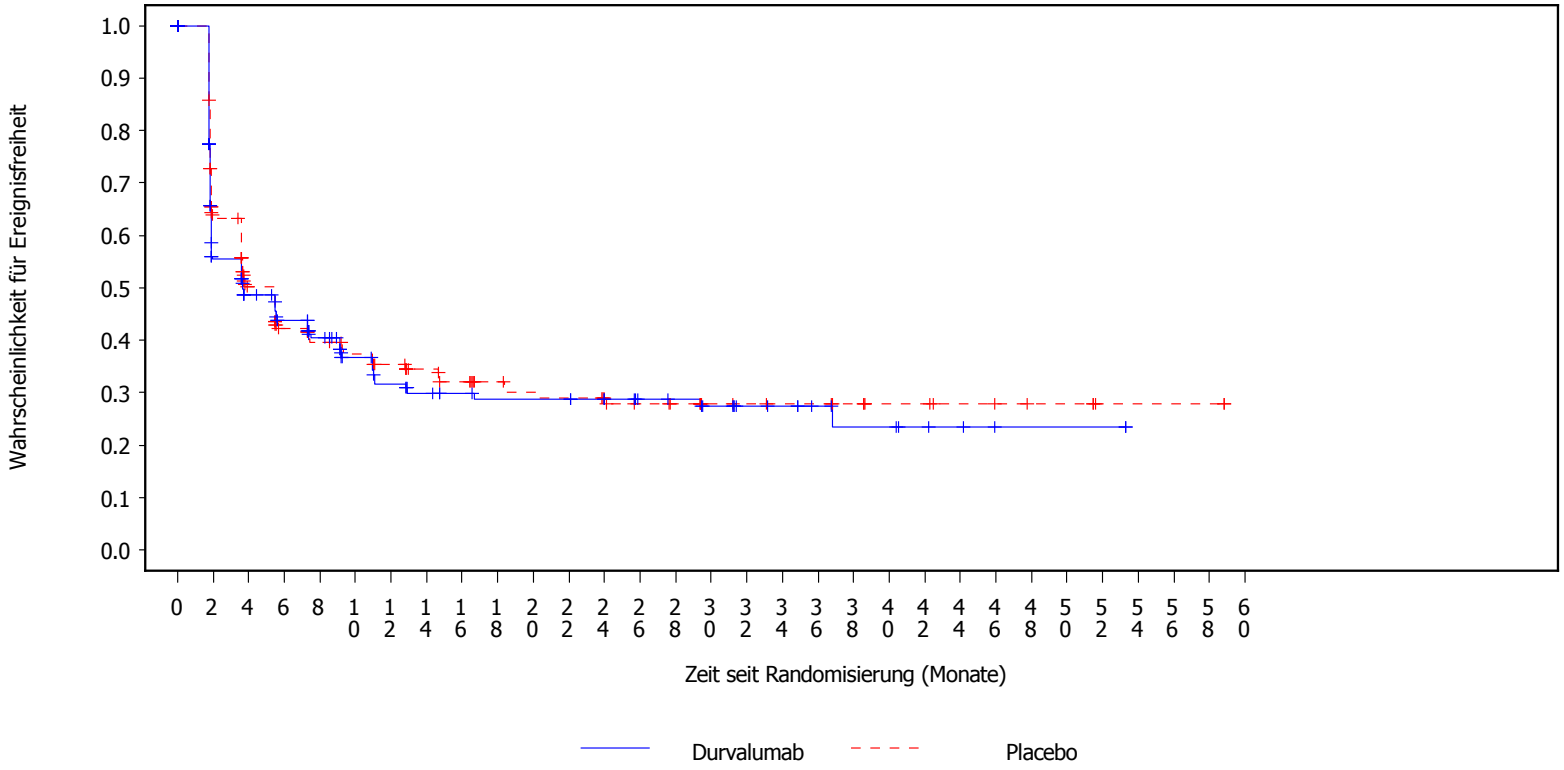
Figure 3.5.4.2 ADRIATIC: Kaplan-Meier plot of Zeit bis zur Verschlechterung PGIS
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

264	10685	71	59	45	37	32	29	27	27	27	23	20	19	16	12	11	8	6	6	4	3	1	1	1	1	0	0	0	0	Durvalumab
266	11984	65	58	53	48	42	37	32	29	28	25	22	20	15	14	13	13	11	8	8	6	5	4	4	1	1	1	1	0	Placebo

Time to deterioration is defined as time from randomisation date until the earliest date of deterioration in the respective score. Patients with no evaluable assessments or no baseline data are censored at day 1. Patients alive or who died more than 2 visits after last assessment, with no deterioration are censored at last evaluable assessment. Patients with available baseline values who did not experience a deterioration up to the timepoint of analyses who died within 2 visits of last assessment are censored at their death date.

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Anhang 4-G6.5.2: PGIS - Subgruppenanalysen

Nutzenbewertung nach AMNOG Seite 1 von 4

Table 3.6.4.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung PGIS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	13 (36,1)	7,5 [1,8; NE]	37	18 (48,6)	3,6 [1,9;20,2]	0,73	[0,35; 1,48]	0,3833
Stadium III	228	119 (52,2)	3,6 [1,9; 5,6]	229	109 (47,6)	5,5 [3,6; 7,4]	1,17	[0,90; 1,51]	0,2455
Interaktions p-Wert									0,2227
TNM Status (eCRF) - DEU									
Stadium I/II	33	12 (36,4)	12,8 [1,8; NE]	34	17 (50,0)	3,6 [1,8;20,2]	0,63	[0,29; 1,32]	0,2213
Stadium III	231	120 (51,9)	3,6 [1,9; 5,6]	232	110 (47,4)	5,5 [3,6; 7,4]	1,19	[0,91; 1,54]	0,1983
Interaktions p-Wert									0,1135
Erhalt einer PCI (IVRS) - DEU									
Ja	142	78 (54,9)	2,0 [1,9; 5,5]	144	68 (47,2)	3,7 [3,6; 5,5]	1,08	[0,78; 1,50]	0,6464
Nein	122	54 (44,3)	5,5 [3,6; 9,1]	122	59 (48,4)	5,5 [3,6; 9,3]	1,10	[0,76; 1,59]	0,6218
Interaktions p-Wert									0,9462
Erhalt einer PCI (eCRF) - DEU									
Ja	142	78 (54,9)	2,0 [1,9; 5,5]	143	68 (47,6)	3,7 [3,6; 5,5]	1,08	[0,78; 1,50]	0,6464
Nein	122	54 (44,3)	5,5 [3,6; 9,1]	123	59 (48,0)	5,5 [3,6; 9,3]	1,10	[0,76; 1,59]	0,6218
Interaktions p-Wert									0,9462
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	32	16 (50,0)	3,7 [1,8; NE]	32	15 (46,9)	7,4 [3,6; NE]	1,36	[0,67; 2,79]	0,3894
>=14 bis <28 Tage	79	41 (51,9)	5,5 [1,9; 7,5]	80	43 (53,8)	3,6 [1,9; 5,5]	1,07	[0,70; 1,64]	0,7555
>=28 Tage	153	75 (49,0)	3,7 [1,9; 9,2]	154	69 (44,8)	3,8 [3,6;11,0]	1,07	[0,77; 1,49]	0,6735
Interaktions p-Wert									0,8219
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.

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Table 3.6.4.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung PGIS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<28 Tage	16	10 (62,5)	1,8 [1,8; NE]	24	12 (50,0)	7,4 [3,6; NE]	2,58	[1,09; 5,99]	0,0320*
>=28 bis <56 Tage	104	46 (44,2)	7,5 [2,0;11,0]	104	47 (45,2)	3,6 [1,9; 5,5]	0,86	[0,57; 1,29]	0,4524
>=56 bis <84 Tage	98	54 (55,1)	3,6 [1,9; 7,3]	76	39 (51,3)	3,7 [1,9; 5,5]	1,06	[0,70; 1,61]	0,7899
>=84 Tage	46	22 (47,8)	5,5 [1,8; NE]	62	29 (46,8)	7,4 [1,9;24,0]	1,26	[0,71; 2,18]	0,4226
Interaktions p-Wert									0,1412
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	91	44 (48,4)	3,6 [1,8; 5,5]	88	50 (56,8)	3,6 [1,8; 3,7]	0,82	[0,54; 1,22]	0,3272
Cisplatin	173	88 (50,9)	5,5 [1,9; 9,1]	178	77 (43,3)	7,4 [3,7;14,7]	1,28	[0,94; 1,74]	0,1120
Interaktions p-Wert									0,0821
Vorheriges Radiochemotherapieregime - DEU									
Täglich	195	97 (49,7)	3,7 [1,9; 7,3]	187	89 (47,6)	3,6 [3,6; 5,5]	1,01	[0,76; 1,35]	0,9479
Zweimal täglich	69	35 (50,7)	5,5 [1,8;12,8]	79	38 (48,1)	5,6 [3,7;24,0]	1,28	[0,81; 2,03]	0,2939
Interaktions p-Wert									0,3918
Bestes Ansprechen auf cCRT - DEU									
CR	31	17 (54,8)	3,6 [1,8; 7,4]	34	8 (23,5)	NE [NE; NE]	2,30	[1,02; 5,66]	0,0438*
PR	191	91 (47,6)	5,5 [3,6; 9,2]	200	106 (53,0)	3,7 [3,6; 5,5]	0,94	[0,71; 1,24]	0,6635
SD	42	24 (57,1)	1,9 [1,8; 3,7]	32	13 (40,6)	5,5 [1,8; NE]	1,54	[0,80; 3,12]	0,2002
Interaktions p-Wert									0,0680
Geschlecht - DEU									
Männer	178	94 (52,8)	5,5 [3,6; 9,1]	188	90 (47,9)	5,5 [3,7; 9,2]	1,11	[0,83; 1,48]	0,4924
Frauen	86	38 (44,2)	1,9 [1,8; 5,5]	78	37 (47,4)	3,6 [1,9; 5,5]	1,09	[0,69; 1,72]	0,7087
Interaktions p-Wert									0,9564
Altersgruppe - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.4.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung PGIS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
<65 Jahre	160	83 (51,9)	3,7 [2,0; 9,1]	162	76 (46,9)	3,8 [3,6; 9,2]	1,10	[0,80; 1,50]	0,5541
>=65 Jahre	104	49 (47,1)	3,6 [1,9; 7,5]	104	51 (49,0)	5,5 [3,6; 7,4]	1,11	[0,75; 1,64]	0,6077
Interaktions p-Wert									0,9723
PD-L1-Status - DEU									
TC and IC <1%	78	44 (56,4)	1,9 [1,8; 7,3]	73	39 (53,4)	3,8 [3,6; 9,2]	1,26	[0,82; 1,95]	0,2928
TC or IC >=1%	84	46 (54,8)	3,7 [1,8;11,0]	98	44 (44,9)	5,6 [3,6;14,7]	1,29	[0,85; 1,95]	0,2309
Interaktions p-Wert									0,9433
Raucherstatus - DEU									
Raucher	241	115 (47,7)	5,5 [3,6; 9,1]	240	116 (48,3)	5,5 [3,6; 5,6]	1,02	[0,79; 1,32]	0,8913
Nichtraucher	23	17 (73,9)	1,8 [1,8; 1,9]	26	11 (42,3)	3,6 [1,8; NE]	2,40	[1,14; 5,28]	0,0218*
Interaktions p-Wert									0,0337*
Abstammung - DEU									
Weiß	130	58 (44,6)	3,6 [1,9; 9,1]	137	58 (42,3)	5,5 [3,6; 7,4]	1,11	[0,77; 1,61]	0,5589
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	74 (56,5)	3,7 [1,9; 7,4]	121	68 (56,2)	3,7 [3,6; 7,4]	1,07	[0,77; 1,49]	0,6927
Andere	2	0	NE [NE; NE]	5	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8662
Geographische Region - DEU									
Asien	129	74 (57,4)	3,7 [1,9; 7,4]	120	68 (56,7)	3,7 [3,6; 7,4]	1,06	[0,76; 1,47]	0,7327
Europa	94	48 (51,1)	3,7 [1,9;11,0]	112	53 (47,3)	5,5 [3,6; 5,5]	1,05	[0,71; 1,55]	0,8195
Nordamerika	41	10 (24,4)	3,6 [1,8; NE]	34	6 (17,6)	NE [NE; NE]	2,11	[0,78; 6,21]	0,1405
Interaktions p-Wert									0,4144
ECOG-Status zu Baseline - DEU									

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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Table 3.6.4.1 ADRIATIC: Summary of subgroup analysis of time to first Zeit bis zur Verschlechterung PGIS
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
0	133	65 (48,9)	5,5 [1,9; 9,1]	131	65 (49,6)	3,8 [3,6; 9,2]	1,15	[0,82; 1,62]	0,4236
1	131	67 (51,1)	3,6 [1,9; 9,1]	135	62 (45,9)	5,5 [1,9; 7,4]	1,05	[0,74; 1,48]	0,8009
Interaktions p-Wert									0,6993

[a] Median time to event based on the Kaplan Meier estimate. NE = not estimable as median (or 95% CLs) not reached.
[b] HR, 95% profile likelihood CIs and likelihood-ratio test p-values estimated from Cox PH model. Efron method for handling ties. If >=10 patients for all subgroup levels, >=10 events for 1 subgroup level, >0 events for all subgroup levels/ treatments, results from model including treatment, subgroup, treatment by subgroup interaction. For subgroups with >2 levels, levels with insufficient data were dropped and, if appropriate, interaction model re-fitted. If interaction model conditions not met but 1 level had >=10 events, and >0 events for both treatments, results from model for 1 level including treatment only.
* Interaction p-value <0.05. HR <1 favours durvalumab. NC = not calculable.
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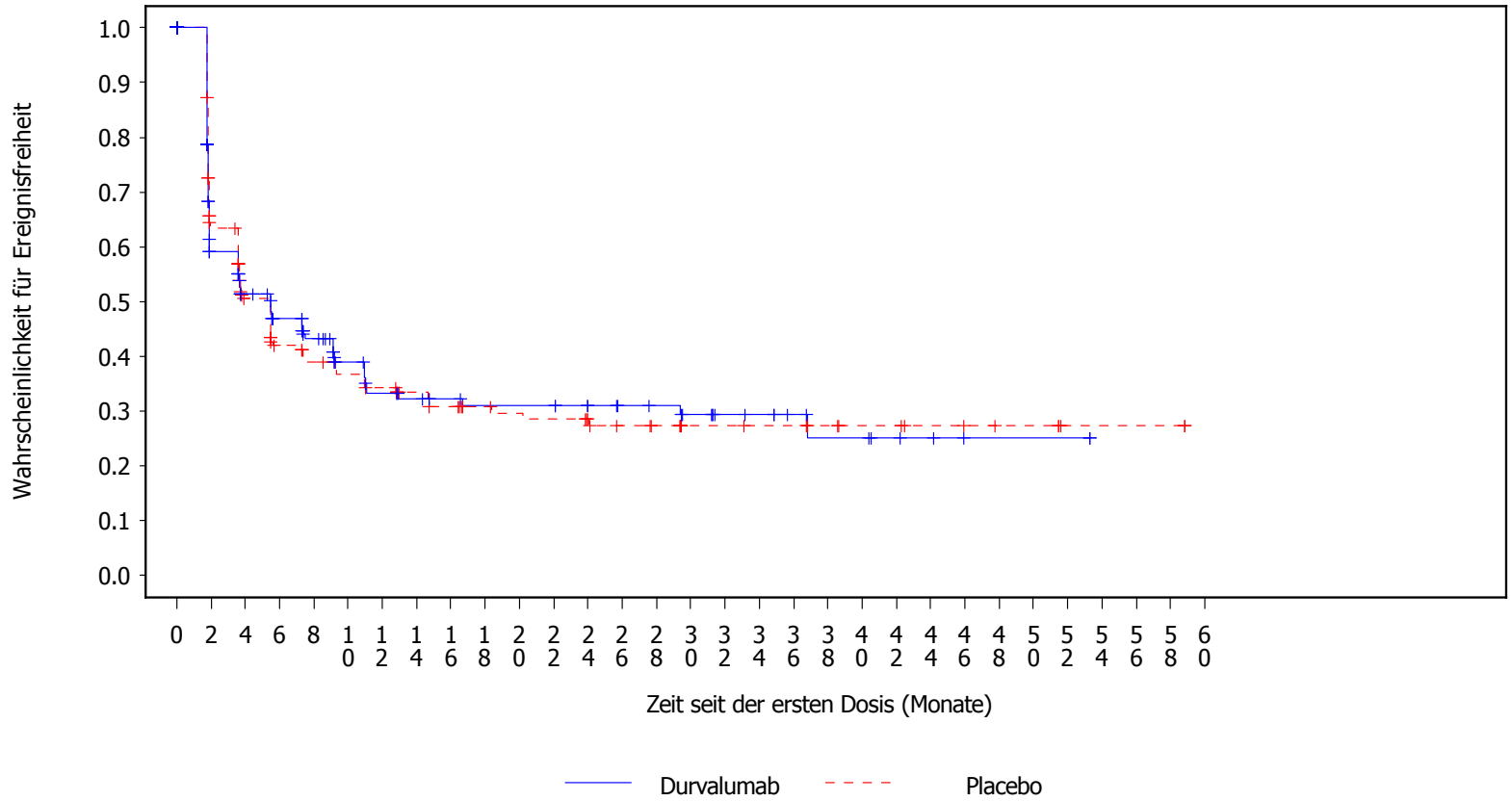
Anhang 4-G6.5.3: PGIS - Subgruppenanalysen Kaplan-Meier-Plot

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.4.2 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung PGIS for Raucherstatus - DEU=Raucher
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

241	102	81	68	56	42	34	31	28	26	26	26	22	20	19	16	12	11	8	6	6	4	3	1	1	1	1	0	0	0	0	Durvalumab
240	108	77	59	52	47	43	37	33	29	27	26	23	20	18	13	13	12	12	10	8	8	6	5	4	4	1	1	1	1	0	Placebo

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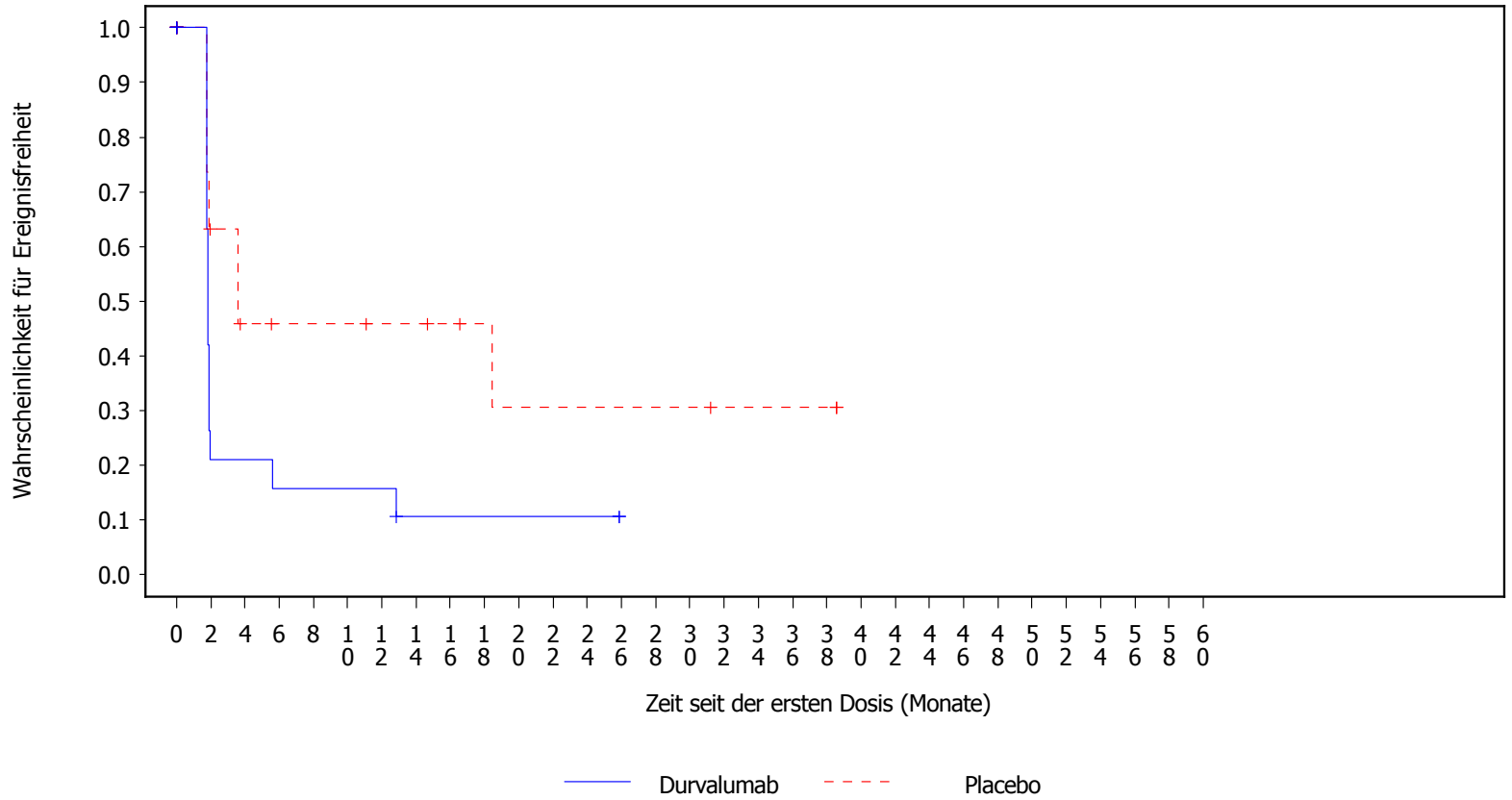
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.6.4.3 ADRIATIC: Subgroup analysis Kaplan-Meier plot of time to first occurrence of Zeit bis zur Verschlechterung PGIS for Raucherstatus - DEU=Nichtraucher
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

23	4	4	3	3	3	3	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Durvalumab
26	11	7	6	6	6	5	5	4	3	2	2	2	2	2	2	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	Placebo

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Anhang 4-G7: Patientenberichtete Morbidität und gesundheitsbezogene Lebensqualität - ergänzende Analysen

Anhang 4-G7.1: EORTC QLQ-C30 - MMRM-Analyse

Table 3.8.1.1 ADRIATIC: Summary of analysis of change from baseline over time in Globaler Gesundheitsstatus (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	73,41 (17,581)	-3,90 (1,398)	192	70,01 (18,171)	-5,34 (1,436)	1,44 [-2,508; 5,388]	0,4737
Woche 8	193	73,58 (17,320)	-7,19 (1,574)	179	70,02 (17,678)	-6,16 (1,621)	-1,03 [-5,478; 3,426]	0,6506
Woche 12	176	73,82 (17,268)	-5,70 (1,445)	169	70,17 (17,337)	-6,01 (1,479)	0,32 [-3,756; 4,392]	0,8781
Woche 16	168	73,61 (17,770)	-4,47 (1,373)	166	69,33 (17,505)	-4,75 (1,399)	0,28 [-3,582; 4,149]	0,8855
Woche 20	160	73,75 (17,738)	-4,14 (1,417)	155	69,19 (17,700)	-2,67 (1,448)	-1,47 [-5,462; 2,528]	0,4707
Woche 24	147	73,81 (18,090)	-3,87 (1,490)	149	69,46 (17,931)	-3,20 (1,510)	-0,67 [-4,852; 3,515]	0,7535
Woche 28	145	73,51 (17,614)	-3,74 (1,396)	133	68,86 (17,823)	-3,96 (1,442)	0,21 [-3,745; 4,169]	0,9161
Woche 32	141	73,82 (18,137)	-3,83 (1,400)	128	69,86 (16,406)	-3,69 (1,452)	-0,14 [-4,114; 3,839]	0,9458
Woche 36	132	73,04 (18,037)	-3,33 (1,350)	123	69,58 (16,391)	-4,55 (1,396)	1,22 [-2,612; 5,046]	0,5323
Woche 40	119	73,46 (17,760)	-3,17 (1,445)	105	69,52 (17,405)	-3,07 (1,513)	-0,09 [-4,218; 4,033]	0,9648
Woche 44	117	73,58 (17,137)	-2,80 (1,404)	106	70,20 (16,625)	-3,24 (1,463)	0,45 [-3,550; 4,445]	0,8258
Woche 48	109	73,32 (17,413)	-4,83 (1,462)	105	70,08 (16,331)	-3,76 (1,509)	-1,07 [-5,212; 3,072]	0,6117
Woche 52	112	73,21 (17,381)	-4,89 (1,386)	101	70,46 (15,922)	-3,38 (1,449)	-1,51 [-5,462; 2,441]	0,4527
Woche 56	106	73,98 (17,881)	-3,99 (1,385)	90	69,26 (16,319)	-3,18 (1,470)	-0,81 [-4,796; 3,173]	0,6890
Woche 60	103	73,46 (18,218)	-3,50 (1,294)	85	68,53 (16,636)	-1,71 (1,389)	-1,79 [-5,534; 1,957]	0,3483
Woche 64	101	73,93 (18,015)	-2,70 (1,303)	82	67,58 (15,549)	-2,98 (1,409)	0,28 [-3,510; 4,076]	0,8834
Woche 68	91	74,36 (17,926)	-2,52 (1,305)	80	68,65 (15,533)	-2,27 (1,387)	-0,25 [-4,017; 3,510]	0,8948

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.1 ADRIATIC: Summary of analysis of change from baseline over time in Globaler Gesundheitsstatus (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	73,24 (18,592)	-3,43 (1,301)	77	68,94 (15,273)	-3,29 (1,396)	-0,14 [-3,907; 3,627]	0,9416
Woche 76	90	73,15 (19,018)	-1,57 (1,396)	68	67,40 (16,525)	-2,76 (1,553)	1,19 [-2,933; 5,315]	0,5703
Woche 80	87	72,41 (18,298)	-0,97 (1,430)	64	67,58 (16,341)	-2,95 (1,610)	1,97 [-2,275; 6,224]	0,3613
Woche 84	87	73,66 (18,278)	-1,83 (1,360)	66	67,80 (16,138)	-4,63 (1,525)	2,80 [-1,241; 6,840]	0,1738
Woche 88	83	73,19 (18,361)	-3,06 (1,440)	60	68,06 (16,322)	-4,40 (1,639)	1,34 [-2,975; 5,647]	0,5423
Woche 92	84	73,02 (18,139)	-3,51 (1,443)	59	68,50 (15,324)	-4,46 (1,660)	0,95 [-3,399; 5,291]	0,6688
Woche 96	79	72,78 (18,428)	-2,34 (1,371)	54	68,52 (15,667)	-4,10 (1,599)	1,76 [-2,396; 5,925]	0,4045
Woche 100	85	74,31 (18,149)	-2,15 (1,377)	57	68,27 (15,304)	-4,06 (1,613)	1,91 [-2,287; 6,110]	0,3710
Woche 104	73	74,32 (17,053)	-3,69 (1,433)	54	68,83 (14,496)	-4,57 (1,647)	0,89 [-3,432; 5,208]	0,6860
Woche 108	71	71,95 (17,997)	-2,12 (1,466)	51	70,75 (14,470)	-2,18 (1,698)	0,06 [-4,364; 4,492]	0,9774
Woche 112	68	71,81 (17,458)	-2,19 (1,504)	46	70,47 (14,022)	-4,30 (1,764)	2,11 [-2,463; 6,690]	0,3640
Woche 116	62	73,66 (17,414)	-2,99 (1,478)	50	69,17 (14,409)	-4,21 (1,670)	1,22 [-3,190; 5,635]	0,5858
Woche 120	57	74,71 (17,884)	-3,77 (1,655)	46	68,12 (14,305)	-5,73 (1,867)	1,96 [-2,990; 6,912]	0,4359
Woche 124	53	74,69 (18,269)	-2,57 (1,788)	43	69,77 (15,540)	-6,60 (2,011)	4,03 [-1,304; 9,360]	0,1379
Woche 128	54	75,93 (18,075)	-3,30 (1,632)	39	68,38 (16,016)	-5,08 (1,884)	1,78 [-3,175; 6,733]	0,4797
Woche 132	49	74,49 (19,647)	-3,34 (1,525)	38	67,32 (15,904)	-3,98 (1,751)	0,64 [-3,969; 5,256]	0,7835
Woche 136	48	75,52 (18,306)	-3,59 (1,596)	33	67,68 (16,504)	-3,63 (1,878)	0,04 [-4,864; 4,944]	0,9871

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.1 ADRIATIC: Summary of analysis of change from baseline over time in Globaler Gesundheitsstatus (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	76,11 (17,642)	-3,39 (1,654)	33	68,18 (15,514)	-5,20 (1,912)	1,81 [-3,222; 6,849]	0,4783
Woche 144	36	72,22 (19,107)	-3,79 (1,791)	29	67,53 (15,162)	-2,78 (2,048)	-1,01 [-6,410; 4,389]	0,7121
Woche 148	40	72,08 (18,829)	-2,62 (1,992)	26	66,67 (15,986)	-3,80 (2,409)	1,18 [-5,022; 7,380]	0,7078
Woche 152	38	72,81 (19,441)	-2,60 (1,968)	27	67,59 (15,389)	-2,08 (2,325)	-0,52 [-6,570; 5,535]	0,8660
Woche 156	34	74,51 (20,509)	-2,74 (2,073)	27	69,44 (15,504)	-4,46 (2,367)	1,72 [-4,537; 7,972]	0,5882
Woche 160	31	72,58 (19,976)	-4,62 (2,322)	25	67,67 (16,015)	-6,48 (2,652)	1,86 [-5,147; 8,871]	0,6001
Woche 164	31	73,12 (20,266)	-4,44 (2,074)	21	68,25 (17,001)	-5,86 (2,458)	1,42 [-4,974; 7,815]	0,6611
Woche 168	27	75,93 (17,953)	-4,89 (2,312)	24	66,32 (16,389)	-5,60 (2,565)	0,71 [-6,208; 7,637]	0,8386
Woche 172	30	76,94 (18,399)	-4,79 (2,143)	20	68,75 (14,016)	-4,18 (2,511)	-0,61 [-7,217; 6,002]	0,8560
Woche 176	22	76,52 (18,480)	-2,62 (2,324)	18	67,13 (16,035)	-5,30 (2,609)	2,69 [-4,350; 9,722]	0,4506
Woche 180	20	77,08 (19,285)	-1,88 (2,887)	16	66,67 (16,942)	-7,03 (3,250)	5,15 [-3,623; 13,930]	0,2465
Woche 184	18	75,46 (19,061)	-4,77 (2,604)	17	66,67 (16,404)	-4,46 (2,828)	-0,31 [-8,056; 7,431]	0,9363
Woche 188	16	76,04 (20,610)	-10,54 (3,444)	15	66,11 (16,204)	-3,13 (3,707)	-7,41 [-17,653; 2,825]	0,1532
Durchschnitt über alle Visiten	215	73,22 (17,522)	-3,59 (0,981)	205	70,16 (18,152)	-4,15 (1,079)	0,57 [-2,313; 3,444]	0,6996
Hedges' g SMD							0,04 [-0,153; 0,229]	0,6982

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.2 ADRIATIC: Summary of analysis of change from baseline over time in Emotionale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	86,07 (17,142)	-0,42 (1,174)	192	85,68 (15,571)	-1,82 (1,207)	1,40 [-1,910; 4,710]	0,4061
Woche 8	193	86,92 (16,441)	-2,10 (1,450)	179	85,24 (15,772)	-5,14 (1,495)	3,04 [-1,060; 7,131]	0,1459
Woche 12	176	86,88 (17,009)	-2,27 (1,407)	169	85,26 (15,749)	-3,82 (1,441)	1,55 [-2,406; 5,515]	0,4407
Woche 16	168	86,41 (17,269)	-2,19 (1,319)	166	84,99 (15,923)	-2,45 (1,344)	0,25 [-3,449; 3,958]	0,8926
Woche 20	160	86,61 (16,929)	-1,65 (1,189)	155	85,38 (15,730)	-1,99 (1,215)	0,35 [-2,995; 3,690]	0,8381
Woche 24	147	86,62 (17,298)	-3,90 (1,331)	149	85,96 (15,772)	-2,19 (1,347)	-1,71 [-5,434; 2,015]	0,3672
Woche 28	145	85,75 (17,400)	-0,87 (1,229)	133	85,09 (16,025)	-1,90 (1,269)	1,03 [-2,444; 4,504]	0,5601
Woche 32	141	85,93 (18,125)	-1,72 (1,320)	128	86,20 (15,098)	-2,67 (1,369)	0,95 [-2,790; 4,690]	0,6177
Woche 36	132	85,42 (18,111)	-1,93 (1,276)	123	86,45 (15,067)	-0,84 (1,318)	-1,09 [-4,702; 2,515]	0,5516
Woche 40	119	85,99 (17,825)	-2,90 (1,432)	105	85,79 (14,751)	-3,22 (1,500)	0,32 [-3,756; 4,405]	0,8758
Woche 44	117	86,75 (16,708)	-3,25 (1,428)	106	85,61 (15,708)	-3,00 (1,490)	-0,25 [-4,313; 3,807]	0,9026
Woche 48	109	85,70 (18,672)	-4,47 (1,395)	105	86,11 (15,490)	-1,05 (1,438)	-3,41 [-7,354; 0,532]	0,0897
Woche 52	112	86,16 (17,671)	-2,71 (1,403)	101	86,39 (15,080)	-4,18 (1,467)	1,47 [-2,527; 5,461]	0,4704
Woche 56	106	85,85 (17,861)	-3,90 (1,409)	90	85,65 (15,803)	-1,88 (1,496)	-2,02 [-6,064; 2,022]	0,3261
Woche 60	103	85,60 (17,743)	-0,88 (1,339)	85	84,61 (15,827)	-2,23 (1,435)	1,36 [-2,506; 5,217]	0,4903
Woche 64	101	86,30 (17,818)	-2,70 (1,435)	82	84,45 (15,971)	-3,92 (1,547)	1,22 [-2,933; 5,374]	0,5635
Woche 68	91	86,54 (17,863)	-0,94 (1,297)	80	85,42 (16,158)	-3,51 (1,374)	2,57 [-1,145; 6,293]	0,1743

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.2 ADRIATIC: Summary of analysis of change from baseline over time in Emotionale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	86,76 (17,794)	-0,35 (1,253)	77	86,04 (15,261)	-3,98 (1,337)	3,63 [0,023; 7,236]	0,0486*
Woche 76	90	84,91 (18,982)	-1,80 (1,436)	68	83,95 (16,309)	-2,86 (1,590)	1,07 [-3,146; 5,277]	0,6188
Woche 80	87	86,11 (18,401)	-2,11 (1,440)	64	83,20 (15,607)	-3,50 (1,616)	1,38 [-2,879; 5,645]	0,5234
Woche 84	87	86,97 (17,411)	0,36 (1,479)	66	82,83 (16,465)	-3,25 (1,654)	3,61 [-0,764; 7,983]	0,1054
Woche 88	83	87,25 (17,526)	-1,67 (1,448)	60	82,78 (16,728)	-4,15 (1,643)	2,47 [-1,843; 6,792]	0,2602
Woche 92	84	86,90 (17,656)	-2,18 (1,490)	59	85,17 (15,402)	-4,34 (1,705)	2,16 [-2,303; 6,619]	0,3417
Woche 96	79	86,29 (17,905)	-0,92 (1,367)	54	84,26 (15,667)	-3,14 (1,587)	2,22 [-1,908; 6,344]	0,2907
Woche 100	85	86,86 (17,742)	0,33 (1,267)	57	84,80 (15,520)	-0,96 (1,478)	1,29 [-2,542; 5,129]	0,5072
Woche 104	73	87,56 (17,074)	0,41 (1,590)	54	84,88 (15,106)	-4,77 (1,815)	5,18 [0,421; 9,940]	0,0330*
Woche 108	71	88,26 (17,794)	-0,08 (1,567)	51	84,64 (15,034)	-4,36 (1,800)	4,28 [-0,432; 8,988]	0,0749
Woche 112	68	87,38 (18,689)	0,26 (1,548)	46	83,70 (15,412)	-2,31 (1,808)	2,56 [-2,135; 7,264]	0,2834
Woche 116	62	88,98 (17,582)	0,03 (1,608)	50	82,33 (16,806)	-1,53 (1,802)	1,56 [-3,228; 6,339]	0,5223
Woche 120	57	90,06 (17,067)	-1,69 (1,719)	46	81,16 (16,891)	-3,29 (1,925)	1,60 [-3,531; 6,735]	0,5392
Woche 124	53	90,41 (15,191)	-0,90 (1,642)	43	81,59 (15,490)	-3,55 (1,833)	2,65 [-2,259; 7,556]	0,2887
Woche 128	54	91,20 (15,978)	-0,16 (1,488)	39	80,77 (15,432)	-1,42 (1,712)	1,26 [-3,279; 5,795]	0,5853
Woche 132	49	90,14 (17,895)	-0,36 (1,656)	38	82,46 (15,952)	-1,69 (1,880)	1,34 [-3,644; 6,315]	0,5976
Woche 136	48	90,45 (16,930)	-0,16 (1,558)	33	84,34 (13,938)	-1,31 (1,813)	1,15 [-3,601; 5,892]	0,6343

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.2 ADRIATIC: Summary of analysis of change from baseline over time in Emotionale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	91,11 (12,102)	-1,99 (1,755)	33	85,35 (13,345)	-0,92 (1,983)	-1,07 [-6,318; 4,178]	0,6879
Woche 144	36	89,58 (17,970)	-0,73 (1,575)	29	85,63 (13,711)	1,11 (1,764)	-1,84 [-6,524; 2,844]	0,4388
Woche 148	40	89,38 (17,191)	-2,69 (1,872)	26	83,33 (13,944)	0,17 (2,234)	-2,86 [-8,658; 2,938]	0,3310
Woche 152	38	90,35 (17,059)	2,52 (1,746)	27	83,02 (14,337)	0,67 (2,030)	1,84 [-3,501; 7,189]	0,4959
Woche 156	34	87,50 (18,942)	-1,26 (1,812)	27	83,95 (13,659)	-0,06 (2,061)	-1,20 [-6,645; 4,252]	0,6647
Woche 160	31	87,37 (19,822)	-2,20 (2,101)	25	82,33 (13,676)	-2,12 (2,385)	-0,08 [-6,399; 6,236]	0,9797
Woche 164	31	87,90 (19,701)	1,26 (1,785)	21	82,14 (13,251)	-0,99 (2,118)	2,25 [-3,272; 7,774]	0,4209
Woche 168	27	91,98 (12,549)	-0,06 (1,765)	24	82,99 (13,787)	1,30 (1,894)	-1,36 [-6,580; 3,864]	0,6069
Woche 172	30	91,39 (12,663)	4,17 (1,680)	20	83,75 (12,529)	0,47 (1,940)	3,69 [-1,469; 8,856]	0,1590
Woche 176	22	93,94 (7,793)	0,85 (1,983)	18	82,87 (13,550)	-0,07 (2,061)	0,92 [-4,970; 6,811]	0,7567
Woche 180	20	93,33 (7,929)	2,21 (1,858)	16	82,81 (13,077)	2,78 (1,939)	-0,57 [-6,123; 4,981]	0,8380
Woche 184	18	93,06 (8,210)	2,96 (2,176)	17	83,82 (13,330)	1,42 (2,165)	1,54 [-4,767; 7,847]	0,6266
Woche 188	16	92,71 (7,979)	-0,85 (2,700)	15	85,56 (13,897)	1,12 (2,674)	-1,97 [-9,678; 5,740]	0,6101
Durchschnitt über alle Visiten	215	85,62 (17,584)	-0,97 (0,916)	205	85,93 (15,415)	-1,94 (0,996)	0,97 [-1,692; 3,637]	0,4734
Hedges' g SMD							0,07 [-0,121; 0,262]	0,4726

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraab 04NOV2024:19:16

Table 3.8.1.3 ADRIATIC: Summary of analysis of change from baseline over time in Kognitive Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	89,87 (15,190)	-0,51 (1,200)	192	86,81 (16,783)	-2,81 (1,244)	2,30 [-1,097; 5,699]	0,1838
Woche 8	193	90,33 (14,682)	-2,08 (1,203)	179	86,96 (16,407)	-3,24 (1,251)	1,15 [-2,261; 4,569]	0,5069
Woche 12	176	90,34 (14,523)	-1,42 (1,378)	169	87,08 (16,440)	-2,50 (1,423)	1,08 [-2,818; 4,976]	0,5863
Woche 16	168	90,28 (14,177)	-2,54 (1,185)	166	86,85 (16,597)	-2,85 (1,217)	0,31 [-3,034; 3,650]	0,8564
Woche 20	160	90,10 (14,394)	-2,67 (1,324)	155	86,99 (16,369)	-3,13 (1,365)	0,46 [-3,280; 4,200]	0,8091
Woche 24	147	90,48 (13,793)	-5,52 (1,462)	149	87,02 (16,076)	-5,19 (1,494)	-0,34 [-4,449; 3,777]	0,8723
Woche 28	145	89,66 (15,223)	-4,17 (1,448)	133	86,84 (17,171)	-2,65 (1,509)	-1,52 [-5,635; 2,588]	0,4665
Woche 32	141	89,13 (15,557)	-5,08 (1,396)	128	87,11 (16,497)	-6,00 (1,460)	0,92 [-3,047; 4,890]	0,6480
Woche 36	132	89,27 (15,701)	-3,23 (1,311)	123	87,53 (16,335)	-5,51 (1,363)	2,28 [-1,440; 5,995]	0,2290
Woche 40	119	90,34 (14,474)	-5,08 (1,397)	105	88,73 (15,067)	-6,60 (1,469)	1,52 [-2,469; 5,511]	0,4537
Woche 44	117	90,60 (14,743)	-4,97 (1,352)	106	88,52 (16,324)	-4,74 (1,415)	-0,24 [-4,088; 3,614]	0,9037
Woche 48	109	90,37 (14,923)	-6,00 (1,443)	105	89,68 (14,687)	-6,54 (1,492)	0,54 [-3,542; 4,624]	0,7945
Woche 52	112	90,77 (14,813)	-5,50 (1,390)	101	89,11 (16,572)	-6,01 (1,457)	0,51 [-3,454; 4,472]	0,8007
Woche 56	106	90,09 (15,045)	-6,91 (1,349)	90	90,37 (14,564)	-7,23 (1,436)	0,32 [-3,553; 4,199]	0,8698
Woche 60	103	89,97 (14,638)	-6,33 (1,339)	85	89,41 (14,962)	-5,39 (1,436)	-0,95 [-4,810; 2,916]	0,6299
Woche 64	101	90,26 (14,770)	-6,28 (1,392)	82	89,63 (15,190)	-5,28 (1,502)	-1,00 [-5,027; 3,030]	0,6260
Woche 68	91	90,84 (14,112)	-5,83 (1,400)	80	89,58 (15,320)	-6,45 (1,485)	0,62 [-3,398; 4,636]	0,7619

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.3 ADRIATIC: Summary of analysis of change from baseline over time in Kognitive Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	90,56 (14,363)	-5,52 (1,318)	77	91,13 (13,676)	-6,79 (1,409)	1,28 [-2,522; 5,072]	0,5090
Woche 76	90	89,63 (16,110)	-4,07 (1,275)	68	90,44 (14,772)	-6,87 (1,410)	2,80 [-0,939; 6,543]	0,1415
Woche 80	87	91,38 (13,655)	-5,09 (1,316)	64	90,10 (14,764)	-7,83 (1,469)	2,74 [-1,143; 6,617]	0,1661
Woche 84	87	91,38 (14,120)	-5,45 (1,362)	66	90,40 (15,208)	-5,74 (1,512)	0,29 [-3,716; 4,286]	0,8886
Woche 88	83	91,97 (13,364)	-5,71 (1,352)	60	90,56 (15,147)	-6,35 (1,521)	0,65 [-3,356; 4,648]	0,7508
Woche 92	84	91,87 (13,317)	-5,53 (1,396)	59	92,94 (11,664)	-7,27 (1,594)	1,74 [-2,408; 5,896]	0,4091
Woche 96	79	91,35 (13,572)	-6,60 (1,414)	54	91,67 (14,019)	-7,70 (1,630)	1,10 [-3,142; 5,337]	0,6108
Woche 100	85	90,98 (13,981)	-6,15 (1,320)	57	90,94 (15,128)	-6,47 (1,528)	0,31 [-3,657; 4,286]	0,8763
Woche 104	73	91,78 (13,643)	-4,21 (1,523)	54	90,74 (15,070)	-9,16 (1,725)	4,95 [0,424; 9,475]	0,0322*
Woche 108	71	91,55 (14,330)	-7,52 (1,503)	51	91,18 (15,038)	-8,12 (1,717)	0,59 [-3,894; 5,084]	0,7943
Woche 112	68	90,93 (14,522)	-7,07 (1,526)	46	90,22 (15,938)	-7,21 (1,771)	0,14 [-4,461; 4,740]	0,9524
Woche 116	62	91,67 (14,394)	-6,00 (1,505)	50	90,67 (15,489)	-7,62 (1,675)	1,61 [-2,817; 6,046]	0,4738
Woche 120	57	91,81 (13,409)	-8,27 (1,650)	46	89,49 (16,238)	-9,10 (1,836)	0,82 [-4,043; 5,688]	0,7393
Woche 124	53	94,03 (10,385)	-7,54 (1,567)	43	92,64 (11,674)	-8,01 (1,727)	0,48 [-4,070; 5,020]	0,8370
Woche 128	54	93,83 (10,882)	-5,49 (1,572)	39	90,60 (13,677)	-8,99 (1,784)	3,50 [-1,170; 8,172]	0,1412
Woche 132	49	92,86 (11,785)	-7,39 (1,686)	38	91,67 (13,836)	-10,32 (1,903)	2,94 [-2,054; 7,925]	0,2475
Woche 136	48	93,06 (11,827)	-5,70 (1,764)	33	90,91 (13,876)	-7,96 (2,051)	2,26 [-3,063; 7,577]	0,4037

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.3 ADRIATIC: Summary of analysis of change from baseline over time in Kognitive Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	92,22 (13,577)	-6,91 (1,901)	33	92,42 (11,852)	-9,22 (2,190)	2,31 [-3,378; 8,002]	0,4240
Woche 144	36	92,59 (12,244)	-7,84 (1,781)	29	90,80 (13,791)	-4,99 (1,994)	-2,84 [-8,111; 2,422]	0,2878
Woche 148	40	92,08 (13,602)	-6,29 (1,935)	26	90,38 (12,625)	-10,82 (2,304)	4,53 [-1,406; 10,456]	0,1339
Woche 152	38	92,54 (13,808)	-5,70 (1,882)	27	90,74 (13,344)	-9,11 (2,185)	3,41 [-2,268; 9,091]	0,2374
Woche 156	34	91,67 (14,361)	-5,67 (1,658)	27	91,98 (11,667)	-9,90 (1,878)	4,23 [-0,698; 9,152]	0,0921
Woche 160	31	91,40 (14,827)	-5,44 (1,824)	25	91,33 (12,838)	-9,97 (2,053)	4,53 [-0,878; 9,941]	0,1000
Woche 164	31	90,86 (14,807)	-8,46 (2,005)	21	91,27 (13,560)	-10,12 (2,370)	1,66 [-4,464; 7,779]	0,5936
Woche 168	27	91,98 (14,886)	-7,23 (1,953)	24	90,97 (13,883)	-9,80 (2,134)	2,57 [-3,131; 8,272]	0,3745
Woche 172	30	92,22 (14,339)	-9,34 (2,119)	20	93,33 (12,566)	-8,63 (2,516)	-0,72 [-7,180; 5,746]	0,8266
Woche 176	22	94,70 (10,772)	-6,66 (2,255)	18	91,67 (13,098)	-12,65 (2,467)	5,99 [-0,573; 12,553]	0,0732
Woche 180	20	94,17 (11,180)	-9,54 (2,726)	16	91,67 (13,608)	-11,59 (3,008)	2,05 [-5,941; 10,035]	0,6120
Woche 184	18	94,44 (11,433)	-8,01 (2,515)	17	92,16 (13,330)	-9,47 (2,631)	1,45 [-5,684; 8,592]	0,6869
Woche 188	16	92,71 (12,124)	-9,28 (2,414)	15	93,33 (12,280)	-11,12 (2,553)	1,83 [-5,080; 8,750]	0,5990
Durchschnitt über alle Visiten	215	89,92 (15,174)	-5,83 (0,973)	205	87,15 (16,594)	-7,26 (1,060)	1,43 [-1,396; 4,254]	0,3208
Hedges' g SMD							0,10 [-0,095; 0,288]	0,3212

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.4 ADRIATIC: Summary of analysis of change from baseline over time in Körperfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	85,95 (14,480)	-2,03 (1,041)	192	83,54 (14,851)	-1,99 (1,074)	-0,04 [-2,982; 2,907]	0,9802
Woche 8	193	87,08 (13,602)	-3,96 (1,229)	179	83,43 (14,997)	-4,88 (1,269)	0,92 [-2,556; 4,405]	0,6017
Woche 12	176	86,63 (13,957)	-3,21 (1,188)	169	83,47 (15,085)	-3,03 (1,221)	-0,18 [-3,541; 3,172]	0,9139
Woche 16	168	86,79 (13,600)	-4,11 (1,236)	166	83,01 (15,265)	-3,10 (1,266)	-1,01 [-4,496; 2,477]	0,5695
Woche 20	160	86,75 (13,143)	-4,26 (1,303)	155	83,01 (14,950)	-1,79 (1,337)	-2,47 [-6,154; 1,206]	0,1871
Woche 24	147	87,26 (12,676)	-4,44 (1,243)	149	83,04 (15,255)	-3,69 (1,266)	-0,75 [-4,245; 2,753]	0,6753
Woche 28	145	86,39 (14,248)	-3,63 (1,261)	133	82,61 (15,480)	-3,06 (1,306)	-0,57 [-4,146; 3,006]	0,7542
Woche 32	141	86,57 (14,320)	-5,46 (1,339)	128	83,18 (14,562)	-3,86 (1,393)	-1,60 [-5,408; 2,205]	0,4086
Woche 36	132	86,57 (13,333)	-3,23 (1,260)	123	83,58 (14,668)	-5,15 (1,307)	1,92 [-1,658; 5,495]	0,2922
Woche 40	119	87,45 (12,937)	-4,46 (1,255)	105	83,43 (14,326)	-5,42 (1,316)	0,97 [-2,619; 4,554]	0,5961
Woche 44	117	86,78 (14,330)	-6,10 (1,358)	106	83,46 (14,555)	-5,05 (1,423)	-1,05 [-4,925; 2,829]	0,5954
Woche 48	109	86,18 (13,839)	-5,29 (1,343)	105	84,19 (14,360)	-4,58 (1,394)	-0,70 [-4,514; 3,112]	0,7179
Woche 52	112	86,73 (14,050)	-4,54 (1,216)	101	84,03 (14,455)	-3,41 (1,276)	-1,14 [-4,610; 2,336]	0,5200
Woche 56	106	85,79 (14,810)	-5,84 (1,199)	90	84,89 (14,267)	-4,79 (1,276)	-1,05 [-4,497; 2,396]	0,5492
Woche 60	103	85,70 (14,684)	-4,43 (1,164)	85	83,92 (14,739)	-3,85 (1,249)	-0,58 [-3,945; 2,778]	0,7329
Woche 64	101	85,87 (14,431)	-4,41 (1,162)	82	83,25 (14,750)	-3,38 (1,255)	-1,03 [-4,398; 2,337]	0,5477
Woche 68	91	86,08 (13,431)	-3,93 (1,144)	80	83,92 (14,801)	-3,25 (1,219)	-0,68 [-3,974; 2,611]	0,6843

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.4 ADRIATIC: Summary of analysis of change from baseline over time in Körperfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	86,59 (13,126)	-5,05 (1,208)	77	84,50 (14,687)	-5,31 (1,294)	0,26 [-3,229; 3,746]	0,8842
Woche 76	90	86,81 (13,518)	-4,01 (1,298)	68	83,14 (15,431)	-4,20 (1,436)	0,18 [-3,637; 4,001]	0,9254
Woche 80	87	86,90 (12,303)	-3,55 (1,251)	64	82,29 (15,268)	-5,22 (1,405)	1,67 [-2,043; 5,387]	0,3766
Woche 84	87	86,97 (13,446)	-1,76 (1,234)	66	82,12 (15,609)	-5,01 (1,385)	3,24 [-0,422; 6,906]	0,0827
Woche 88	83	87,31 (11,853)	-4,26 (1,288)	60	83,00 (15,739)	-4,79 (1,462)	0,53 [-3,323; 4,377]	0,7878
Woche 92	84	86,83 (12,112)	-3,88 (1,178)	59	84,75 (14,280)	-4,01 (1,351)	0,14 [-3,402; 3,672]	0,9401
Woche 96	79	86,75 (12,241)	-5,17 (1,321)	54	83,33 (15,200)	-5,39 (1,538)	0,22 [-3,785; 4,222]	0,9146
Woche 100	85	87,22 (12,523)	-3,82 (1,137)	57	83,63 (14,858)	-2,67 (1,331)	-1,15 [-4,612; 2,303]	0,5117
Woche 104	73	86,58 (12,095)	-4,48 (1,323)	54	83,83 (15,081)	-3,70 (1,525)	-0,78 [-4,766; 3,210]	0,7013
Woche 108	71	87,32 (11,719)	-3,21 (1,206)	51	84,05 (15,090)	-2,36 (1,396)	-0,85 [-4,502; 2,792]	0,6446
Woche 112	68	87,45 (12,540)	-4,88 (1,347)	46	83,48 (15,185)	-4,92 (1,575)	0,04 [-4,062; 4,141]	0,9850
Woche 116	62	88,28 (11,495)	-6,17 (1,487)	50	83,87 (15,538)	-5,07 (1,676)	-1,10 [-5,533; 3,342]	0,6271
Woche 120	57	88,54 (10,672)	-7,10 (1,596)	46	82,61 (16,479)	-3,90 (1,797)	-3,20 [-7,975; 1,576]	0,1881
Woche 124	53	89,06 (11,101)	-5,13 (1,527)	43	84,03 (15,198)	-4,26 (1,708)	-0,87 [-5,424; 3,682]	0,7062
Woche 128	54	90,00 (9,926)	-4,19 (1,381)	39	83,42 (14,818)	-3,06 (1,572)	-1,13 [-5,297; 3,044]	0,5948
Woche 132	49	90,07 (11,149)	-4,20 (1,266)	38	81,58 (15,915)	-2,22 (1,437)	-1,98 [-5,812; 1,856]	0,3101
Woche 136	48	90,83 (10,530)	-5,81 (1,345)	33	83,03 (14,443)	-3,01 (1,546)	-2,80 [-6,903; 1,302]	0,1796

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.4 ADRIATIC: Summary of analysis of change from baseline over time in Körperfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	89,33 (11,137)	-6,18 (1,477)	33	83,84 (12,805)	-3,70 (1,689)	-2,48 [-6,953; 1,991]	0,2750
Woche 144	36	88,15 (10,938)	-4,92 (1,705)	29	85,52 (11,693)	-3,01 (1,919)	-1,91 [-7,016; 3,190]	0,4598
Woche 148	40	88,67 (11,115)	-5,32 (1,783)	26	84,10 (12,938)	-2,82 (2,101)	-2,51 [-7,999; 2,984]	0,3683
Woche 152	38	88,60 (11,380)	-5,28 (1,550)	27	84,44 (14,202)	-1,26 (1,797)	-4,02 [-8,744; 0,703]	0,0947
Woche 156	34	88,24 (11,612)	-6,53 (1,609)	27	84,94 (12,621)	-1,23 (1,820)	-5,30 [-10,140; -0,460]	0,0321*
Woche 160	31	87,96 (11,211)	-7,10 (1,849)	25	83,73 (13,754)	-1,65 (2,086)	-5,45 [-11,004; 0,114]	0,0548
Woche 164	31	88,60 (11,313)	-4,76 (1,718)	21	84,44 (13,878)	-2,59 (1,990)	-2,17 [-7,415; 3,066]	0,4133
Woche 168	27	89,63 (10,350)	-4,32 (1,672)	24	83,33 (14,711)	-2,22 (1,824)	-2,10 [-7,047; 2,851]	0,4033
Woche 172	30	88,89 (11,391)	-6,12 (1,780)	20	85,00 (12,773)	-3,16 (2,053)	-2,97 [-8,382; 2,446]	0,2799
Woche 176	22	87,88 (11,200)	-7,93 (1,920)	18	85,56 (11,490)	-3,13 (2,142)	-4,80 [-10,526; 0,930]	0,0997
Woche 180	20	86,33 (11,129)	-3,88 (2,232)	16	85,00 (11,547)	-4,07 (2,510)	0,19 [-6,499; 6,874]	0,9557
Woche 184	18	87,41 (11,635)	-7,22 (2,553)	17	85,88 (11,757)	-4,53 (2,749)	-2,70 [-10,171; 4,779]	0,4751
Woche 188	16	85,83 (12,383)	-6,46 (2,847)	15	88,00 (10,750)	-5,27 (3,059)	-1,19 [-9,545; 7,165]	0,7768
Durchschnitt über alle Visiten	215	85,92 (14,550)	-4,81 (0,862)	205	83,77 (14,689)	-3,66 (0,945)	-1,15 [-3,673; 1,374]	0,3711
Hedges' g SMD							-0,09 [-0,279; 0,104]	0,3690

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.5 ADRIATIC: Summary of analysis of change from baseline over time in Rollenfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	87,58 (20,421)	-0,44 (1,455)	192	88,54 (18,259)	-6,24 (1,493)	5,80 [1,706; 9,895]	0,0056*
Woche 8	193	89,46 (18,590)	-3,75 (1,729)	179	88,08 (18,549)	-8,30 (1,782)	4,55 [-0,329; 9,428]	0,0675
Woche 12	176	88,92 (19,240)	-5,65 (1,716)	169	88,76 (18,053)	-5,57 (1,757)	-0,08 [-4,903; 4,750]	0,9752
Woche 16	168	88,29 (19,692)	-4,13 (1,595)	166	88,15 (18,628)	-6,01 (1,623)	1,88 [-2,591; 6,347]	0,4092
Woche 20	160	89,06 (18,975)	-5,14 (1,666)	155	88,39 (17,956)	-5,60 (1,701)	0,45 [-4,227; 5,131]	0,8495
Woche 24	147	89,12 (18,978)	-3,73 (1,658)	149	89,04 (18,459)	-6,37 (1,677)	2,64 [-1,994; 7,276]	0,2632
Woche 28	145	88,51 (19,496)	-5,28 (1,775)	133	88,60 (19,176)	-7,56 (1,832)	2,28 [-2,735; 7,288]	0,3723
Woche 32	141	88,18 (20,465)	-5,12 (1,768)	128	89,71 (18,486)	-8,09 (1,832)	2,97 [-2,029; 7,979]	0,2432
Woche 36	132	88,51 (19,442)	-4,04 (1,657)	123	90,24 (18,223)	-8,83 (1,711)	4,79 [0,102; 9,470]	0,0453*
Woche 40	119	89,36 (19,130)	-5,25 (1,705)	105	90,32 (17,720)	-8,58 (1,786)	3,32 [-1,537; 8,178]	0,1796
Woche 44	117	89,74 (17,893)	-5,99 (1,795)	106	90,09 (17,635)	-7,22 (1,873)	1,23 [-3,875; 6,328]	0,6366
Woche 48	109	88,38 (20,350)	-6,16 (1,656)	105	90,79 (17,138)	-6,54 (1,708)	0,38 [-4,299; 5,062]	0,8727
Woche 52	112	89,73 (18,346)	-6,38 (1,608)	101	90,43 (17,535)	-7,44 (1,684)	1,06 [-3,519; 5,640]	0,6490
Woche 56	106	89,62 (17,736)	-6,53 (1,593)	90	90,56 (17,851)	-7,34 (1,694)	0,81 [-3,761; 5,386]	0,7269
Woche 60	103	89,16 (18,034)	-5,36 (1,508)	85	90,78 (17,725)	-5,67 (1,617)	0,31 [-4,042; 4,657]	0,8895
Woche 64	101	89,77 (17,790)	-6,48 (1,595)	82	90,45 (17,960)	-6,84 (1,720)	0,36 [-4,254; 4,975]	0,8778
Woche 68	91	90,29 (18,099)	-4,49 (1,503)	80	90,42 (18,137)	-6,61 (1,595)	2,13 [-2,183; 6,440]	0,3321

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.5 ADRIATIC: Summary of analysis of change from baseline over time in Rollenfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	89,44 (18,436)	-3,50 (1,391)	77	91,13 (17,224)	-5,32 (1,488)	1,82 [-2,193; 5,824]	0,3733
Woche 76	90	88,89 (18,529)	-3,42 (1,673)	68	89,46 (19,296)	-7,32 (1,853)	3,90 [-1,014; 8,813]	0,1194
Woche 80	87	89,66 (17,653)	-5,65 (1,693)	64	89,84 (18,213)	-7,85 (1,897)	2,19 [-2,811; 7,199]	0,3889
Woche 84	87	89,46 (18,348)	-4,28 (1,645)	66	89,14 (19,280)	-8,37 (1,837)	4,09 [-0,763; 8,944]	0,0982
Woche 88	83	89,96 (17,642)	-4,63 (1,697)	60	90,00 (18,716)	-8,11 (1,924)	3,48 [-1,568; 8,535]	0,1756
Woche 92	84	89,88 (17,550)	-5,06 (1,626)	59	91,53 (16,485)	-9,35 (1,866)	4,29 [-0,582; 9,165]	0,0841
Woche 96	79	88,82 (18,046)	-5,30 (1,680)	54	91,05 (17,943)	-9,76 (1,952)	4,46 [-0,611; 9,539]	0,0845
Woche 100	85	90,78 (16,568)	-3,30 (1,461)	57	90,94 (18,113)	-6,89 (1,709)	3,59 [-0,832; 8,020]	0,1110
Woche 104	73	89,27 (18,081)	-5,28 (1,606)	54	91,98 (16,104)	-6,69 (1,843)	1,41 [-3,405; 6,232]	0,5639
Woche 108	71	89,44 (18,091)	-5,43 (1,691)	51	92,81 (15,002)	-8,60 (1,956)	3,17 [-1,931; 8,264]	0,2222
Woche 112	68	89,71 (17,043)	-5,40 (1,821)	46	91,67 (15,615)	-6,45 (2,131)	1,05 [-4,479; 6,574]	0,7090
Woche 116	62	90,32 (17,217)	-6,46 (1,955)	50	91,33 (16,578)	-8,35 (2,192)	1,89 [-3,896; 7,679]	0,5201
Woche 120	57	90,35 (18,079)	-8,40 (2,093)	46	88,77 (18,939)	-8,71 (2,345)	0,32 [-5,882; 6,517]	0,9196
Woche 124	53	90,25 (18,326)	-6,17 (2,029)	43	91,47 (16,416)	-8,87 (2,274)	2,70 [-3,311; 8,716]	0,3762
Woche 128	54	91,67 (17,953)	-5,73 (1,978)	39	92,74 (16,129)	-10,08 (2,289)	4,35 [-1,608; 10,307]	0,1513
Woche 132	49	89,12 (19,706)	-7,90 (2,104)	38	90,79 (16,755)	-8,75 (2,400)	0,85 [-5,452; 7,150]	0,7905
Woche 136	48	90,28 (17,475)	-5,00 (1,970)	33	93,43 (14,988)	-8,39 (2,337)	3,39 [-2,643; 9,415]	0,2690

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.5 ADRIATIC: Summary of analysis of change from baseline over time in Rollenfunktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	91,11 (15,731)	-3,68 (1,935)	33	95,45 (10,436)	-4,27 (2,288)	0,59 [-5,294; 6,475]	0,8431
Woche 144	36	89,35 (18,324)	-6,38 (2,145)	29	95,98 (9,611)	-7,60 (2,481)	1,23 [-5,271; 7,726]	0,7093
Woche 148	40	87,08 (20,145)	-6,64 (2,240)	26	92,95 (15,757)	-3,88 (2,695)	-2,76 [-9,720; 4,193]	0,4334
Woche 152	38	86,84 (20,562)	-4,57 (2,226)	27	91,36 (17,523)	-6,80 (2,608)	2,23 [-4,564; 9,028]	0,5170
Woche 156	34	86,27 (21,110)	-5,97 (2,228)	27	95,06 (11,147)	-8,74 (2,553)	2,77 [-3,985; 9,527]	0,4187
Woche 160	31	86,02 (21,983)	-4,40 (2,263)	25	92,00 (16,750)	-8,46 (2,554)	4,06 [-2,710; 10,837]	0,2375
Woche 164	31	88,71 (19,430)	-3,75 (2,196)	21	92,06 (17,175)	-7,82 (2,602)	4,07 [-2,671; 10,816]	0,2344
Woche 168	27	91,98 (16,902)	-3,04 (2,069)	24	90,97 (18,376)	-5,22 (2,265)	2,18 [-3,879; 8,244]	0,4774
Woche 172	30	91,11 (16,800)	-3,74 (2,000)	20	93,33 (12,566)	-6,07 (2,388)	2,33 [-3,821; 8,472]	0,4553
Woche 176	22	92,42 (16,846)	-2,45 (2,318)	18	95,37 (11,152)	-6,95 (2,646)	4,50 [-2,405; 11,403]	0,1990
Woche 180	20	90,00 (18,257)	-4,12 (2,609)	16	94,79 (11,736)	-7,64 (2,996)	3,52 [-4,329; 11,369]	0,3763
Woche 184	18	89,81 (19,079)	-4,26 (3,442)	17	95,10 (11,433)	-9,07 (3,775)	4,81 [-5,320; 14,941]	0,3481
Woche 188	16	89,58 (19,124)	-8,49 (3,003)	15	95,56 (9,894)	-4,88 (3,281)	-3,61 [-12,480; 5,257]	0,4196
Durchschnitt über alle Visiten	215	87,98 (20,100)	-5,03 (1,105)	205	88,94 (17,918)	-7,32 (1,206)	2,29 [-0,920; 5,506]	0,1615
Hedges' g SMD							0,14 [-0,055; 0,328]	0,1617

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.6 ADRIATIC: Summary of analysis of change from baseline over time in Soziale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	87,58 (18,449)	0,46 (1,416)	192	86,37 (19,839)	-1,70 (1,456)	2,16 [-1,831; 6,155]	0,2878
Woche 8	193	87,39 (19,001)	-2,21 (1,676)	179	85,75 (20,152)	-2,78 (1,729)	0,57 [-4,161; 5,309]	0,8117
Woche 12	176	87,59 (19,334)	-0,63 (1,671)	169	86,39 (18,514)	-2,62 (1,712)	1,99 [-2,717; 6,691]	0,4067
Woche 16	168	87,00 (19,849)	-1,76 (1,578)	166	86,45 (18,857)	-1,30 (1,608)	-0,46 [-4,893; 3,968]	0,8375
Woche 20	160	87,19 (19,625)	-2,55 (1,611)	155	86,24 (19,661)	-1,33 (1,647)	-1,23 [-5,760; 3,303]	0,5943
Woche 24	147	87,87 (20,042)	-0,83 (1,546)	149	86,91 (19,137)	-1,60 (1,565)	0,77 [-3,559; 5,094]	0,7275
Woche 28	145	87,01 (20,362)	-1,40 (1,563)	133	86,34 (20,292)	-2,75 (1,615)	1,35 [-3,065; 5,774]	0,5472
Woche 32	141	86,41 (20,664)	-0,79 (1,672)	128	86,33 (20,108)	-3,72 (1,737)	2,93 [-1,809; 7,670]	0,2249
Woche 36	132	86,49 (20,812)	-0,59 (1,672)	123	87,26 (19,799)	-4,34 (1,729)	3,75 [-0,980; 8,481]	0,1198
Woche 40	119	86,97 (21,607)	-0,46 (1,717)	105	87,14 (20,446)	-6,04 (1,801)	5,58 [0,685; 10,476]	0,0256*
Woche 44	117	87,46 (20,046)	-1,88 (1,643)	106	86,16 (21,513)	-3,72 (1,717)	1,85 [-2,829; 6,520]	0,4379
Woche 48	109	85,63 (21,927)	-2,85 (1,551)	105	87,30 (20,740)	-1,52 (1,601)	-1,33 [-5,717; 3,056]	0,5510
Woche 52	112	86,46 (20,690)	-2,18 (1,534)	101	86,63 (21,216)	-2,80 (1,607)	0,62 [-3,754; 4,987]	0,7815
Woche 56	106	85,53 (21,341)	-4,09 (1,610)	90	86,85 (21,708)	-4,59 (1,712)	0,50 [-4,129; 5,121]	0,8331
Woche 60	103	86,89 (20,828)	-0,64 (1,434)	85	86,86 (20,101)	-3,47 (1,540)	2,83 [-1,309; 6,971]	0,1795
Woche 64	101	85,31 (21,639)	-2,38 (1,608)	82	86,59 (20,360)	-5,68 (1,735)	3,31 [-1,344; 7,961]	0,1628
Woche 68	91	86,63 (19,755)	-0,11 (1,456)	80	87,08 (20,192)	-2,58 (1,545)	2,47 [-1,705; 6,651]	0,2450

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.6 ADRIATIC: Summary of analysis of change from baseline over time in Soziale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	85,19 (21,701)	-0,38 (1,296)	77	87,66 (18,810)	0,40 (1,385)	-0,78 [-4,510; 2,956]	0,6823
Woche 76	90	85,19 (21,987)	-1,84 (1,586)	68	85,54 (20,342)	-3,61 (1,758)	1,77 [-2,885; 6,427]	0,4547
Woche 80	87	85,25 (21,779)	-1,49 (1,522)	64	85,94 (19,969)	-2,76 (1,707)	1,27 [-3,230; 5,768]	0,5792
Woche 84	87	86,59 (21,240)	0,54 (1,495)	66	84,85 (21,429)	-2,09 (1,673)	2,63 [-1,789; 7,041]	0,2427
Woche 88	83	86,75 (21,583)	-1,82 (1,762)	60	87,22 (20,208)	-3,39 (2,002)	1,56 [-3,689; 6,818]	0,5580
Woche 92	84	85,52 (21,766)	-1,70 (1,497)	59	88,70 (17,628)	-1,64 (1,719)	-0,06 [-4,551; 4,435]	0,9797
Woche 96	79	85,02 (22,264)	-0,49 (1,462)	54	88,58 (18,829)	-1,69 (1,701)	1,20 [-3,216; 5,626]	0,5918
Woche 100	85	86,67 (21,486)	0,72 (1,432)	57	87,13 (19,163)	-1,19 (1,678)	1,90 [-2,443; 6,250]	0,3891
Woche 104	73	85,62 (22,103)	-0,83 (1,706)	54	88,89 (18,315)	-4,95 (1,956)	4,11 [-1,006; 9,233]	0,1148
Woche 108	71	85,92 (22,826)	-2,51 (1,574)	51	90,20 (17,054)	-2,12 (1,821)	-0,38 [-5,133; 4,366]	0,8736
Woche 112	68	86,03 (22,966)	-1,35 (1,714)	46	88,77 (17,935)	-1,83 (2,007)	0,48 [-4,729; 5,687]	0,8563
Woche 116	62	87,90 (20,727)	-2,61 (1,934)	50	89,00 (18,629)	-2,65 (2,170)	0,04 [-5,689; 5,771]	0,9888
Woche 120	57	86,55 (22,146)	-2,55 (2,024)	46	85,51 (20,670)	-4,16 (2,267)	1,60 [-4,390; 7,599]	0,5982
Woche 124	53	88,05 (18,309)	-2,90 (1,724)	43	89,53 (17,826)	-3,08 (1,932)	0,18 [-4,928; 5,295]	0,9435
Woche 128	54	88,27 (20,637)	-2,02 (1,954)	39	88,89 (18,470)	-3,62 (2,257)	1,59 [-4,296; 7,486]	0,5937
Woche 132	49	85,37 (22,982)	-2,65 (1,940)	38	89,04 (18,695)	0,53 (2,212)	-3,18 [-8,997; 2,632]	0,2815
Woche 136	48	86,11 (22,369)	-1,06 (1,934)	33	91,41 (16,203)	-3,00 (2,289)	1,94 [-3,996; 7,872]	0,5197

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.6 ADRIATIC: Summary of analysis of change from baseline over time in Soziale Funktion (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	84,81 (22,140)	-1,47 (1,902)	33	94,95 (11,399)	-0,14 (2,246)	-1,34 [-7,188; 4,515]	0,6526
Woche 144	36	85,65 (23,955)	-5,21 (2,164)	29	92,53 (13,791)	1,10 (2,470)	-6,31 [-12,832; 0,216]	0,0580
Woche 148	40	84,17 (24,445)	-2,09 (1,901)	26	90,38 (17,747)	1,39 (2,276)	-3,48 [-9,366; 2,405]	0,2443
Woche 152	38	86,40 (20,815)	-0,11 (1,900)	27	89,51 (17,991)	0,79 (2,228)	-0,90 [-6,705; 4,899]	0,7588
Woche 156	34	83,82 (26,107)	-2,04 (1,956)	27	93,83 (12,359)	-0,20 (2,252)	-1,84 [-7,783; 4,094]	0,5402
Woche 160	31	83,87 (27,040)	-1,69 (2,012)	25	90,67 (17,401)	-0,65 (2,283)	-1,03 [-7,077; 5,013]	0,7362
Woche 164	31	82,80 (26,696)	0,60 (1,843)	21	91,27 (17,965)	-0,13 (2,169)	0,73 [-4,935; 6,396]	0,7991
Woche 168	27	87,65 (23,837)	-0,72 (2,157)	24	90,97 (17,706)	-2,42 (2,383)	1,70 [-4,673; 8,067]	0,5989
Woche 172	30	86,11 (24,006)	2,80 (1,837)	20	94,17 (12,419)	4,56 (2,194)	-1,77 [-7,444; 3,913]	0,5395
Woche 176	22	93,18 (12,236)	0,41 (2,211)	18	96,30 (10,779)	3,79 (2,573)	-3,38 [-9,764; 3,011]	0,2970
Woche 180	20	93,33 (12,566)	2,65 (2,502)	16	95,83 (11,386)	3,62 (2,892)	-0,97 [-8,139; 6,207]	0,7897
Woche 184	18	93,52 (11,630)	2,15 (2,604)	17	96,08 (11,070)	2,09 (2,903)	0,06 [-7,205; 7,317]	0,9878
Woche 188	16	91,67 (13,608)	-5,50 (4,191)	15	95,56 (11,729)	6,27 (4,665)	-11,77 [-23,751; 0,205]	0,0539
Durchschnitt über alle Visiten	215	86,98 (19,359)	-1,28 (1,035)	205	86,59 (19,533)	-1,56 (1,134)	0,28 [-2,734; 3,297]	0,8544
Hedges' g SMD							0,02 [-0,173; 0,209]	0,8545

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.7 ADRIATIC: Summary of analysis of change from baseline over time in Fatigue (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	23,42 (20,090)	1,99 (1,506)	192	25,00 (19,986)	3,72 (1,551)	-1,73 [-5,979; 2,518]	0,4238
Woche 8	193	22,05 (19,228)	6,10 (1,744)	179	26,01 (20,164)	7,60 (1,802)	-1,50 [-6,434; 3,434]	0,5504
Woche 12	176	21,65 (18,754)	2,35 (1,647)	169	25,71 (20,220)	4,05 (1,690)	-1,70 [-6,344; 2,944]	0,4720
Woche 16	168	21,30 (18,775)	2,93 (1,497)	166	25,77 (21,048)	3,71 (1,526)	-0,78 [-4,991; 3,428]	0,7154
Woche 20	160	21,39 (18,211)	3,08 (1,472)	155	26,38 (20,384)	1,01 (1,507)	2,07 [-2,078; 6,222]	0,3268
Woche 24	147	21,16 (17,894)	3,76 (1,584)	149	25,43 (20,959)	3,48 (1,605)	0,28 [-4,162; 4,722]	0,9015
Woche 28	145	21,84 (19,263)	2,66 (1,547)	133	26,23 (21,510)	2,33 (1,601)	0,32 [-4,059; 4,707]	0,8845
Woche 32	141	21,83 (19,446)	2,76 (1,638)	128	25,43 (20,309)	4,02 (1,703)	-1,26 [-5,910; 3,394]	0,5952
Woche 36	132	22,22 (18,470)	0,48 (1,571)	123	24,84 (20,571)	5,29 (1,627)	-4,81 [-9,259; -0,356]	0,0344*
Woche 40	119	21,48 (17,818)	1,94 (1,649)	105	24,66 (19,970)	5,33 (1,728)	-3,38 [-8,086; 1,321]	0,1582
Woche 44	117	21,56 (19,426)	3,03 (1,638)	106	25,37 (20,387)	2,65 (1,713)	0,38 [-4,284; 5,052]	0,8716
Woche 48	109	22,53 (20,085)	3,67 (1,691)	105	24,76 (20,340)	2,85 (1,749)	0,82 [-3,968; 5,610]	0,7361
Woche 52	112	21,43 (20,160)	1,52 (1,696)	101	25,08 (20,224)	4,19 (1,777)	-2,67 [-7,510; 2,169]	0,2785
Woche 56	106	22,33 (19,964)	2,12 (1,516)	90	25,19 (20,250)	2,84 (1,615)	-0,72 [-5,084; 3,642]	0,7452
Woche 60	103	22,01 (19,054)	0,96 (1,473)	85	26,27 (20,987)	2,34 (1,585)	-1,38 [-5,644; 2,885]	0,5249
Woche 64	101	21,78 (19,046)	1,24 (1,614)	82	26,96 (20,734)	3,93 (1,747)	-2,69 [-7,383; 1,998]	0,2596
Woche 68	91	21,37 (19,047)	1,44 (1,662)	80	26,94 (21,418)	2,62 (1,771)	-1,18 [-5,977; 3,609]	0,6271

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.7 ADRIATIC: Summary of analysis of change from baseline over time in Fatigue (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	20,99 (18,950)	1,61 (1,742)	77	25,25 (20,914)	4,93 (1,865)	-3,32 [-8,353; 1,717]	0,1957
Woche 76	90	21,85 (18,730)	-0,06 (1,707)	68	27,45 (21,071)	2,88 (1,900)	-2,94 [-7,980; 2,103]	0,2522
Woche 80	87	21,20 (17,249)	1,16 (1,629)	64	27,26 (21,224)	4,34 (1,834)	-3,19 [-8,033; 1,660]	0,1966
Woche 84	87	21,71 (20,042)	-0,71 (1,720)	66	27,44 (21,281)	4,30 (1,933)	-5,00 [-10,115; 0,106]	0,0549
Woche 88	83	21,42 (18,428)	0,97 (1,758)	60	26,67 (21,378)	4,54 (2,002)	-3,57 [-8,829; 1,698]	0,1834
Woche 92	84	21,43 (17,486)	0,03 (1,551)	59	25,24 (19,772)	3,84 (1,783)	-3,81 [-8,471; 0,859]	0,1094
Woche 96	79	22,64 (18,270)	1,28 (1,687)	54	26,34 (20,396)	5,26 (1,972)	-3,97 [-9,097; 1,150]	0,1279
Woche 100	85	21,96 (17,898)	1,96 (1,705)	57	27,88 (21,220)	4,34 (2,011)	-2,38 [-7,588; 2,833]	0,3697
Woche 104	73	22,68 (17,513)	1,23 (1,736)	54	26,34 (21,399)	5,16 (2,002)	-3,93 [-9,156; 1,306]	0,1407
Woche 108	71	21,60 (17,507)	2,65 (1,672)	51	26,58 (20,856)	4,29 (1,940)	-1,64 [-6,701; 3,425]	0,5245
Woche 112	68	22,06 (17,956)	1,71 (1,745)	46	28,26 (20,781)	3,91 (2,057)	-2,20 [-7,535; 3,134]	0,4172
Woche 116	62	20,61 (17,978)	3,38 (1,819)	50	27,11 (21,782)	3,38 (2,050)	0,00 [-5,434; 5,425]	0,9986
Woche 120	57	19,69 (17,318)	3,67 (1,991)	46	30,19 (23,267)	4,08 (2,256)	-0,41 [-6,404; 5,575]	0,8916
Woche 124	53	19,08 (16,791)	1,92 (1,961)	43	27,39 (20,907)	3,64 (2,201)	-1,73 [-7,595; 4,142]	0,5623
Woche 128	54	17,08 (16,255)	3,14 (2,047)	39	27,92 (21,909)	3,85 (2,349)	-0,71 [-6,942; 5,517]	0,8217
Woche 132	49	18,37 (17,938)	2,50 (2,042)	38	28,65 (22,466)	2,75 (2,332)	-0,25 [-6,446; 5,941]	0,9359
Woche 136	48	18,29 (15,961)	1,90 (1,885)	33	27,27 (20,618)	-0,09 (2,211)	1,99 [-3,816; 7,795]	0,4994
Woche 140	45	18,77 (15,502)	3,13 (2,222)	33	24,24 (16,305)	3,49 (2,552)	-0,36 [-7,082; 6,368]	0,9166

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.7 ADRIATIC: Summary of analysis of change from baseline over time in Fatigue (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	20,37 (17,518)	0,24 (1,984)	29	24,14 (16,284)	-1,90 (2,242)	2,14 [-3,823; 8,104]	0,4782
Woche 148	40	20,56 (17,351)	1,07 (2,281)	26	26,92 (18,371)	0,21 (2,740)	0,87 [-6,244; 7,978]	0,8097
Woche 152	38	19,30 (17,839)	-1,01 (2,348)	27	27,57 (20,059)	-1,00 (2,757)	0,00 [-7,246; 7,236]	0,9989
Woche 156	34	20,92 (17,888)	0,81 (1,985)	27	24,69 (16,111)	-2,68 (2,262)	3,49 [-2,501; 9,486]	0,2509
Woche 160	31	21,15 (18,449)	-0,01 (2,545)	25	28,44 (20,051)	-0,30 (2,903)	0,30 [-7,408; 8,002]	0,9393
Woche 164	31	20,07 (18,012)	-1,17 (2,220)	21	25,40 (18,968)	1,69 (2,609)	-2,86 [-9,698; 3,969]	0,4081
Woche 168	27	16,46 (17,533)	0,71 (2,197)	24	25,93 (20,374)	0,62 (2,374)	0,09 [-6,383; 6,569]	0,9774
Woche 172	30	17,04 (17,443)	-0,71 (2,262)	20	22,22 (16,122)	1,91 (2,613)	-2,62 [-9,470; 4,235]	0,4507
Woche 176	22	17,68 (18,357)	1,28 (2,468)	18	20,37 (12,783)	4,27 (2,720)	-2,98 [-10,224; 4,257]	0,4151
Woche 180	20	18,33 (18,827)	-1,16 (2,420)	16	20,83 (12,087)	4,33 (2,682)	-5,49 [-12,613; 1,626]	0,1288
Woche 184	18	19,75 (18,497)	0,33 (2,795)	17	19,61 (12,747)	4,47 (2,991)	-4,14 [-12,215; 3,937]	0,3107
Woche 188	16	20,83 (19,824)	0,04 (2,973)	15	18,52 (13,057)	6,22 (3,196)	-6,18 [-14,813; 2,449]	0,1575
Durchschnitt über alle Visiten	215	23,51 (20,240)	1,57 (1,092)	205	25,20 (20,230)	3,16 (1,196)	-1,59 [-4,782; 1,602]	0,3282
Hedges' g SMD							-0,10 [-0,287; 0,096]	0,3266

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraag 04NOV2024:19:16

Table 3.8.1.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	10,54 (16,185)	2,71 (1,361)	192	12,15 (16,266)	6,41 (1,403)	-3,71 [-7,553; 0,134]	0,0585
Woche 8	193	9,33 (15,194)	4,76 (1,542)	179	12,48 (16,464)	8,02 (1,594)	-3,25 [-7,621; 1,112]	0,1436
Woche 12	176	9,09 (15,099)	3,31 (1,401)	169	13,12 (16,782)	6,58 (1,439)	-3,27 [-7,224; 0,690]	0,1053
Woche 16	168	9,92 (15,609)	5,15 (1,394)	166	12,95 (16,855)	6,01 (1,423)	-0,86 [-4,784; 3,060]	0,6660
Woche 20	160	9,38 (14,800)	3,90 (1,332)	155	13,23 (17,062)	5,76 (1,365)	-1,86 [-5,615; 1,900]	0,3317
Woche 24	147	9,18 (14,359)	4,81 (1,472)	149	12,53 (16,768)	7,15 (1,491)	-2,34 [-6,467; 1,788]	0,2657
Woche 28	145	9,31 (14,813)	5,45 (1,512)	133	13,78 (17,227)	8,96 (1,571)	-3,50 [-7,802; 0,795]	0,1099
Woche 32	141	9,69 (15,060)	4,17 (1,489)	128	13,93 (17,219)	7,62 (1,558)	-3,44 [-7,690; 0,804]	0,1118
Woche 36	132	10,10 (15,239)	5,71 (1,560)	123	13,41 (17,159)	6,94 (1,622)	-1,22 [-5,658; 3,212]	0,5880
Woche 40	119	8,68 (14,203)	4,22 (1,582)	105	14,13 (17,870)	9,04 (1,671)	-4,81 [-9,360; -0,267]	0,0381*
Woche 44	117	9,12 (14,598)	5,72 (1,583)	106	13,68 (17,182)	8,39 (1,664)	-2,68 [-7,209; 1,858]	0,2465
Woche 48	109	8,26 (14,456)	6,35 (1,683)	105	13,17 (17,093)	7,74 (1,740)	-1,38 [-6,166; 3,400]	0,5698
Woche 52	112	8,04 (14,322)	6,26 (1,621)	101	13,37 (17,163)	7,93 (1,703)	-1,67 [-6,317; 2,981]	0,4807
Woche 56	106	8,81 (14,766)	7,51 (1,642)	90	13,52 (17,470)	7,79 (1,757)	-0,28 [-5,029; 4,472]	0,9083
Woche 60	103	8,74 (14,732)	4,82 (1,411)	85	14,31 (17,660)	8,23 (1,528)	-3,42 [-7,528; 0,697]	0,1033
Woche 64	101	7,92 (13,863)	6,64 (1,569)	82	14,43 (18,099)	7,81 (1,706)	-1,17 [-5,762; 3,423]	0,6166
Woche 68	91	8,24 (14,136)	3,94 (1,420)	80	14,17 (18,005)	5,42 (1,516)	-1,48 [-5,593; 2,635]	0,4797

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	8,33 (14,407)	4,04 (1,603)	77	12,99 (16,362)	8,60 (1,721)	-4,56 [-9,214; 0,092]	0,0547
Woche 76	90	8,70 (14,617)	4,14 (1,515)	68	15,69 (19,291)	5,94 (1,705)	-1,80 [-6,318; 2,724]	0,4345
Woche 80	87	8,43 (13,892)	4,57 (1,479)	64	14,58 (17,442)	5,93 (1,678)	-1,37 [-5,804; 3,072]	0,5448
Woche 84	87	6,32 (12,253)	3,90 (1,475)	66	15,40 (19,240)	7,94 (1,658)	-4,05 [-8,476; 0,384]	0,0733
Woche 88	83	6,02 (12,091)	5,33 (1,666)	60	15,28 (19,235)	8,50 (1,899)	-3,16 [-8,212; 1,886]	0,2184
Woche 92	84	6,75 (12,706)	3,60 (1,454)	59	13,84 (16,995)	7,14 (1,673)	-3,54 [-7,953; 0,878]	0,1158
Woche 96	79	6,96 (12,689)	4,58 (1,573)	54	14,20 (19,535)	5,76 (1,839)	-1,18 [-5,995; 3,644]	0,6312
Woche 100	85	6,67 (12,387)	2,51 (1,506)	57	14,91 (19,077)	6,84 (1,775)	-4,33 [-8,974; 0,311]	0,0673
Woche 104	73	6,62 (12,650)	1,58 (1,469)	54	12,96 (17,030)	5,10 (1,679)	-3,53 [-7,966; 0,910]	0,1186
Woche 108	71	8,22 (14,050)	4,82 (1,772)	51	13,73 (17,226)	7,09 (2,058)	-2,27 [-7,666; 3,125]	0,4078
Woche 112	68	7,35 (12,677)	6,66 (1,749)	46	14,13 (17,557)	3,31 (2,055)	3,35 [-2,030; 8,729]	0,2209
Woche 116	62	6,72 (12,244)	4,75 (1,766)	50	14,00 (17,288)	6,17 (1,977)	-1,42 [-6,716; 3,868]	0,5961
Woche 120	57	5,85 (11,990)	8,12 (1,997)	46	15,58 (17,709)	3,34 (2,237)	4,78 [-1,244; 10,805]	0,1191
Woche 124	53	5,97 (13,113)	5,81 (1,917)	43	14,34 (14,810)	7,30 (2,136)	-1,49 [-7,253; 4,267]	0,6094
Woche 128	54	7,41 (13,988)	4,92 (1,942)	39	13,68 (14,745)	10,01 (2,247)	-5,09 [-11,022; 0,841]	0,0920
Woche 132	49	6,80 (13,140)	4,72 (1,961)	38	14,04 (14,769)	5,16 (2,231)	-0,44 [-6,385; 5,504]	0,8838
Woche 136	48	7,29 (13,274)	6,43 (2,051)	33	10,10 (12,458)	6,60 (2,399)	-0,17 [-6,431; 6,094]	0,9576
Woche 140	45	7,04 (13,050)	1,78 (1,884)	33	10,61 (13,056)	3,69 (2,161)	-1,90 [-7,591; 3,783]	0,5090

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	6,02 (12,053)	6,30 (2,120)	29	11,49 (13,440)	2,93 (2,351)	3,37 [-2,947; 9,691]	0,2924
Woche 148	40	7,08 (13,549)	3,77 (1,846)	26	12,18 (13,790)	0,68 (2,201)	3,09 [-2,642; 8,820]	0,2878
Woche 152	38	9,21 (15,352)	4,86 (1,869)	27	11,73 (13,724)	2,47 (2,193)	2,39 [-3,345; 8,122]	0,4107
Woche 156	34	10,29 (15,899)	3,48 (1,919)	27	10,49 (13,195)	3,45 (2,183)	0,03 [-5,745; 5,798]	0,9928
Woche 160	31	9,68 (15,971)	8,08 (2,194)	25	10,67 (12,620)	3,15 (2,477)	4,93 [-1,646; 11,499]	0,1403
Woche 164	31	6,45 (11,924)	4,24 (2,075)	21	10,32 (13,412)	2,46 (2,397)	1,78 [-4,520; 8,081]	0,5762
Woche 168	27	4,94 (9,028)	2,96 (2,030)	24	11,81 (13,441)	2,36 (2,139)	0,60 [-5,300; 6,501]	0,8405
Woche 172	30	6,11 (11,973)	3,77 (2,201)	20	10,83 (13,545)	2,99 (2,533)	0,78 [-5,891; 7,458]	0,8165
Woche 176	22	4,55 (9,175)	5,20 (2,214)	18	11,11 (14,003)	3,92 (2,366)	1,28 [-5,203; 7,763]	0,6953
Woche 180	20	5,00 (9,521)	-0,23 (2,362)	16	10,42 (13,437)	1,46 (2,528)	-1,69 [-8,570; 5,199]	0,6274
Woche 184	18	5,56 (9,901)	1,62 (2,553)	17	9,80 (13,253)	-1,24 (2,635)	2,86 [-4,414; 10,131]	0,4366
Woche 188	16	5,21 (10,035)	4,60 (3,325)	15	7,78 (12,387)	-0,84 (3,391)	5,44 [-3,867; 14,757]	0,2473
Durchschnitt über alle Visiten	215	10,16 (15,998)	4,60 (0,973)	205	11,95 (16,067)	5,62 (1,066)	-1,01 [-3,864; 1,837]	0,4850
Hedges' g SMD							-0,07 [-0,260; 0,123]	0,4826

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraah 04NOV2024:19:16

Table 3.8.1.9 ADRIATIC: Summary of analysis of change from baseline over time in Übelkeit und Erbrechen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	6,29 (13,436)	-2,02 (0,727)	192	6,25 (11,248)	-0,26 (0,749)	-1,76 [-3,810; 0,287]	0,0918
Woche 8	193	6,30 (13,682)	1,43 (0,739)	179	6,89 (11,545)	1,34 (0,765)	0,10 [-1,990; 2,183]	0,9279
Woche 12	176	6,06 (13,495)	-2,22 (0,761)	169	6,21 (11,025)	-0,96 (0,779)	-1,26 [-3,396; 0,876]	0,2473
Woche 16	168	5,95 (13,562)	-1,07 (0,775)	166	6,43 (11,261)	-1,11 (0,787)	0,04 [-2,128; 2,205]	0,9722
Woche 20	160	6,15 (13,688)	-2,05 (0,791)	155	6,77 (11,815)	-1,96 (0,807)	-0,09 [-2,305; 2,127]	0,9374
Woche 24	147	5,44 (11,567)	-2,16 (0,816)	149	6,60 (11,099)	-1,26 (0,821)	-0,89 [-3,165; 1,377]	0,4400
Woche 28	145	6,21 (14,020)	-1,85 (0,823)	133	6,39 (10,995)	-1,08 (0,853)	-0,77 [-3,099; 1,551]	0,5140
Woche 32	141	6,50 (14,194)	-2,29 (0,833)	128	7,42 (11,980)	-1,14 (0,871)	-1,14 [-3,507; 1,221]	0,3433
Woche 36	132	6,44 (14,215)	-2,93 (0,854)	123	6,91 (11,867)	-1,07 (0,887)	-1,86 [-4,274; 0,556]	0,1312
Woche 40	119	5,60 (13,771)	-3,34 (0,887)	105	7,14 (12,199)	0,24 (0,937)	-3,58 [-6,107; -1,045]	0,0056*
Woche 44	117	5,98 (14,092)	-2,61 (0,896)	106	7,86 (12,642)	-2,14 (0,943)	-0,47 [-3,019; 2,085]	0,7196
Woche 48	109	6,27 (14,836)	-1,75 (0,921)	105	7,94 (12,679)	-1,89 (0,954)	0,14 [-2,462; 2,739]	0,9168
Woche 52	112	6,10 (14,498)	-2,78 (0,921)	101	8,09 (13,041)	-0,19 (0,972)	-2,59 [-5,218; 0,035]	0,0532
Woche 56	106	6,13 (14,787)	-3,77 (0,943)	90	7,22 (12,505)	-1,32 (1,012)	-2,45 [-5,166; 0,260]	0,0764
Woche 60	103	6,15 (14,758)	-2,15 (0,949)	85	7,84 (12,490)	-2,80 (1,029)	0,65 [-2,097; 3,395]	0,6430
Woche 64	101	6,27 (14,879)	-1,92 (0,955)	82	7,93 (12,890)	-1,65 (1,042)	-0,27 [-3,044; 2,500]	0,8475
Woche 68	91	5,86 (12,012)	-3,68 (0,990)	80	7,92 (13,253)	-2,25 (1,057)	-1,42 [-4,264; 1,418]	0,3262

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.9 ADRIATIC: Summary of analysis of change from baseline over time in Übelkeit und Erbrechen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	5,37 (11,937)	-4,28 (0,997)	77	8,87 (13,406)	-1,86 (1,077)	-2,42 [-5,302; 0,467]	0,1004
Woche 76	90	6,48 (15,339)	-1,73 (1,000)	68	7,11 (11,983)	-2,37 (1,125)	0,64 [-2,313; 3,591]	0,6712
Woche 80	87	6,13 (15,484)	-2,97 (1,010)	64	7,81 (12,933)	-3,06 (1,152)	0,09 [-2,921; 3,093]	0,9553
Woche 84	87	6,32 (15,511)	-3,22 (1,016)	66	8,08 (13,153)	-1,98 (1,153)	-1,24 [-4,256; 1,772]	0,4192
Woche 88	83	5,62 (15,460)	-3,12 (1,035)	60	7,22 (12,029)	-1,36 (1,191)	-1,76 [-4,855; 1,335]	0,2650
Woche 92	84	5,95 (15,446)	-0,95 (1,027)	59	7,34 (12,484)	-1,01 (1,195)	0,06 [-3,030; 3,152]	0,9691
Woche 96	79	6,12 (15,829)	-2,52 (1,037)	54	7,10 (12,372)	-1,99 (1,223)	-0,53 [-3,675; 2,614]	0,7409
Woche 100	85	6,86 (15,914)	-3,10 (1,010)	57	7,31 (12,206)	-2,31 (1,201)	-0,79 [-3,863; 2,290]	0,6162
Woche 104	73	6,16 (16,079)	-2,90 (1,063)	54	7,10 (11,493)	-1,91 (1,223)	-1,00 [-4,175; 2,181]	0,5384
Woche 108	71	4,69 (11,678)	-3,31 (1,089)	51	5,56 (9,230)	-3,26 (1,259)	-0,05 [-3,307; 3,209]	0,9767
Woche 112	68	7,35 (17,129)	-3,46 (1,112)	46	5,80 (9,439)	-2,84 (1,310)	-0,62 [-3,994; 2,747]	0,7168
Woche 116	62	5,38 (12,360)	-3,06 (1,155)	50	5,00 (9,066)	-2,76 (1,285)	-0,30 [-3,684; 3,082]	0,8614
Woche 120	57	5,26 (12,263)	-1,17 (1,197)	46	6,88 (10,873)	-2,10 (1,327)	0,94 [-2,570; 4,446]	0,6000
Woche 124	53	5,66 (15,994)	-2,43 (1,234)	43	5,81 (10,212)	-1,24 (1,367)	-1,20 [-4,806; 2,414]	0,5161
Woche 128	54	4,01 (9,120)	-2,03 (1,246)	39	7,26 (11,339)	0,24 (1,427)	-2,27 [-5,998; 1,455]	0,2321
Woche 132	49	6,12 (16,906)	-2,17 (1,275)	38	7,02 (11,384)	-1,51 (1,448)	-0,66 [-4,445; 3,122]	0,7317
Woche 136	48	5,90 (16,663)	-2,60 (1,294)	33	6,57 (10,976)	-3,60 (1,533)	0,99 [-2,939; 4,928]	0,6201

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.9 ADRIATIC: Summary of analysis of change from baseline over time in Übelkeit und Erbrechen (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	6,30 (17,148)	-3,85 (1,326)	33	5,56 (9,919)	-2,22 (1,538)	-1,63 [-5,607; 2,356]	0,4233
Woche 144	36	4,63 (10,244)	-3,48 (1,455)	29	6,32 (10,364)	-3,21 (1,618)	-0,27 [-4,542; 4,000]	0,9010
Woche 148	40	2,50 (8,051)	-2,34 (1,460)	26	7,05 (11,712)	-3,45 (1,699)	1,11 [-3,306; 5,531]	0,6214
Woche 152	38	3,51 (8,800)	-1,85 (1,474)	27	6,17 (10,488)	-3,53 (1,693)	1,68 [-2,725; 6,082]	0,4548
Woche 156	34	3,92 (9,229)	-3,45 (1,541)	27	6,17 (9,415)	-2,09 (1,711)	-1,36 [-5,877; 3,157]	0,5548
Woche 160	31	3,76 (9,339)	-4,72 (1,505)	25	6,67 (10,758)	-3,61 (1,656)	-1,10 [-5,501; 3,291]	0,6219
Woche 164	31	3,76 (9,339)	-3,98 (1,522)	21	6,35 (11,151)	-0,30 (1,763)	-3,68 [-8,257; 0,893]	0,1145
Woche 168	27	3,09 (8,056)	-3,90 (1,631)	24	4,86 (9,167)	-2,56 (1,719)	-1,34 [-5,939; 3,256]	0,5670
Woche 172	30	3,89 (9,472)	-4,52 (1,576)	20	5,83 (9,786)	-0,87 (1,828)	-3,65 [-8,384; 1,075]	0,1296
Woche 176	22	5,30 (10,772)	-5,56 (1,749)	18	5,56 (9,901)	-0,16 (1,928)	-5,40 [-10,508; -0,297]	0,0381*
Woche 180	20	5,83 (11,180)	-1,62 (1,826)	16	6,25 (10,319)	0,25 (2,031)	-1,87 [-7,238; 3,493]	0,4933
Woche 184	18	6,48 (11,630)	-2,82 (1,913)	17	5,88 (10,106)	-2,54 (2,005)	-0,28 [-5,724; 5,167]	0,9201
Woche 188	16	6,25 (11,980)	-3,12 (1,799)	15	5,56 (10,287)	-0,25 (1,855)	-2,87 [-7,986; 2,242]	0,2688
Durchschnitt über alle Visiten	215	6,12 (13,187)	-2,71 (0,570)	205	6,50 (11,240)	-1,68 (0,621)	-1,03 [-2,689; 0,628]	0,2226
Hedges' g SMD							-0,12 [-0,311; 0,072]	0,2222

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraai 04NOV2024:19:16

Nutzenbewertung nach AMNOG

Table 3.8.1.10 ADRIATIC: Summary of analysis of change from baseline over time in Appetitverlust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	18,95 (25,633)	0,83 (1,460)	192	15,97 (23,374)	2,44 (1,504)	-1,61 [-5,724; 2,503]	0,4426
Woche 8	193	18,13 (24,753)	9,33 (1,482)	179	17,13 (24,057)	5,61 (1,532)	3,72 [-0,461; 7,901]	0,0811
Woche 12	176	18,18 (25,152)	4,23 (1,521)	169	16,96 (23,603)	1,25 (1,558)	2,98 [-1,290; 7,251]	0,1713
Woche 16	168	18,25 (25,223)	1,97 (1,547)	166	17,07 (24,271)	-1,15 (1,572)	3,13 [-1,199; 7,453]	0,1565
Woche 20	160	18,13 (25,036)	-0,32 (1,577)	155	17,20 (24,722)	-3,45 (1,609)	3,13 [-1,288; 7,548]	0,1649
Woche 24	147	18,82 (24,385)	-1,20 (1,622)	149	17,45 (24,685)	-4,43 (1,635)	3,23 [-1,290; 7,747]	0,1612
Woche 28	145	18,39 (24,511)	-0,58 (1,639)	133	16,29 (23,789)	-5,98 (1,698)	5,40 [0,774; 10,030]	0,0222*
Woche 32	141	19,15 (25,271)	-0,31 (1,660)	128	16,41 (23,661)	-3,29 (1,731)	2,98 [-1,727; 7,686]	0,2146
Woche 36	132	20,20 (25,641)	-4,35 (1,703)	123	16,53 (23,906)	-3,20 (1,764)	-1,16 [-5,970; 3,655]	0,6372
Woche 40	119	20,73 (24,926)	-5,67 (1,765)	105	15,87 (24,062)	-4,87 (1,860)	-0,80 [-5,838; 4,237]	0,7554
Woche 44	117	20,23 (25,127)	-4,13 (1,787)	106	17,30 (24,443)	-3,72 (1,873)	-0,41 [-5,491; 4,669]	0,8740
Woche 48	109	21,10 (25,524)	-3,46 (1,835)	105	17,14 (24,510)	-6,74 (1,892)	3,28 [-1,894; 8,452]	0,2140
Woche 52	112	19,64 (25,134)	-4,68 (1,828)	101	16,50 (24,324)	-7,16 (1,921)	2,49 [-2,718; 7,689]	0,3490
Woche 56	106	20,44 (25,849)	-2,42 (1,866)	90	16,30 (25,106)	-5,43 (1,998)	3,01 [-2,359; 8,376]	0,2718
Woche 60	103	18,77 (24,553)	-3,77 (1,888)	85	17,25 (24,993)	-7,44 (2,042)	3,67 [-1,786; 9,125]	0,1873
Woche 64	101	19,80 (25,896)	-4,47 (1,909)	82	16,67 (25,256)	-8,03 (2,077)	3,56 [-1,974; 9,098]	0,2072
Woche 68	91	19,78 (25,327)	-6,58 (1,975)	80	15,42 (24,845)	-8,71 (2,104)	2,13 [-3,540; 7,792]	0,4620

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraaj 04NOV2024:19:16

Table 3.8.1.10 ADRIATIC: Summary of analysis of change from baseline over time in Appetitverlust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	20,00 (25,381)	-4,85 (1,991)	77	16,88 (25,720)	-7,58 (2,137)	2,73 [-3,000; 8,465]	0,3500
Woche 76	90	21,85 (26,517)	-7,19 (2,004)	68	15,69 (24,072)	-6,78 (2,242)	-0,41 [-6,323; 5,499]	0,8914
Woche 80	87	19,92 (25,140)	-6,15 (2,027)	64	18,23 (25,840)	-7,38 (2,300)	1,22 [-4,790; 7,233]	0,6904
Woche 84	87	20,31 (25,597)	-6,57 (2,031)	66	17,17 (24,973)	-3,73 (2,292)	-2,84 [-8,854; 3,166]	0,3535
Woche 88	83	19,68 (25,522)	-2,82 (2,061)	60	16,11 (24,923)	-5,62 (2,369)	2,80 [-3,362; 8,963]	0,3729
Woche 92	84	19,44 (24,927)	-2,29 (2,061)	59	17,51 (25,033)	-6,48 (2,398)	4,19 [-2,009; 10,397]	0,1851
Woche 96	79	20,68 (25,767)	-7,42 (2,105)	54	16,67 (24,869)	-7,27 (2,483)	-0,15 [-6,539; 6,239]	0,9633
Woche 100	85	20,39 (25,247)	-4,42 (2,065)	57	18,13 (25,253)	-7,50 (2,454)	3,07 [-3,216; 9,365]	0,3380
Woche 104	73	19,18 (24,164)	-8,10 (2,162)	54	17,90 (25,668)	-7,51 (2,495)	-0,59 [-7,065; 5,886]	0,8584
Woche 108	71	17,84 (21,699)	-7,90 (2,199)	51	15,69 (23,431)	-7,69 (2,561)	-0,21 [-6,828; 6,407]	0,9503
Woche 112	68	18,63 (21,841)	-5,85 (2,248)	46	18,12 (24,044)	-9,11 (2,655)	3,26 [-3,562; 10,081]	0,3489
Woche 116	62	17,74 (22,355)	-5,23 (2,331)	50	16,00 (24,504)	-7,99 (2,607)	2,76 [-4,102; 9,612]	0,4308
Woche 120	57	17,54 (21,917)	-5,96 (2,413)	46	16,67 (25,092)	-9,34 (2,692)	3,38 [-3,708; 10,466]	0,3500
Woche 124	53	15,72 (21,287)	-5,16 (2,493)	43	17,83 (26,576)	-8,61 (2,770)	3,45 [-3,856; 10,757]	0,3545
Woche 128	54	14,81 (21,148)	-7,58 (2,501)	39	20,51 (28,217)	-7,37 (2,889)	-0,21 [-7,720; 7,301]	0,9564
Woche 132	49	18,37 (22,629)	-7,75 (2,584)	38	22,81 (29,106)	-7,55 (2,951)	-0,21 [-7,900; 7,489]	0,9582
Woche 136	48	15,28 (21,699)	-9,74 (2,622)	33	20,20 (28,795)	-10,92 (3,101)	1,18 [-6,799; 9,160]	0,7718

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraaj 04NOV2024:19:16

Table 3.8.1.10 ADRIATIC: Summary of analysis of change from baseline over time in Appetitverlust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	17,04 (22,045)	-7,41 (2,700)	33	18,18 (25,126)	-9,45 (3,135)	2,04 [-6,079; 10,159]	0,6223
Woche 144	36	16,67 (21,822)	-8,54 (2,942)	29	21,84 (27,133)	-9,29 (3,325)	0,75 [-7,981; 9,476]	0,8666
Woche 148	40	15,83 (21,334)	-9,75 (2,881)	26	23,08 (29,468)	-8,64 (3,496)	-1,11 [-10,032; 7,805]	0,8066
Woche 152	38	16,67 (21,575)	-7,53 (2,964)	27	20,99 (29,451)	-7,84 (3,488)	0,31 [-8,689; 9,304]	0,9466
Woche 156	34	16,67 (22,096)	-6,39 (3,090)	27	18,52 (25,036)	-6,09 (3,502)	-0,30 [-9,478; 8,869]	0,9481
Woche 160	31	17,20 (22,560)	-3,12 (3,223)	25	22,67 (30,000)	-9,34 (3,643)	6,22 [-3,341; 15,782]	0,2021
Woche 164	31	16,13 (22,560)	-7,34 (3,275)	21	23,81 (31,873)	-4,07 (3,899)	-3,26 [-13,284; 6,757]	0,5230
Woche 168	27	17,28 (23,334)	-8,44 (3,467)	24	18,06 (29,454)	-7,48 (3,758)	-0,96 [-10,995; 9,079]	0,8515
Woche 172	30	15,56 (22,715)	-8,75 (3,407)	20	16,67 (25,363)	-7,32 (4,043)	-1,43 [-11,800; 8,936]	0,7865
Woche 176	22	19,70 (24,471)	-9,64 (3,825)	18	20,37 (28,328)	-9,31 (4,274)	-0,33 [-11,577; 10,917]	0,9542
Woche 180	20	20,00 (25,131)	-7,76 (4,025)	16	22,92 (29,107)	-7,40 (4,541)	-0,36 [-12,244; 11,527]	0,9528
Woche 184	18	20,37 (25,918)	-4,73 (4,224)	17	21,57 (28,726)	-6,66 (4,480)	1,93 [-10,135; 13,998]	0,7534
Woche 188	16	22,92 (26,440)	-8,35 (4,542)	15	24,44 (29,457)	-7,30 (4,794)	-1,05 [-13,921; 11,828]	0,8732
Durchschnitt über alle Visiten	215	18,76 (25,261)	-4,86 (1,192)	205	16,75 (23,250)	-6,23 (1,303)	1,37 [-2,098; 4,847]	0,4372
Hedges' g SMD							0,08 [-0,115; 0,267]	0,4367

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraaj 04NOV2024:19:16

Table 3.8.1.11 ADRIATIC: Summary of analysis of change from baseline over time in Diarrhö (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	3,43 (10,680)	0,45 (1,043)	192	5,90 (17,051)	1,75 (1,071)	-1,31 [-4,254; 1,636]	0,3827
Woche 8	193	3,63 (10,949)	0,14 (0,988)	179	6,15 (17,474)	1,07 (1,020)	-0,93 [-3,732; 1,865]	0,5124
Woche 12	176	3,41 (10,738)	0,21 (1,078)	169	6,11 (17,312)	1,03 (1,100)	-0,82 [-3,852; 2,219]	0,5972
Woche 16	168	3,57 (10,965)	0,75 (1,113)	166	6,63 (18,061)	0,93 (1,128)	-0,17 [-3,297; 2,951]	0,9133
Woche 20	160	3,96 (11,445)	1,18 (1,077)	155	7,10 (18,605)	0,72 (1,099)	0,45 [-2,579; 3,487]	0,7686
Woche 24	147	3,85 (11,386)	0,04 (1,229)	149	7,16 (18,810)	2,47 (1,236)	-2,43 [-5,867; 1,008]	0,1654
Woche 28	145	3,22 (9,879)	0,87 (1,055)	133	7,02 (18,826)	0,95 (1,093)	-0,08 [-3,076; 2,923]	0,9601
Woche 32	141	3,07 (9,678)	1,50 (1,135)	128	7,03 (18,066)	0,79 (1,182)	0,71 [-2,522; 3,952]	0,6643
Woche 36	132	2,53 (8,854)	0,29 (1,029)	123	7,32 (18,375)	0,85 (1,063)	-0,55 [-3,482; 2,374]	0,7099
Woche 40	119	3,08 (9,696)	0,88 (1,185)	105	7,62 (19,203)	1,98 (1,252)	-1,11 [-4,516; 2,304]	0,5237
Woche 44	117	2,56 (8,921)	0,84 (1,193)	106	7,55 (18,564)	3,15 (1,248)	-2,31 [-5,726; 1,115]	0,1857
Woche 48	109	3,06 (9,667)	0,21 (1,190)	105	7,94 (18,790)	1,30 (1,226)	-1,09 [-4,471; 2,297]	0,5276
Woche 52	112	2,08 (8,105)	0,46 (1,038)	101	8,25 (19,667)	-0,43 (1,089)	0,89 [-2,099; 3,877]	0,5587
Woche 56	106	2,52 (8,847)	-0,47 (1,064)	90	8,15 (19,552)	1,07 (1,142)	-1,54 [-4,639; 1,556]	0,3280
Woche 60	103	2,91 (9,459)	-0,78 (0,945)	85	6,67 (16,903)	-0,02 (1,021)	-0,76 [-3,511; 1,994]	0,5879
Woche 64	101	2,64 (9,047)	0,87 (1,232)	82	8,54 (20,158)	1,13 (1,348)	-0,26 [-3,890; 3,365]	0,8869
Woche 68	91	3,30 (10,006)	-0,98 (1,071)	80	7,50 (19,104)	1,73 (1,141)	-2,71 [-5,808; 0,390]	0,0863

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraak 04NOV2024:19:16

Table 3.8.1.11 ADRIATIC: Summary of analysis of change from baseline over time in Diarrhö (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	2,96 (9,539)	-1,00 (0,958)	77	7,36 (17,625)	0,09 (1,027)	-1,09 [-3,872; 1,696]	0,4418
Woche 76	90	2,59 (8,977)	0,53 (1,184)	68	6,37 (16,549)	0,57 (1,325)	-0,04 [-3,559; 3,481]	0,9827
Woche 80	87	2,68 (9,119)	1,35 (1,172)	64	6,77 (16,986)	0,55 (1,328)	0,80 [-2,716; 4,308]	0,6553
Woche 84	87	3,45 (10,210)	-0,21 (1,236)	66	7,07 (17,062)	3,32 (1,395)	-3,54 [-7,228; 0,155]	0,0603
Woche 88	83	3,21 (9,897)	-1,62 (0,909)	60	7,22 (17,458)	-0,53 (1,045)	-1,10 [-3,842; 1,650]	0,4322
Woche 92	84	3,17 (9,844)	2,23 (1,447)	59	7,34 (17,582)	0,04 (1,685)	2,19 [-2,215; 6,595]	0,3281
Woche 96	79	3,38 (10,120)	0,87 (1,371)	54	8,64 (18,526)	2,61 (1,628)	-1,74 [-5,964; 2,491]	0,4187
Woche 100	85	2,75 (9,218)	-0,19 (1,224)	57	8,19 (18,127)	2,86 (1,457)	-3,05 [-6,837; 0,734]	0,1135
Woche 104	73	2,74 (9,219)	-0,70 (1,283)	54	6,79 (13,551)	2,20 (1,467)	-2,90 [-6,775; 0,977]	0,1417
Woche 108	71	2,82 (9,338)	-0,56 (1,221)	51	7,19 (13,846)	1,10 (1,414)	-1,66 [-5,381; 2,057]	0,3790
Woche 112	68	2,94 (9,525)	0,50 (1,265)	46	7,25 (13,901)	0,00 (1,497)	0,50 [-3,407; 4,403]	0,8013
Woche 116	62	3,23 (9,935)	0,10 (1,228)	50	6,67 (13,469)	0,76 (1,365)	-0,66 [-4,304; 2,991]	0,7227
Woche 120	57	2,92 (9,513)	0,09 (1,363)	46	7,25 (13,901)	-0,24 (1,516)	0,32 [-3,736; 4,385]	0,8746
Woche 124	53	3,14 (9,837)	-1,18 (1,797)	43	6,20 (13,125)	4,76 (1,990)	-5,95 [-11,276; -0,619]	0,0290*
Woche 128	54	3,09 (9,753)	1,74 (1,634)	39	5,98 (12,959)	4,25 (1,889)	-2,51 [-7,464; 2,453]	0,3195
Woche 132	49	3,40 (10,195)	1,77 (1,821)	38	6,14 (13,095)	-1,71 (2,064)	3,48 [-1,995; 8,956]	0,2105
Woche 136	48	3,47 (10,290)	-0,59 (1,267)	33	7,07 (13,838)	-1,47 (1,509)	0,88 [-3,049; 4,811]	0,6575
Woche 140	45	3,70 (10,594)	1,00 (1,702)	33	8,08 (14,506)	0,81 (1,993)	0,20 [-5,032; 5,426]	0,9406

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraak 04NOV2024:19:16

Table 3.8.1.11 ADRIATIC: Summary of analysis of change from baseline over time in Diarrhö (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	4,63 (11,691)	-1,27 (1,336)	29	6,90 (13,742)	-2,75 (1,507)	1,48 [-2,531; 5,499]	0,4643
Woche 148	40	4,17 (11,164)	-1,55 (1,524)	26	8,97 (15,078)	0,24 (1,884)	-1,79 [-6,635; 3,053]	0,4644
Woche 152	38	3,51 (10,367)	-0,50 (1,860)	27	8,64 (14,886)	1,61 (2,216)	-2,10 [-7,920; 3,710]	0,4730
Woche 156	34	3,92 (10,901)	0,70 (1,852)	27	9,88 (15,511)	-0,05 (2,137)	0,75 [-4,924; 6,433]	0,7920
Woche 160	31	4,30 (11,359)	-2,67 (1,509)	25	9,33 (15,275)	0,14 (1,726)	-2,80 [-7,398; 1,793]	0,2280
Woche 164	31	3,23 (10,018)	-1,26 (2,072)	21	9,52 (15,430)	3,64 (2,522)	-4,90 [-11,484; 1,685]	0,1423
Woche 168	27	3,70 (10,675)	0,40 (1,916)	24	9,72 (15,477)	1,21 (2,109)	-0,81 [-6,552; 4,925]	0,7781
Woche 172	30	3,33 (10,171)	-0,44 (1,671)	20	10,00 (15,672)	0,74 (2,052)	-1,18 [-6,529; 4,161]	0,6597
Woche 176	22	3,03 (9,808)	0,53 (1,922)	18	11,11 (16,169)	0,66 (2,214)	-0,13 [-6,103; 5,837]	0,9646
Woche 180	20	5,00 (12,212)	-2,21 (1,640)	16	12,50 (16,667)	0,16 (1,935)	-2,37 [-7,463; 2,728]	0,3557
Woche 184	18	5,56 (12,783)	-0,70 (1,853)	17	11,76 (16,420)	0,08 (2,030)	-0,79 [-6,302; 4,727]	0,7753
Woche 188	16	4,17 (11,386)	-1,17 (2,552)	15	11,11 (16,265)	1,39 (2,742)	-2,56 [-10,165; 5,044]	0,5005
Durchschnitt über alle Visiten	215	3,26 (10,429)	0,01 (0,666)	205	6,02 (16,881)	1,01 (0,729)	-1,00 [-2,954; 0,952]	0,3141
Hedges' g SMD							-0,10 [-0,290; 0,093]	0,3112

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraak 04NOV2024:19:16

Table 3.8.1.12 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	15,20 (20,207)	2,61 (1,541)	192	18,58 (22,801)	3,68 (1,580)	-1,07 [-5,413; 3,275]	0,6288
Woche 8	193	14,34 (19,736)	5,98 (1,700)	179	18,99 (23,421)	5,95 (1,748)	0,03 [-4,770; 4,838]	0,9889
Woche 12	176	14,20 (19,361)	4,69 (1,737)	169	19,33 (22,883)	6,60 (1,773)	-1,91 [-6,798; 2,986]	0,4442
Woche 16	168	13,69 (19,756)	4,17 (1,672)	166	20,08 (23,749)	5,96 (1,694)	-1,79 [-6,485; 2,906]	0,4542
Woche 20	160	14,58 (20,024)	4,71 (1,718)	155	20,00 (23,293)	5,29 (1,749)	-0,58 [-5,417; 4,253]	0,8129
Woche 24	147	14,51 (20,298)	4,37 (1,619)	149	20,36 (24,109)	4,76 (1,632)	-0,40 [-4,931; 4,140]	0,8640
Woche 28	145	14,71 (20,365)	4,17 (1,632)	133	20,80 (24,482)	2,82 (1,687)	1,35 [-3,285; 5,978]	0,5678
Woche 32	141	15,37 (20,516)	6,27 (1,766)	128	19,53 (23,487)	4,86 (1,834)	1,41 [-3,611; 6,426]	0,5815
Woche 36	132	14,90 (20,309)	3,21 (1,627)	123	20,33 (24,752)	4,40 (1,681)	-1,19 [-5,803; 3,426]	0,6127
Woche 40	119	13,73 (19,606)	3,86 (1,844)	105	20,63 (24,188)	5,04 (1,932)	-1,18 [-6,456; 4,098]	0,6606
Woche 44	117	13,96 (20,171)	4,55 (1,802)	106	20,44 (24,156)	5,25 (1,879)	-0,69 [-5,836; 4,446]	0,7905
Woche 48	109	13,76 (20,393)	4,28 (1,889)	105	19,68 (24,326)	3,90 (1,939)	0,38 [-4,962; 5,727]	0,8880
Woche 52	112	13,39 (20,239)	4,57 (1,827)	101	19,80 (22,695)	4,57 (1,906)	0,00 [-5,210; 5,218]	0,9987
Woche 56	106	14,47 (20,583)	6,14 (1,829)	90	18,89 (23,464)	6,55 (1,945)	-0,41 [-5,680; 4,852]	0,8772
Woche 60	103	15,21 (20,757)	2,36 (1,709)	85	19,22 (23,218)	4,61 (1,837)	-2,25 [-7,199; 2,697]	0,3713
Woche 64	101	14,52 (20,230)	4,02 (1,994)	82	20,33 (23,281)	7,94 (2,156)	-3,91 [-9,713; 1,886]	0,1851
Woche 68	91	13,92 (19,917)	3,88 (1,907)	80	19,58 (23,537)	5,24 (2,018)	-1,36 [-6,843; 4,126]	0,6262

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.12 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	15,19 (20,700)	3,54 (1,827)	77	19,48 (21,865)	7,42 (1,953)	-3,88 [-9,161; 1,396]	0,1487
Woche 76	90	14,44 (20,633)	4,68 (1,889)	68	21,08 (24,369)	5,56 (2,104)	-0,88 [-6,467; 4,712]	0,7575
Woche 80	87	15,71 (20,859)	2,84 (1,892)	64	20,31 (22,707)	6,57 (2,134)	-3,73 [-9,359; 1,903]	0,1935
Woche 84	87	13,41 (19,987)	1,84 (1,808)	66	21,72 (24,455)	6,61 (2,027)	-4,78 [-10,162; 0,604]	0,0816
Woche 88	83	14,46 (20,291)	4,39 (1,998)	60	22,78 (24,923)	8,59 (2,288)	-4,20 [-10,219; 1,822]	0,1707
Woche 92	84	14,68 (20,273)	3,91 (1,901)	59	20,90 (22,230)	8,91 (2,195)	-5,01 [-10,752; 0,740]	0,0874
Woche 96	79	15,61 (20,559)	2,96 (1,867)	54	22,22 (24,228)	6,14 (2,192)	-3,18 [-8,873; 2,519]	0,2729
Woche 100	85	14,12 (20,169)	2,87 (1,771)	57	22,22 (24,667)	6,75 (2,090)	-3,88 [-9,306; 1,548]	0,1605
Woche 104	73	15,98 (20,868)	3,90 (1,898)	54	19,75 (24,673)	5,57 (2,182)	-1,67 [-7,381; 4,044]	0,5654
Woche 108	71	17,37 (21,719)	1,90 (2,001)	51	20,26 (23,169)	4,81 (2,321)	-2,91 [-8,960; 3,139]	0,3440
Woche 112	68	17,16 (21,155)	5,82 (2,131)	46	21,74 (23,536)	5,49 (2,521)	0,32 [-6,197; 6,842]	0,9224
Woche 116	62	16,13 (21,545)	4,96 (2,119)	50	22,67 (23,752)	7,50 (2,389)	-2,54 [-8,856; 3,777]	0,4289
Woche 120	57	15,79 (21,917)	7,14 (2,516)	46	23,91 (26,909)	7,89 (2,843)	-0,75 [-8,269; 6,779]	0,8453
Woche 124	53	15,09 (21,249)	1,31 (2,190)	43	22,48 (23,817)	7,79 (2,465)	-6,48 [-13,018; 0,065]	0,0523
Woche 128	54	14,20 (21,084)	3,96 (2,064)	39	21,37 (23,554)	5,59 (2,398)	-1,63 [-7,909; 4,649]	0,6090
Woche 132	49	15,65 (21,626)	0,41 (2,046)	38	22,81 (24,636)	7,38 (2,348)	-6,96 [-13,138; -0,790]	0,0273*
Woche 136	48	17,36 (22,795)	1,71 (2,107)	33	21,21 (23,301)	6,30 (2,507)	-4,60 [-11,075; 1,880]	0,1630
Woche 140	45	14,81 (21,968)	3,18 (2,380)	33	21,21 (18,292)	7,27 (2,773)	-4,09 [-11,348; 3,166]	0,2672

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.12 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	15,74 (21,802)	1,22 (2,508)	29	17,24 (16,952)	4,41 (2,831)	-3,19 [-10,684; 4,305]	0,4013
Woche 148	40	16,67 (22,646)	-0,16 (2,262)	26	21,79 (22,983)	7,32 (2,750)	-7,48 [-14,540; -0,422]	0,0380*
Woche 152	38	14,91 (22,855)	0,96 (2,639)	27	24,69 (23,738)	7,45 (3,143)	-6,49 [-14,666; 1,693]	0,1190
Woche 156	34	16,67 (23,570)	2,15 (2,548)	27	20,99 (18,829)	5,27 (2,914)	-3,12 [-10,807; 4,566]	0,4232
Woche 160	31	17,20 (24,146)	2,41 (2,916)	25	26,67 (23,570)	5,51 (3,372)	-3,10 [-11,954; 5,747]	0,4888
Woche 164	31	17,20 (24,146)	-1,39 (2,786)	21	25,40 (23,345)	6,48 (3,372)	-7,87 [-16,558; 0,821]	0,0755
Woche 168	27	13,58 (23,130)	0,27 (3,317)	24	26,39 (24,035)	5,99 (3,699)	-5,72 [-15,688; 4,255]	0,2581
Woche 172	30	15,56 (24,343)	-1,73 (2,983)	20	25,00 (18,337)	5,62 (3,636)	-7,35 [-16,741; 2,049]	0,1239
Woche 176	22	12,12 (16,412)	-0,72 (3,815)	18	24,07 (15,363)	5,10 (4,323)	-5,82 [-17,576; 5,928]	0,3269
Woche 180	20	15,00 (25,305)	-6,46 (3,637)	16	25,00 (14,907)	5,34 (4,186)	-11,80 [-22,953; -0,642]	0,0385*
Woche 184	18	16,67 (26,197)	0,96 (5,056)	17	23,53 (15,656)	6,11 (5,458)	-5,15 [-20,088; 9,791]	0,4932
Woche 188	16	16,67 (27,217)	2,03 (4,583)	15	22,22 (16,265)	-1,12 (4,897)	3,15 [-10,342; 16,651]	0,6410
Durchschnitt über alle Visiten	215	14,88 (20,012)	2,87 (1,216)	205	18,21 (22,724)	5,81 (1,333)	-2,94 [-6,500; 0,614]	0,1046
Hedges' g SMD							-0,16 [-0,351; 0,032]	0,1034

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.13 ADRIATIC: Summary of analysis of change from baseline over time in Finanzielle Schwierigkeiten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	16,01 (24,640)	-4,08 (1,687)	192	16,84 (23,631)	-0,56 (1,734)	-3,53 [-8,285; 1,228]	0,1455
Woche 8	193	16,41 (24,795)	-3,60 (1,731)	179	16,95 (23,535)	-0,18 (1,785)	-3,42 [-8,306; 1,473]	0,1703
Woche 12	176	15,53 (24,403)	-1,36 (1,774)	169	16,77 (22,749)	-0,83 (1,817)	-0,53 [-5,521; 4,461]	0,8347
Woche 16	168	17,06 (25,532)	-2,13 (1,781)	166	17,87 (23,682)	-1,30 (1,813)	-0,83 [-5,823; 4,171]	0,7453
Woche 20	160	17,29 (25,071)	-2,31 (1,663)	155	18,71 (24,643)	-1,96 (1,700)	-0,35 [-5,027; 4,323]	0,8823
Woche 24	147	17,69 (25,969)	-1,86 (1,635)	149	18,34 (24,640)	-1,07 (1,656)	-0,79 [-5,369; 3,780]	0,7329
Woche 28	145	16,78 (24,884)	-1,10 (1,624)	133	18,55 (25,430)	-0,25 (1,678)	-0,85 [-5,443; 3,739]	0,7154
Woche 32	141	17,97 (25,979)	-1,05 (1,661)	128	18,75 (25,011)	-1,18 (1,726)	0,14 [-4,571; 4,845]	0,9544
Woche 36	132	17,68 (25,201)	-1,35 (1,709)	123	17,62 (24,265)	-0,26 (1,766)	-1,08 [-5,917; 3,749]	0,6594
Woche 40	119	16,81 (24,882)	-1,44 (1,779)	105	16,51 (24,514)	-1,32 (1,864)	-0,12 [-5,188; 4,944]	0,9623
Woche 44	117	16,52 (24,613)	-2,51 (1,675)	106	16,04 (24,007)	-0,07 (1,748)	-2,44 [-7,198; 2,325]	0,3149
Woche 48	109	18,04 (26,267)	0,63 (1,818)	105	15,87 (24,062)	-1,14 (1,874)	1,77 [-3,366; 6,906]	0,4983
Woche 52	112	16,37 (24,093)	-1,99 (1,580)	101	16,83 (24,324)	-1,83 (1,654)	-0,17 [-4,667; 4,330]	0,9413
Woche 56	106	16,98 (25,300)	-0,85 (1,526)	90	15,93 (25,098)	-1,25 (1,623)	0,40 [-3,980; 4,784]	0,8569
Woche 60	103	16,18 (24,192)	-1,06 (1,743)	85	16,08 (23,351)	-0,23 (1,871)	-0,82 [-5,854; 4,204]	0,7472
Woche 64	101	19,14 (26,811)	-2,82 (1,616)	82	15,04 (22,316)	0,41 (1,742)	-3,24 [-7,916; 1,441]	0,1743
Woche 68	91	18,32 (24,976)	-5,51 (1,652)	80	15,00 (24,247)	-1,05 (1,752)	-4,46 [-9,205; 0,279]	0,0650

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.13 ADRIATIC: Summary of analysis of change from baseline over time in Finanzielle Schwierigkeiten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	18,89 (25,504)	-2,04 (1,677)	77	15,58 (23,311)	-1,56 (1,791)	-0,48 [-5,309; 4,350]	0,8452
Woche 76	90	18,89 (26,465)	-2,24 (1,629)	68	17,65 (24,751)	-0,83 (1,802)	-1,41 [-6,189; 3,368]	0,5620
Woche 80	87	19,92 (26,148)	-3,37 (1,771)	64	15,63 (24,465)	0,03 (1,979)	-3,40 [-8,625; 1,830]	0,2019
Woche 84	87	16,48 (23,224)	-3,80 (1,669)	66	16,16 (24,279)	-3,22 (1,861)	-0,58 [-5,499; 4,337]	0,8164
Woche 88	83	17,67 (24,047)	-2,73 (1,765)	60	16,67 (24,929)	-0,58 (1,998)	-2,15 [-7,397; 3,094]	0,4203
Woche 92	84	18,65 (24,463)	-3,80 (1,667)	59	15,82 (25,033)	-4,71 (1,908)	0,91 [-4,075; 5,901]	0,7188
Woche 96	79	18,57 (24,891)	-1,45 (1,773)	54	14,81 (23,046)	-3,42 (2,056)	1,97 [-3,376; 7,319]	0,4685
Woche 100	85	19,22 (27,399)	-4,85 (1,567)	57	18,71 (26,739)	-1,32 (1,828)	-3,53 [-8,262; 1,209]	0,1438
Woche 104	73	16,89 (24,295)	-3,42 (1,819)	54	15,43 (24,837)	1,13 (2,080)	-4,56 [-9,999; 0,886]	0,1004
Woche 108	71	16,90 (24,478)	-1,56 (1,843)	51	15,69 (23,431)	-2,63 (2,123)	1,07 [-4,464; 6,609]	0,7032
Woche 112	68	19,61 (27,761)	-3,90 (1,730)	46	16,67 (25,092)	-5,19 (2,020)	1,28 [-3,960; 6,525]	0,6302
Woche 116	62	15,59 (22,355)	-2,54 (1,836)	50	13,33 (20,203)	-4,09 (2,063)	1,55 [-3,889; 6,988]	0,5748
Woche 120	57	16,96 (23,673)	-3,63 (1,921)	46	16,67 (25,092)	-2,53 (2,153)	-1,10 [-6,786; 4,590]	0,7040
Woche 124	53	15,09 (21,249)	-1,39 (2,023)	43	13,18 (23,162)	-0,32 (2,270)	-1,07 [-7,063; 4,933]	0,7262
Woche 128	54	16,05 (23,113)	-3,51 (1,898)	39	13,68 (23,839)	-4,54 (2,197)	1,04 [-4,689; 6,763]	0,7212
Woche 132	49	19,05 (24,533)	-1,44 (1,994)	38	13,16 (23,936)	-3,19 (2,275)	1,75 [-4,240; 7,734]	0,5652
Woche 136	48	19,44 (24,633)	-3,97 (2,068)	33	12,12 (23,301)	-1,28 (2,440)	-2,69 [-9,033; 3,655]	0,4034

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.13 ADRIATIC: Summary of analysis of change from baseline over time in Finanzielle Schwierigkeiten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	22,22 (26,591)	-3,76 (1,953)	33	9,09 (17,225)	-5,25 (2,269)	1,49 [-4,480; 7,465]	0,6222
Woche 144	36	23,15 (28,530)	-0,80 (2,260)	29	14,94 (22,863)	-6,87 (2,531)	6,06 [-0,683; 12,808]	0,0776
Woche 148	40	20,00 (25,930)	-2,58 (2,109)	26	16,67 (27,080)	-5,27 (2,519)	2,70 [-3,809; 9,206]	0,4132
Woche 152	38	18,42 (22,855)	-5,64 (2,072)	27	17,28 (26,747)	-3,75 (2,424)	-1,89 [-8,204; 4,424]	0,5545
Woche 156	34	18,63 (26,197)	0,01 (2,533)	27	12,35 (18,829)	-1,62 (2,887)	1,63 [-5,987; 9,253]	0,6721
Woche 160	31	19,35 (26,908)	-1,84 (2,341)	25	16,00 (25,676)	-1,90 (2,638)	0,06 [-6,934; 7,045]	0,9874
Woche 164	31	20,43 (26,774)	-5,00 (2,243)	21	15,87 (27,119)	-4,36 (2,640)	-0,64 [-7,512; 6,227]	0,8533
Woche 168	27	19,75 (26,569)	-0,55 (3,024)	24	15,28 (25,968)	-1,34 (3,309)	0,79 [-8,132; 9,705]	0,8613
Woche 172	30	20,00 (27,123)	-5,86 (2,476)	20	11,67 (19,571)	-3,00 (2,943)	-2,85 [-10,519; 4,812]	0,4618
Woche 176	22	12,12 (16,412)	-8,49 (2,040)	18	5,56 (12,783)	-6,04 (2,430)	-2,45 [-8,526; 3,620]	0,4243
Woche 180	20	10,00 (15,672)	-8,31 (2,368)	16	6,25 (13,437)	-4,79 (2,772)	-3,52 [-10,402; 3,362]	0,3112
Woche 184	18	7,41 (14,260)	-6,78 (2,815)	17	5,88 (13,098)	-6,47 (3,066)	-0,32 [-7,964; 7,333]	0,9343
Woche 188	16	12,50 (16,667)	-3,57 (3,908)	15	8,89 (15,258)	-3,88 (4,277)	0,30 [-10,987; 11,595]	0,9573
Durchschnitt über alle Visiten	215	16,28 (25,139)	-2,92 (1,139)	205	17,24 (23,476)	-2,27 (1,240)	-0,65 [-3,951; 2,660]	0,7013
Hedges' g SMD							-0,04 [-0,229; 0,154]	0,7014

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraam 04NOV2024:19:16

Table 3.8.1.14 ADRIATIC: Summary of analysis of change from baseline over time in Schlaflosigkeit (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	16,18 (24,195)	-1,80 (1,514)	192	17,53 (24,817)	0,53 (1,560)	-2,34 [-6,607; 1,936]	0,2832
Woche 8	193	15,37 (24,051)	4,16 (1,795)	179	17,32 (24,311)	2,92 (1,857)	1,23 [-3,846; 6,309]	0,6336
Woche 12	176	14,20 (24,042)	1,53 (1,769)	169	17,16 (23,879)	1,38 (1,812)	0,15 [-4,834; 5,128]	0,9538
Woche 16	168	15,28 (24,431)	1,73 (1,717)	166	17,67 (24,802)	2,92 (1,746)	-1,20 [-6,012; 3,618]	0,6253
Woche 20	160	13,96 (22,577)	4,68 (1,708)	155	18,28 (25,253)	0,26 (1,746)	4,42 [-0,391; 9,224]	0,0717
Woche 24	147	15,19 (23,157)	5,71 (1,892)	149	18,12 (25,552)	1,63 (1,911)	4,08 [-1,211; 9,370]	0,1302
Woche 28	145	14,71 (22,864)	4,71 (1,748)	133	18,05 (24,792)	-0,71 (1,815)	5,41 [0,456; 10,373]	0,0324*
Woche 32	141	14,42 (23,335)	3,22 (1,816)	128	19,53 (25,281)	3,75 (1,900)	-0,53 [-5,705; 4,645]	0,8405
Woche 36	132	15,15 (23,790)	5,74 (1,901)	123	18,43 (25,680)	2,64 (1,973)	3,10 [-2,292; 8,494]	0,2587
Woche 40	119	12,61 (21,256)	2,10 (1,787)	105	18,41 (26,141)	3,15 (1,883)	-1,05 [-6,170; 4,072]	0,6871
Woche 44	117	13,68 (22,808)	3,64 (1,748)	106	17,61 (26,108)	1,87 (1,831)	1,78 [-3,211; 6,763]	0,4838
Woche 48	109	13,76 (22,776)	5,45 (1,957)	105	18,41 (26,141)	2,82 (2,019)	2,63 [-2,911; 8,175]	0,3509
Woche 52	112	13,10 (21,156)	2,36 (1,712)	101	18,48 (26,024)	1,19 (1,799)	1,17 [-3,725; 6,070]	0,6378
Woche 56	106	13,84 (22,475)	5,85 (1,904)	90	18,89 (26,465)	1,91 (2,042)	3,94 [-1,566; 9,446]	0,1600
Woche 60	103	14,24 (22,190)	3,69 (1,818)	85	20,39 (27,262)	2,68 (1,977)	1,01 [-4,290; 6,305]	0,7084
Woche 64	101	14,19 (23,260)	2,81 (1,681)	82	19,51 (26,683)	1,12 (1,836)	1,69 [-3,218; 6,599]	0,4983
Woche 68	91	15,38 (23,990)	4,72 (1,715)	80	18,33 (26,992)	1,98 (1,829)	2,74 [-2,197; 7,682]	0,2753

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.1.14 ADRIATIC: Summary of analysis of change from baseline over time in Schlaflosigkeit (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	13,70 (22,841)	4,03 (1,766)	77	19,48 (27,758)	-0,15 (1,903)	4,18 [-0,945; 9,305]	0,1094
Woche 76	90	15,19 (23,523)	3,28 (1,918)	68	20,10 (27,704)	6,63 (2,161)	-3,35 [-9,046; 2,347]	0,2480
Woche 80	87	14,94 (23,712)	3,35 (1,909)	64	21,88 (27,995)	3,68 (2,186)	-0,33 [-6,053; 5,398]	0,9104
Woche 84	87	12,26 (21,030)	4,69 (2,053)	66	22,22 (27,632)	2,08 (2,333)	2,61 [-3,551; 8,767]	0,4052
Woche 88	83	12,45 (21,281)	1,74 (1,897)	60	20,56 (28,185)	2,45 (2,184)	-0,70 [-6,431; 5,023]	0,8089
Woche 92	84	12,70 (21,274)	3,55 (1,891)	59	18,64 (27,173)	2,96 (2,196)	0,59 [-5,135; 6,321]	0,8386
Woche 96	79	13,50 (21,694)	3,37 (2,024)	54	19,14 (26,384)	-1,10 (2,388)	4,47 [-1,717; 10,666]	0,1557
Woche 100	85	12,94 (22,475)	3,12 (2,097)	57	19,30 (27,420)	5,85 (2,491)	-2,73 [-9,168; 3,714]	0,4048
Woche 104	73	11,42 (20,949)	1,77 (1,977)	54	16,05 (24,003)	0,05 (2,267)	1,72 [-4,229; 7,663]	0,5696
Woche 108	71	11,27 (20,271)	1,56 (1,896)	51	16,99 (25,274)	1,02 (2,192)	0,54 [-5,196; 6,274]	0,8531
Woche 112	68	14,22 (23,965)	2,50 (2,057)	46	17,39 (26,048)	3,75 (2,436)	-1,25 [-7,555; 5,049]	0,6953
Woche 116	62	11,83 (20,992)	3,51 (2,103)	50	16,67 (25,422)	1,52 (2,348)	1,98 [-4,248; 8,215]	0,5308
Woche 120	57	9,94 (19,885)	6,33 (2,292)	46	17,39 (25,082)	6,32 (2,541)	0,01 [-6,774; 6,792]	0,9979
Woche 124	53	8,81 (19,775)	5,31 (2,425)	43	13,95 (23,268)	4,11 (2,666)	1,20 [-5,900; 8,308]	0,7382
Woche 128	54	8,02 (19,356)	5,73 (2,589)	39	15,38 (23,996)	7,54 (2,940)	-1,81 [-9,557; 5,934]	0,6448
Woche 132	49	7,48 (19,562)	1,43 (2,377)	38	16,67 (25,410)	6,87 (2,645)	-5,44 [-12,494; 1,615]	0,1298
Woche 136	48	9,03 (20,328)	7,82 (2,465)	33	15,15 (23,704)	1,64 (2,875)	6,18 [-1,310; 13,671]	0,1051

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.14 ADRIATIC: Summary of analysis of change from baseline over time in Schlaflosigkeit (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 140	45	9,63 (18,288)	0,54 (2,033)	33	20,20 (26,272)	-0,10 (2,346)	0,64 [-5,561; 6,843]	0,8384
Woche 144	36	12,04 (22,752)	4,14 (2,609)	29	14,94 (21,056)	1,40 (2,928)	2,74 [-5,046; 10,516]	0,4873
Woche 148	40	12,50 (23,495)	2,19 (2,347)	26	14,10 (19,260)	2,16 (2,835)	0,03 [-7,259; 7,327]	0,9926
Woche 152	38	13,16 (23,936)	2,48 (2,339)	27	14,81 (21,350)	-0,90 (2,747)	3,38 [-3,767; 10,534]	0,3505
Woche 156	34	14,71 (24,878)	3,46 (2,748)	27	12,35 (18,829)	0,03 (3,127)	3,43 [-4,822; 11,679]	0,4119
Woche 160	31	15,05 (25,587)	4,34 (2,710)	25	13,33 (19,245)	-1,54 (3,055)	5,89 [-2,215; 13,986]	0,1526
Woche 164	31	13,98 (25,494)	0,51 (2,779)	21	12,70 (19,653)	2,53 (3,309)	-2,02 [-10,593; 6,556]	0,6412
Woche 168	27	9,88 (20,286)	2,14 (2,803)	24	15,28 (21,934)	-0,76 (3,000)	2,89 [-5,277; 11,067]	0,4828
Woche 172	30	8,89 (17,361)	0,63 (2,891)	20	13,33 (19,941)	0,10 (3,374)	0,53 [-8,233; 9,299]	0,9041
Woche 176	22	7,58 (14,298)	6,13 (3,874)	18	12,96 (20,256)	-2,03 (4,153)	8,15 [-3,040; 19,348]	0,1505
Woche 180	20	8,33 (14,809)	4,86 (4,150)	16	12,50 (20,638)	-2,25 (4,519)	7,11 [-5,004; 19,226]	0,2445
Woche 184	18	9,26 (15,363)	-0,03 (3,348)	17	11,76 (20,211)	-2,60 (3,477)	2,57 [-6,939; 12,081]	0,5903
Woche 188	16	6,25 (13,437)	7,67 (3,906)	15	6,67 (13,801)	2,77 (4,064)	4,90 [-5,533; 15,328]	0,3497
Durchschnitt über alle Visiten	215	16,12 (24,082)	3,46 (1,130)	205	17,56 (24,820)	1,83 (1,239)	1,62 [-1,674; 4,924]	0,3336
Hedges' g SMD							0,09 [-0,097; 0,286]	0,3330

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraan 04NOV2024:19:16

Table 3.8.1.15 ADRIATIC: Summary of analysis of change from baseline over time in Verstopfung (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 4	204	11,44 (21,183)	-1,69 (1,282)	192	11,28 (21,707)	-0,72 (1,320)	-0,97 [-4,582; 2,651]	0,6001
Woche 8	193	10,71 (20,139)	0,26 (1,511)	179	11,17 (21,765)	0,85 (1,563)	-0,59 [-4,863; 3,684]	0,7864
Woche 12	176	10,04 (19,361)	2,40 (1,533)	169	11,44 (22,434)	0,53 (1,571)	1,87 [-2,447; 6,184]	0,3952
Woche 16	168	10,12 (19,900)	3,81 (1,622)	166	11,04 (22,138)	2,41 (1,648)	1,39 [-3,151; 5,941]	0,5467
Woche 20	160	10,21 (20,131)	1,58 (1,559)	155	10,97 (21,525)	2,32 (1,590)	-0,74 [-5,123; 3,635]	0,7386
Woche 24	147	11,11 (20,397)	3,04 (1,623)	149	11,63 (22,900)	1,34 (1,636)	1,70 [-2,831; 6,230]	0,4611
Woche 28	145	10,34 (20,229)	1,99 (1,589)	133	12,53 (23,784)	0,88 (1,646)	1,11 [-3,393; 5,607]	0,6287
Woche 32	141	9,93 (20,215)	0,83 (1,549)	128	12,50 (23,663)	3,05 (1,616)	-2,22 [-6,623; 2,185]	0,3225
Woche 36	132	9,09 (18,461)	2,53 (1,633)	123	12,47 (23,915)	0,55 (1,693)	1,99 [-2,643; 6,620]	0,3990
Woche 40	119	8,96 (18,765)	2,64 (1,628)	105	12,06 (22,228)	1,56 (1,716)	1,09 [-3,574; 5,744]	0,6471
Woche 44	117	8,83 (17,721)	3,31 (1,679)	106	12,26 (22,690)	-0,02 (1,760)	3,34 [-1,456; 8,130]	0,1717
Woche 48	109	11,31 (19,887)	4,89 (1,577)	105	11,75 (22,160)	2,05 (1,627)	2,84 [-1,623; 7,294]	0,2117
Woche 52	112	10,12 (18,898)	4,64 (1,760)	101	10,89 (21,139)	-0,73 (1,848)	5,37 [0,349; 10,398]	0,0362*
Woche 56	106	10,06 (18,499)	4,11 (1,633)	90	11,48 (21,873)	0,45 (1,748)	3,66 [-1,046; 8,372]	0,1269
Woche 60	103	9,71 (17,854)	1,71 (1,422)	85	11,76 (22,246)	-1,59 (1,538)	3,30 [-0,829; 7,423]	0,1168
Woche 64	101	10,89 (18,920)	3,65 (1,738)	82	12,20 (22,536)	0,66 (1,893)	2,99 [-2,069; 8,051]	0,2454
Woche 68	91	10,62 (18,512)	1,86 (1,854)	80	12,50 (22,108)	0,98 (1,977)	0,88 [-4,459; 6,219]	0,7457

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.1.15 ADRIATIC: Summary of analysis of change from baseline over time in Verstopfung (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 72	90	10,00 (18,326)	1,27 (1,895)	77	10,82 (21,926)	3,95 (2,036)	-2,68 [-8,159; 2,802]	0,3366
Woche 76	90	10,37 (18,458)	1,43 (1,678)	68	13,24 (23,843)	2,41 (1,887)	-0,98 [-5,951; 4,000]	0,6997
Woche 80	87	10,73 (18,673)	3,39 (1,730)	64	14,06 (24,347)	2,36 (1,975)	1,03 [-4,146; 6,201]	0,6959
Woche 84	87	9,20 (17,380)	2,58 (1,587)	66	13,64 (24,092)	0,39 (1,798)	2,19 [-2,545; 6,920]	0,3634
Woche 88	83	9,64 (17,677)	1,73 (1,578)	60	12,22 (22,936)	-1,14 (1,816)	2,87 [-1,873; 7,619]	0,2341
Woche 92	84	9,52 (17,601)	1,54 (1,545)	59	10,17 (22,535)	0,62 (1,798)	0,92 [-3,756; 5,589]	0,6995
Woche 96	79	10,13 (17,986)	1,03 (1,695)	54	9,26 (20,899)	1,47 (2,004)	-0,44 [-5,614; 4,733]	0,8669
Woche 100	85	9,02 (16,578)	3,96 (1,694)	57	9,94 (21,790)	2,70 (2,014)	1,26 [-3,924; 6,445]	0,6324
Woche 104	73	9,13 (17,795)	3,21 (1,763)	54	6,79 (15,019)	1,25 (2,048)	1,95 [-3,358; 7,267]	0,4691
Woche 108	71	8,45 (16,636)	-0,08 (1,710)	51	7,19 (16,751)	1,55 (1,997)	-1,62 [-6,792; 3,543]	0,5359
Woche 112	68	10,78 (18,609)	3,78 (1,874)	46	10,14 (19,713)	3,50 (2,220)	0,28 [-5,446; 6,016]	0,9220
Woche 116	62	8,60 (17,003)	1,12 (1,625)	50	8,00 (17,248)	0,45 (1,825)	0,67 [-4,138; 5,481]	0,7832
Woche 120	57	8,19 (16,998)	3,19 (1,857)	46	10,14 (19,713)	1,70 (2,076)	1,49 [-4,005; 6,986]	0,5931
Woche 124	53	9,43 (18,921)	4,67 (1,766)	43	9,30 (19,687)	-1,26 (1,977)	5,93 [0,695; 11,159]	0,0267*
Woche 128	54	6,17 (15,959)	1,22 (1,830)	39	8,55 (18,286)	0,34 (2,110)	0,88 [-4,612; 6,374]	0,7518
Woche 132	49	7,48 (17,031)	0,72 (2,087)	38	11,40 (20,905)	1,62 (2,375)	-0,90 [-7,157; 5,354]	0,7761
Woche 136	48	6,25 (14,838)	3,28 (1,933)	33	9,09 (17,225)	-0,07 (2,271)	3,35 [-2,536; 9,228]	0,2623
Woche 140	45	8,15 (16,136)	2,45 (2,297)	33	10,10 (19,516)	1,24 (2,669)	1,21 [-5,760; 8,184]	0,7311

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/mmrmpra.sas gmmrmpraao 04NOV2024:19:16

Table 3.8.1.15 ADRIATIC: Summary of analysis of change from baseline over time in Verstopfung (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	12,04 (19,765)	8,10 (2,920)	29	8,05 (19,221)	2,38 (3,306)	5,72 [-3,042; 14,481]	0,1983
Woche 148	40	10,83 (19,078)	2,46 (2,140)	26	10,26 (20,590)	-0,20 (2,598)	2,66 [-4,015; 9,334]	0,4313
Woche 152	38	11,40 (19,415)	5,19 (2,312)	27	11,11 (20,672)	-1,00 (2,725)	6,19 [-0,895; 13,277]	0,0861
Woche 156	34	11,76 (19,903)	-1,10 (2,318)	27	6,17 (16,111)	-0,98 (2,648)	-0,11 [-7,115; 6,887]	0,9743
Woche 160	31	10,75 (18,027)	2,54 (2,308)	25	8,00 (17,427)	1,86 (2,610)	0,68 [-6,247; 7,607]	0,8458
Woche 164	31	13,98 (20,681)	1,44 (2,237)	21	9,52 (18,687)	0,63 (2,647)	0,81 [-6,096; 7,724]	0,8152
Woche 168	27	12,35 (18,829)	1,75 (2,210)	24	9,72 (18,334)	-3,24 (2,401)	4,99 [-1,513; 11,495]	0,1307
Woche 172	30	11,11 (18,222)	-1,59 (2,336)	20	8,33 (18,337)	1,00 (2,794)	-2,59 [-9,838; 4,664]	0,4799
Woche 176	22	12,12 (19,370)	4,44 (2,661)	18	9,26 (19,150)	0,05 (2,979)	4,39 [-3,585; 12,361]	0,2763
Woche 180	20	11,67 (19,571)	6,09 (3,507)	16	10,42 (20,069)	-0,45 (3,959)	6,55 [-4,014; 17,105]	0,2203
Woche 184	18	9,26 (15,363)	2,42 (2,503)	17	9,80 (19,596)	-0,47 (2,672)	2,89 [-4,440; 10,212]	0,4337
Woche 188	16	10,42 (20,069)	3,49 (2,623)	15	11,11 (20,574)	0,59 (2,749)	2,90 [-4,783; 10,589]	0,4497
Durchschnitt über alle Visiten	215	11,01 (20,828)	2,50 (0,964)	205	11,38 (21,905)	0,80 (1,058)	1,69 [-1,122; 4,504]	0,2380
Hedges' g SMD							0,12 [-0,076; 0,307]	0,2378

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoints: Nausea and vomiting, Loss of appetite where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Anhang 4-G7.2: EORTC QLQ-C30 - deskriptive Analyse und Verlaufsgrafik

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Globaler Gesundheitsstatus	Durvalumab (N=264)	Baseline [a]	216	73,07	17,613	25,0	75,00	100,0
		Woche 4	236	67,66	19,148	0,0	66,67	100,0
		Woche 8	221	64,56	18,615	0,0	66,67	100,0
		Woche 12	202	66,21	18,813	0,0	66,67	100,0
		Woche 16	189	67,72	18,524	16,7	66,67	100,0
		Woche 20	179	68,25	18,141	25,0	66,67	100,0
		Woche 24	169	69,13	17,785	16,7	66,67	100,0
		Woche 28	163	68,51	17,859	16,7	66,67	100,0
		Woche 32	159	68,61	18,233	25,0	66,67	100,0
		Woche 36	149	69,13	17,849	25,0	66,67	100,0
		Woche 40	135	70,31	18,981	16,7	66,67	100,0
		Woche 44	131	70,04	18,192	25,0	66,67	100,0
		Woche 48	123	68,29	19,751	0,0	66,67	100,0
		Woche 52	124	68,88	18,683	16,7	66,67	100,0
		Woche 56	121	69,35	18,105	33,3	66,67	100,0
		Woche 60	118	69,99	18,462	25,0	66,67	100,0
		Woche 64	113	70,80	18,638	0,0	75,00	100,0
		Woche 68	103	69,74	17,542	16,7	66,67	100,0
		Woche 72	100	69,58	17,180	16,7	66,67	100,0
		Woche 76	98	71,34	17,832	25,0	75,00	100,0
		Woche 80	97	70,70	18,638	25,0	66,67	100,0
		Woche 84	97	71,31	18,280	25,0	75,00	100,0
		Woche 88	91	69,51	19,650	16,7	66,67	100,0
		Woche 92	92	69,20	19,208	25,0	66,67	100,0
		Woche 96	87	69,73	18,289	33,3	66,67	100,0
		Woche 100	94	69,59	17,140	33,3	66,67	100,0
		Woche 104	80	68,13	18,694	25,0	66,67	100,0
		Woche 108	77	68,18	18,274	25,0	66,67	100,0
		Woche 112	73	67,69	19,639	33,3	66,67	100,0
		Woche 116	68	67,28	18,001	33,3	66,67	100,0
		Woche 120	63	67,72	19,428	33,3	66,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Globaler Gesundheitsstatus	Durvalumab (N=264)	Woche 124	58	70,11	18,406	33,3	66,67	100,0
		Woche 128	59	69,07	17,096	33,3	66,67	100,0
		Woche 132	53	70,13	16,297	33,3	66,67	100,0
		Woche 136	52	69,87	17,632	33,3	66,67	100,0
		Woche 140	48	71,01	18,110	16,7	66,67	100,0
		Woche 144	39	69,66	18,973	16,7	66,67	100,0
		Woche 148	43	69,77	20,815	25,0	75,00	100,0
		Woche 152	41	69,72	20,048	25,0	66,67	100,0
		Woche 156	37	70,27	21,385	33,3	75,00	100,0
		Woche 160	33	67,17	20,512	16,7	66,67	100,0
		Woche 164	33	67,17	20,931	33,3	66,67	100,0
		Woche 168	29	69,25	18,648	33,3	66,67	100,0
		Woche 172	32	69,79	16,224	33,3	66,67	100,0
		Woche 176	23	68,84	17,627	33,3	66,67	100,0
		Woche 180	21	68,65	22,190	16,7	75,00	100,0
		Woche 184	19	64,04	18,013	16,7	66,67	91,7
		Woche 188	17	58,82	23,657	0,0	66,67	83,3
		Woche 192	17	64,22	22,777	0,0	66,67	91,7
		Woche 196	14	64,88	17,956	33,3	66,67	91,7
		Woche 200	11	65,15	11,677	50,0	66,67	83,3
		Woche 204	7	66,67	19,245	33,3	66,67	83,3
		Woche 208	8	67,71	15,064	41,7	70,83	83,3
		Woche 212	7	67,86	19,501	33,3	75,00	83,3
		Woche 216	9	70,37	15,652	33,3	75,00	83,3
		Woche 220	7	72,62	18,456	33,3	83,33	83,3
		Woche 224	6	65,28	17,010	33,3	66,67	83,3
		Woche 228	6	72,22	20,184	33,3	83,33	83,3
		Woche 232	6	63,89	15,516	33,3	66,67	75,0
		Woche 236	4	60,42	18,478	33,3	66,67	75,0
		Woche 240	3	69,44	31,549	33,3	83,33	91,7
		Woche 244	2	58,33	35,355	33,3	58,33	83,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

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Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Globaler Gesundheitsstatus	Durvalumab (N=264)	Woche 248	1	33,33	NC	33,3	33,33	33,3
		Woche 252	2	79,17	5,893	75,0	79,17	83,3
	Placebo (N=266)	Baseline [a]	212	69,93	18,092	0,0	66,67	100,0
		Woche 4	230	66,16	18,797	0,0	66,67	100,0
		Woche 8	209	64,91	20,337	0,0	66,67	100,0
		Woche 12	198	65,19	18,726	8,3	66,67	100,0
		Woche 16	197	66,24	17,061	0,0	66,67	100,0
		Woche 20	180	67,96	18,070	0,0	66,67	100,0
		Woche 24	172	68,51	19,093	0,0	66,67	100,0
		Woche 28	158	67,51	18,792	0,0	66,67	100,0
		Woche 32	150	68,33	19,067	0,0	66,67	100,0
		Woche 36	141	67,97	18,156	16,7	66,67	100,0
		Woche 40	122	69,67	17,930	25,0	66,67	100,0
		Woche 44	124	69,96	17,648	33,3	66,67	100,0
		Woche 48	121	69,77	17,715	16,7	66,67	100,0
		Woche 52	118	69,56	16,644	16,7	66,67	100,0
		Woche 56	104	70,59	17,686	16,7	66,67	100,0
		Woche 60	98	71,51	16,360	16,7	75,00	100,0
		Woche 64	94	69,50	16,736	33,3	66,67	100,0
		Woche 68	91	70,24	16,857	33,3	66,67	100,0
		Woche 72	86	69,67	16,954	16,7	66,67	100,0
		Woche 76	77	70,35	19,142	0,0	66,67	100,0
		Woche 80	75	69,78	18,521	16,7	66,67	100,0
		Woche 84	75	67,78	16,909	25,0	66,67	100,0
		Woche 88	70	68,81	17,183	33,3	66,67	100,0
		Woche 92	69	70,65	16,144	16,7	66,67	100,0
		Woche 96	64	69,01	15,676	41,7	66,67	100,0
		Woche 100	66	69,82	16,779	33,3	66,67	100,0
		Woche 104	62	68,82	16,866	33,3	66,67	100,0
		Woche 108	59	70,76	17,669	25,0	66,67	100,0
		Woche 112	54	70,06	15,486	41,7	66,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Globaler Gesundheitsstatus	Placebo (N=266)	Woche 116	56	69,20	16,811	41,7	66,67	100,0
		Woche 120	51	67,81	17,080	33,3	66,67	100,0
		Woche 124	50	69,33	18,323	33,3	66,67	100,0
		Woche 128	45	67,78	17,097	33,3	66,67	100,0
		Woche 132	44	69,32	16,252	33,3	66,67	100,0
		Woche 136	39	69,02	15,989	50,0	66,67	100,0
		Woche 140	39	67,74	16,466	33,3	66,67	100,0
		Woche 144	35	68,81	15,830	33,3	66,67	100,0
		Woche 148	32	68,75	17,065	41,7	66,67	100,0
		Woche 152	33	70,45	16,015	33,3	66,67	100,0
		Woche 156	32	68,23	16,725	33,3	66,67	100,0
		Woche 160	31	64,25	18,782	8,3	66,67	100,0
		Woche 164	24	66,67	16,114	33,3	66,67	100,0
		Woche 168	28	67,86	18,245	33,3	66,67	100,0
		Woche 172	23	68,84	19,498	33,3	66,67	100,0
		Woche 176	21	68,65	16,224	33,3	66,67	100,0
		Woche 180	19	69,30	18,013	33,3	66,67	100,0
		Woche 184	20	70,42	17,412	33,3	70,83	100,0
		Woche 188	18	70,37	18,573	41,7	70,83	100,0
		Woche 192	16	73,44	17,538	50,0	83,33	100,0
		Woche 196	18	71,30	17,203	41,7	75,00	100,0
		Woche 200	19	70,18	15,294	50,0	66,67	100,0
		Woche 204	13	70,51	18,514	33,3	75,00	100,0
		Woche 208	12	72,22	19,570	33,3	83,33	100,0
		Woche 212	15	76,67	13,437	50,0	83,33	100,0
		Woche 216	12	69,44	14,361	50,0	70,83	83,3
		Woche 220	9	67,59	14,699	50,0	66,67	83,3
		Woche 224	11	69,70	14,080	50,0	75,00	83,3
		Woche 228	9	72,22	14,434	50,0	83,33	83,3
		Woche 232	5	66,67	11,785	50,0	66,67	83,3
		Woche 236	5	73,33	9,129	66,7	66,67	83,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Globaler Gesundheitsstatus	Placebo (N=266)	Woche 240	5	71,67	7,454	66,7	66,67	83,3
		Woche 244	4	66,67	0,000	66,7	66,67	66,7
		Woche 248	2	83,33	23,570	66,7	83,33	100,0
		Woche 252	1	75,00	NC	75,0	75,00	75,0
		Woche 256	1	66,67	NC	66,7	66,67	66,7
Emotionale Funktion	Durvalumab (N=264)	Baseline [a]	216	85,65	17,548	8,3	91,67	100,0
		Woche 4	236	85,03	17,278	16,7	91,67	100,0
		Woche 8	221	83,56	19,233	25,0	91,67	100,0
		Woche 12	202	83,95	18,418	0,0	91,67	100,0
		Woche 16	189	84,17	17,710	25,0	91,67	100,0
		Woche 20	179	85,10	17,059	25,0	91,67	100,0
		Woche 24	169	83,23	17,933	8,3	83,33	100,0
		Woche 28	163	85,38	16,252	16,7	91,67	100,0
		Woche 32	159	84,59	18,496	8,3	91,67	100,0
		Woche 36	149	84,06	17,755	25,0	91,67	100,0
		Woche 40	135	83,70	19,473	0,0	91,67	100,0
		Woche 44	131	84,41	18,986	8,3	91,67	100,0
		Woche 48	123	83,06	20,550	0,0	91,67	100,0
		Woche 52	124	85,55	19,042	0,0	91,67	100,0
		Woche 56	121	83,26	20,596	0,0	91,67	100,0
		Woche 60	118	84,75	19,006	16,7	91,67	100,0
		Woche 64	113	84,14	19,732	8,3	91,67	100,0
		Woche 68	103	85,60	17,078	16,7	91,67	100,0
		Woche 72	100	86,67	17,205	25,0	91,67	100,0
		Woche 76	98	84,69	19,796	0,0	91,67	100,0
		Woche 80	97	84,71	18,348	8,3	91,67	100,0
		Woche 84	97	87,29	17,268	8,3	91,67	100,0
		Woche 88	91	85,26	19,957	0,0	91,67	100,0
		Woche 92	92	84,60	20,222	0,0	91,67	100,0
		Woche 96	87	85,44	19,614	0,0	91,67	100,0
		Woche 100	94	86,61	18,217	8,3	100,00	100,0

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Emotionale Funktion	Durvalumab (N=264)	Woche 104	80	86,04	21,081	0,0	91,67	100,0
		Woche 108	77	87,12	19,428	8,3	100,00	100,0
		Woche 112	73	87,10	19,545	8,3	100,00	100,0
		Woche 116	68	88,24	19,168	0,0	100,00	100,0
		Woche 120	63	85,45	23,137	8,3	100,00	100,0
		Woche 124	58	87,07	19,694	8,3	100,00	100,0
		Woche 128	59	88,70	18,683	8,3	100,00	100,0
		Woche 132	53	89,47	20,553	0,0	100,00	100,0
		Woche 136	52	91,03	16,324	8,3	100,00	100,0
		Woche 140	48	88,37	19,880	0,0	100,00	100,0
		Woche 144	39	88,68	20,186	16,7	100,00	100,0
		Woche 148	43	86,82	21,687	8,3	100,00	100,0
		Woche 152	41	90,24	18,902	25,0	100,00	100,0
		Woche 156	37	86,94	20,179	25,0	100,00	100,0
		Woche 160	33	85,61	21,376	25,0	100,00	100,0
		Woche 164	33	88,89	20,055	8,3	100,00	100,0
		Woche 168	29	91,67	12,794	66,7	100,00	100,0
		Woche 172	32	93,23	10,464	66,7	100,00	100,0
		Woche 176	23	92,39	13,510	58,3	100,00	100,0
		Woche 180	21	91,67	13,693	66,7	100,00	100,0
		Woche 184	19	89,47	18,182	33,3	100,00	100,0
		Woche 188	17	86,76	15,607	66,7	100,00	100,0
		Woche 192	17	89,71	22,732	33,3	100,00	100,0
		Woche 196	14	97,02	5,278	83,3	100,00	100,0
		Woche 200	11	97,73	5,389	83,3	100,00	100,0
		Woche 204	7	97,62	4,066	91,7	100,00	100,0
		Woche 208	8	97,92	3,858	91,7	100,00	100,0
		Woche 212	7	96,43	9,449	75,0	100,00	100,0
		Woche 216	9	99,07	2,778	91,7	100,00	100,0
		Woche 220	7	98,81	3,150	91,7	100,00	100,0
		Woche 224	6	93,06	13,351	66,7	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Emotionale Funktion	Durvalumab (N=264)	Woche 228	6	94,44	8,607	83,3	100,00	100,0
		Woche 232	6	94,44	13,608	66,7	100,00	100,0
		Woche 236	4	93,75	12,500	75,0	100,00	100,0
		Woche 240	3	100,00	0,000	100,0	100,00	100,0
		Woche 244	2	100,00	0,000	100,0	100,00	100,0
		Woche 248	1	100,00	NC	100,0	100,00	100,0
		Woche 252	2	100,00	0,000	100,0	100,00	100,0
	Placebo (N=266)	Baseline [a]	212	85,46	16,450	0,0	91,67	100,0
		Woche 4	230	83,41	20,218	0,0	91,67	100,0
		Woche 8	209	79,31	20,771	0,0	83,33	100,0
		Woche 12	198	80,93	21,478	0,0	83,33	100,0
		Woche 16	197	82,02	19,993	8,3	83,33	100,0
		Woche 20	180	83,15	18,030	16,7	83,33	100,0
		Woche 24	172	84,21	17,546	16,7	91,67	100,0
		Woche 28	158	84,65	18,587	0,0	91,67	100,0
		Woche 32	150	84,28	18,408	0,0	91,67	100,0
		Woche 36	141	85,99	17,174	16,7	91,67	100,0
		Woche 40	122	84,63	17,670	8,3	91,67	100,0
		Woche 44	124	84,41	18,281	0,0	91,67	100,0
		Woche 48	121	86,16	17,988	16,7	91,67	100,0
		Woche 52	118	83,40	18,824	33,3	91,67	100,0
		Woche 56	104	85,42	17,792	25,0	91,67	100,0
		Woche 60	98	85,97	17,199	16,7	91,67	100,0
		Woche 64	94	84,04	19,881	16,7	91,67	100,0
		Woche 68	91	84,43	17,133	41,7	91,67	100,0
		Woche 72	86	84,40	16,459	41,7	91,67	100,0
		Woche 76	77	84,63	19,406	0,0	91,67	100,0
		Woche 80	75	84,67	19,182	8,3	91,67	100,0
		Woche 84	75	83,56	21,573	16,7	91,67	100,0
		Woche 88	70	83,81	19,187	8,3	91,67	100,0
		Woche 92	69	85,51	17,189	41,7	91,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Emotionale Funktion	Placebo (N=266)	Woche 96	64	83,85	18,418	33,3	91,67	100,0
		Woche 100	66	86,99	15,820	41,7	91,67	100,0
		Woche 104	62	83,33	20,244	25,0	91,67	100,0
		Woche 108	59	81,50	22,375	8,3	91,67	100,0
		Woche 112	54	83,18	20,572	33,3	91,67	100,0
		Woche 116	56	85,12	21,421	33,3	100,00	100,0
		Woche 120	51	83,66	20,947	8,3	91,67	100,0
		Woche 124	50	84,17	20,430	33,3	100,00	100,0
		Woche 128	45	83,70	20,254	33,3	91,67	100,0
		Woche 132	44	84,09	19,754	33,3	91,67	100,0
		Woche 136	39	84,40	18,651	33,3	91,67	100,0
		Woche 140	39	85,26	17,361	41,7	91,67	100,0
		Woche 144	35	89,05	14,259	58,3	100,00	100,0
		Woche 148	32	85,68	16,698	58,3	100,00	100,0
		Woche 152	33	87,37	14,749	58,3	91,67	100,0
		Woche 156	32	86,98	16,658	41,7	91,67	100,0
		Woche 160	31	82,26	20,832	25,0	91,67	100,0
		Woche 164	24	83,33	17,549	50,0	87,50	100,0
		Woche 168	28	85,71	18,124	41,7	95,83	100,0
		Woche 172	23	85,14	18,284	33,3	91,67	100,0
		Woche 176	21	84,92	15,728	50,0	83,33	100,0
		Woche 180	19	87,28	14,532	58,3	91,67	100,0
		Woche 184	20	86,25	14,629	58,3	91,67	100,0
		Woche 188	18	85,65	15,605	58,3	91,67	100,0
		Woche 192	16	82,29	17,447	50,0	83,33	100,0
		Woche 196	18	88,43	15,162	50,0	95,83	100,0
		Woche 200	19	88,60	14,490	58,3	100,00	100,0
		Woche 204	13	83,97	18,150	50,0	91,67	100,0
		Woche 208	12	87,50	16,088	50,0	95,83	100,0
		Woche 212	15	92,78	12,144	58,3	100,00	100,0
		Woche 216	12	88,19	14,416	58,3	91,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Emotionale Funktion	Placebo (N=266)	Woche 220	9	86,11	21,246	33,3	91,67	100,0
		Woche 224	11	89,39	15,407	58,3	100,00	100,0
		Woche 228	9	87,04	13,889	66,7	83,33	100,0
		Woche 232	5	81,67	17,078	66,7	75,00	100,0
		Woche 236	5	80,00	19,185	58,3	75,00	100,0
		Woche 240	5	80,00	21,731	50,0	83,33	100,0
		Woche 244	4	79,17	27,639	41,7	87,50	100,0
		Woche 248	2	100,00	0,000	100,0	100,00	100,0
		Woche 252	1	100,00	NC	100,0	100,00	100,0
		Woche 256	1	100,00	NC	100,0	100,00	100,0
Kognitive Funktion	Durvalumab (N=264)	Baseline [a]	216	89,89	15,146	33,3	100,00	100,0
		Woche 4	236	88,84	16,424	0,0	100,00	100,0
		Woche 8	221	87,25	17,106	16,7	100,00	100,0
		Woche 12	202	88,20	16,448	16,7	100,00	100,0
		Woche 16	189	87,04	16,784	16,7	100,00	100,0
		Woche 20	179	86,69	16,702	33,3	100,00	100,0
		Woche 24	169	84,81	16,946	33,3	83,33	100,0
		Woche 28	163	86,20	18,294	0,0	83,33	100,0
		Woche 32	159	84,91	18,448	16,7	83,33	100,0
		Woche 36	149	85,68	16,328	0,0	83,33	100,0
		Woche 40	135	85,31	19,429	0,0	83,33	100,0
		Woche 44	131	85,37	18,949	0,0	83,33	100,0
		Woche 48	123	84,69	19,627	0,0	83,33	100,0
		Woche 52	124	85,62	18,690	0,0	100,00	100,0
		Woche 56	121	83,61	18,632	0,0	83,33	100,0
		Woche 60	118	82,77	19,482	16,7	83,33	100,0
		Woche 64	113	84,07	20,460	0,0	83,33	100,0
		Woche 68	103	84,14	17,984	0,0	83,33	100,0
		Woche 72	100	85,33	17,771	16,7	83,33	100,0
		Woche 76	98	85,71	19,442	0,0	100,00	100,0
		Woche 80	97	84,19	20,606	0,0	83,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Kognitive Funktion	Durvalumab (N=264)	Woche 84	97	84,71	19,935	0,0	83,33	100,0
		Woche 88	91	84,98	20,496	0,0	83,33	100,0
		Woche 92	92	84,24	20,578	0,0	83,33	100,0
		Woche 96	87	82,95	21,563	0,0	83,33	100,0
		Woche 100	94	84,04	20,437	0,0	83,33	100,0
		Woche 104	80	85,00	21,641	0,0	100,00	100,0
		Woche 108	77	83,33	20,051	0,0	83,33	100,0
		Woche 112	73	83,56	22,134	0,0	100,00	100,0
		Woche 116	68	84,80	21,498	0,0	100,00	100,0
		Woche 120	63	82,80	21,371	0,0	83,33	100,0
		Woche 124	58	83,91	20,701	0,0	83,33	100,0
		Woche 128	59	86,16	21,026	0,0	100,00	100,0
		Woche 132	53	86,16	21,116	0,0	100,00	100,0
		Woche 136	52	88,46	19,114	0,0	100,00	100,0
		Woche 140	48	84,38	23,167	0,0	100,00	100,0
		Woche 144	39	84,62	23,689	0,0	100,00	100,0
		Woche 148	43	86,05	22,102	0,0	100,00	100,0
		Woche 152	41	86,99	21,250	0,0	100,00	100,0
		Woche 156	37	84,68	22,353	0,0	100,00	100,0
		Woche 160	33	87,37	22,450	0,0	100,00	100,0
		Woche 164	33	85,86	23,244	0,0	100,00	100,0
		Woche 168	29	86,78	21,994	0,0	100,00	100,0
		Woche 172	32	85,42	22,699	0,0	100,00	100,0
		Woche 176	23	86,23	23,917	0,0	100,00	100,0
		Woche 180	21	82,54	26,075	0,0	83,33	100,0
		Woche 184	19	83,33	26,644	0,0	100,00	100,0
		Woche 188	17	79,41	28,583	0,0	100,00	100,0
		Woche 192	17	80,39	33,456	0,0	100,00	100,0
		Woche 196	14	92,86	10,770	66,7	100,00	100,0
		Woche 200	11	95,45	10,778	66,7	100,00	100,0
		Woche 204	7	100,00	0,000	100,0	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Kognitive Funktion	Durvalumab (N=264)	Woche 208	8	95,83	7,715	83,3	100,00	100,0
		Woche 212	7	97,62	6,299	83,3	100,00	100,0
		Woche 216	9	94,44	11,785	66,7	100,00	100,0
		Woche 220	7	95,24	8,133	83,3	100,00	100,0
		Woche 224	6	94,44	13,608	66,7	100,00	100,0
		Woche 228	6	94,44	13,608	66,7	100,00	100,0
		Woche 232	6	94,44	8,607	83,3	100,00	100,0
		Woche 236	4	91,67	9,623	83,3	91,67	100,0
		Woche 240	3	94,44	9,623	83,3	100,00	100,0
		Woche 244	2	83,33	23,570	66,7	83,33	100,0
		Woche 248	1	66,67	NC	66,7	66,67	66,7
		Woche 252	2	100,00	0,000	100,0	100,00	100,0
	Placebo (N=266)	Baseline [a]	212	87,26	16,635	16,7	100,00	100,0
		Woche 4	230	84,49	18,655	0,0	83,33	100,0
		Woche 8	209	84,13	17,354	16,7	83,33	100,0
		Woche 12	198	84,60	18,920	16,7	83,33	100,0
		Woche 16	197	84,77	16,216	33,3	83,33	100,0
		Woche 20	180	84,81	18,248	0,0	83,33	100,0
		Woche 24	172	83,53	19,908	16,7	83,33	100,0
		Woche 28	158	85,55	18,727	0,0	83,33	100,0
		Woche 32	150	83,44	18,870	0,0	83,33	100,0
		Woche 36	141	84,28	17,454	33,3	83,33	100,0
		Woche 40	122	83,88	18,047	16,7	83,33	100,0
		Woche 44	124	86,02	16,378	16,7	83,33	100,0
		Woche 48	121	85,26	15,985	33,3	83,33	100,0
		Woche 52	118	84,89	17,967	16,7	83,33	100,0
		Woche 56	104	84,29	15,549	33,3	83,33	100,0
		Woche 60	98	85,54	16,344	33,3	83,33	100,0
		Woche 64	94	85,64	15,953	33,3	83,33	100,0
		Woche 68	91	85,16	16,750	16,7	83,33	100,0
		Woche 72	86	85,66	14,499	50,0	83,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Kognitive Funktion	Placebo (N=266)	Woche 76	77	85,28	15,759	33,3	83,33	100,0
		Woche 80	75	83,33	17,111	33,3	83,33	100,0
		Woche 84	75	84,22	19,354	16,7	83,33	100,0
		Woche 88	70	85,24	15,682	50,0	83,33	100,0
		Woche 92	69	85,27	16,553	33,3	83,33	100,0
		Woche 96	64	83,59	16,398	33,3	83,33	100,0
		Woche 100	66	84,85	16,467	33,3	83,33	100,0
		Woche 104	62	83,06	18,230	33,3	83,33	100,0
		Woche 108	59	83,62	18,950	33,3	83,33	100,0
		Woche 112	54	83,33	20,477	33,3	83,33	100,0
		Woche 116	56	84,82	20,665	16,7	100,00	100,0
		Woche 120	51	83,99	22,598	0,0	100,00	100,0
		Woche 124	50	86,00	18,553	33,3	100,00	100,0
		Woche 128	45	81,48	21,386	16,7	83,33	100,0
		Woche 132	44	81,44	19,758	16,7	83,33	100,0
		Woche 136	39	79,91	21,690	33,3	83,33	100,0
		Woche 140	39	80,34	22,901	0,0	83,33	100,0
		Woche 144	35	83,81	21,574	33,3	100,00	100,0
		Woche 148	32	76,04	24,662	0,0	83,33	100,0
		Woche 152	33	79,80	23,108	16,7	83,33	100,0
		Woche 156	32	79,17	20,302	33,3	83,33	100,0
		Woche 160	31	79,03	21,068	33,3	83,33	100,0
		Woche 164	24	75,69	24,563	33,3	75,00	100,0
		Woche 168	28	79,17	23,406	33,3	83,33	100,0
		Woche 172	23	81,88	21,269	16,7	83,33	100,0
		Woche 176	21	75,40	23,932	16,7	83,33	100,0
		Woche 180	19	77,19	24,976	16,7	83,33	100,0
		Woche 184	20	79,17	22,213	33,3	83,33	100,0
		Woche 188	18	79,63	23,260	33,3	83,33	100,0
		Woche 192	16	78,13	23,348	33,3	75,00	100,0
		Woche 196	18	79,63	24,625	16,7	83,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Kognitive Funktion	Placebo (N=266)	Woche 200	19	78,07	24,878	16,7	83,33	100,0
		Woche 204	13	74,36	27,735	16,7	83,33	100,0
		Woche 208	12	80,56	29,158	0,0	91,67	100,0
		Woche 212	15	83,33	21,822	33,3	100,00	100,0
		Woche 216	12	81,94	20,669	50,0	83,33	100,0
		Woche 220	9	77,78	26,352	33,3	83,33	100,0
		Woche 224	11	78,79	32,567	0,0	100,00	100,0
		Woche 228	9	75,93	27,778	33,3	83,33	100,0
		Woche 232	5	70,00	29,814	33,3	66,67	100,0
		Woche 236	5	73,33	25,276	50,0	66,67	100,0
		Woche 240	5	76,67	22,361	50,0	66,67	100,0
		Woche 244	4	66,67	40,825	16,7	75,00	100,0
		Woche 248	2	100,00	0,000	100,0	100,00	100,0
		Woche 252	1	100,00	NC	100,0	100,00	100,0
		Woche 256	1	100,00	NC	100,0	100,00	100,0
Körperfunktion	Durvalumab (N=264)	Baseline [a]	216	85,77	14,684	26,7	86,67	100,0
		Woche 4	236	82,63	16,181	20,0	86,67	100,0
		Woche 8	221	81,21	16,223	26,7	86,67	100,0
		Woche 12	202	81,78	16,742	13,3	86,67	100,0
		Woche 16	189	81,76	17,536	13,3	86,67	100,0
		Woche 20	179	82,09	18,117	0,0	86,67	100,0
		Woche 24	169	82,68	16,008	6,7	86,67	100,0
		Woche 28	163	82,90	16,314	26,7	86,67	100,0
		Woche 32	159	81,13	17,385	26,7	86,67	100,0
		Woche 36	149	83,71	15,410	46,7	86,67	100,0
		Woche 40	135	83,36	16,887	26,7	86,67	100,0
		Woche 44	131	81,42	19,180	0,0	86,67	100,0
		Woche 48	123	81,95	19,775	0,0	86,67	100,0
		Woche 52	124	83,49	17,780	20,0	86,67	100,0
		Woche 56	121	81,54	18,293	6,7	86,67	100,0
		Woche 60	118	82,15	18,322	20,0	86,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Körperfunktion	Durvalumab (N=264)	Woche 64	113	82,01	20,156	0,0	86,67	100,0
		Woche 68	103	82,20	18,326	20,0	86,67	100,0
		Woche 72	100	82,13	18,901	20,0	86,67	100,0
		Woche 76	98	82,65	19,187	20,0	86,67	100,0
		Woche 80	97	82,34	20,322	20,0	86,67	100,0
		Woche 84	97	85,09	17,018	20,0	93,33	100,0
		Woche 88	91	82,20	19,653	13,3	86,67	100,0
		Woche 92	92	82,39	18,584	20,0	86,67	100,0
		Woche 96	87	81,76	20,396	6,7	86,67	100,0
		Woche 100	94	82,98	18,668	13,3	86,67	100,0
		Woche 104	80	81,08	19,572	20,0	86,67	100,0
		Woche 108	77	82,16	17,981	13,3	86,67	100,0
		Woche 112	73	81,19	19,095	0,0	86,67	100,0
		Woche 116	68	80,59	18,456	26,7	86,67	100,0
		Woche 120	63	79,89	19,473	26,7	80,00	100,0
		Woche 124	58	83,10	18,020	26,7	86,67	100,0
		Woche 128	59	84,29	16,366	33,3	86,67	100,0
		Woche 132	53	84,91	17,353	33,3	93,33	100,0
		Woche 136	52	83,85	18,357	13,3	86,67	100,0
		Woche 140	48	83,61	20,764	20,0	93,33	100,0
		Woche 144	39	83,76	21,236	13,3	86,67	100,0
		Woche 148	43	82,02	21,358	6,7	86,67	100,0
		Woche 152	41	82,93	19,947	26,7	86,67	100,0
		Woche 156	37	81,08	22,251	26,7	93,33	100,0
		Woche 160	33	80,81	22,283	13,3	86,67	100,0
		Woche 164	33	83,64	20,282	33,3	93,33	100,0
		Woche 168	29	83,68	21,424	26,7	93,33	100,0
		Woche 172	32	81,87	22,543	33,3	86,67	100,0
		Woche 176	23	76,81	24,360	26,7	86,67	100,0
		Woche 180	21	79,68	28,085	0,0	86,67	100,0
		Woche 184	19	77,19	28,916	6,7	93,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Körperfunktion	Durvalumab (N=264)	Woche 188	17	78,04	28,845	0,0	93,33	100,0
		Woche 192	17	76,86	28,975	0,0	86,67	100,0
		Woche 196	14	85,24	21,272	33,3	93,33	100,0
		Woche 200	11	88,48	19,112	40,0	100,00	100,0
		Woche 204	7	98,10	5,040	86,7	100,00	100,0
		Woche 208	8	93,33	12,344	73,3	100,00	100,0
		Woche 212	7	96,19	6,506	86,7	100,00	100,0
		Woche 216	9	94,81	8,012	80,0	100,00	100,0
		Woche 220	7	92,38	9,759	73,3	93,33	100,0
		Woche 224	6	97,78	5,443	86,7	100,00	100,0
		Woche 228	6	96,67	5,578	86,7	100,00	100,0
		Woche 232	6	98,89	2,722	93,3	100,00	100,0
		Woche 236	4	100,00	0,000	100,0	100,00	100,0
		Woche 240	3	100,00	0,000	100,0	100,00	100,0
		Woche 244	2	96,67	4,714	93,3	96,67	100,0
		Woche 248	1	100,00	NC	100,0	100,00	100,0
		Woche 252	2	86,67	9,428	80,0	86,67	93,3
	Placebo (N=266)	Baseline [a]	212	83,71	14,617	26,7	86,67	100,0
		Woche 4	230	81,36	17,002	20,0	86,67	100,0
		Woche 8	209	79,07	16,402	20,0	80,00	100,0
		Woche 12	198	81,62	15,756	20,0	86,67	100,0
		Woche 16	197	81,49	15,795	33,3	86,67	100,0
		Woche 20	180	82,33	16,846	6,7	86,67	100,0
		Woche 24	172	81,59	16,949	13,3	86,67	100,0
		Woche 28	158	82,07	17,255	0,0	86,67	100,0
		Woche 32	150	81,78	18,628	0,0	86,67	100,0
		Woche 36	141	81,42	17,885	13,3	86,67	100,0
		Woche 40	122	81,48	17,174	20,0	86,67	100,0
		Woche 44	124	81,88	16,757	20,0	86,67	100,0
		Woche 48	121	82,98	15,892	26,7	86,67	100,0
		Woche 52	118	83,73	16,481	20,0	86,67	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Körperfunktion	Placebo (N=266)	Woche 56	104	81,86	16,526	20,0	86,67	100,0
		Woche 60	98	82,99	16,445	33,3	86,67	100,0
		Woche 64	94	83,05	15,198	33,3	86,67	100,0
		Woche 68	91	83,44	15,630	33,3	86,67	100,0
		Woche 72	86	82,25	15,428	46,7	86,67	100,0
		Woche 76	77	83,38	17,593	26,7	86,67	100,0
		Woche 80	75	81,24	15,871	33,3	86,67	100,0
		Woche 84	75	81,60	16,434	26,7	86,67	100,0
		Woche 88	70	82,57	14,548	46,7	86,67	100,0
		Woche 92	69	84,73	12,940	53,3	86,67	100,0
		Woche 96	64	81,77	15,544	46,7	86,67	100,0
		Woche 100	66	84,44	13,902	40,0	86,67	100,0
		Woche 104	62	84,62	14,211	46,7	86,67	100,0
		Woche 108	59	84,63	13,744	53,3	86,67	100,0
		Woche 112	54	81,48	15,250	53,3	80,00	100,0
		Woche 116	56	83,10	16,328	13,3	86,67	100,0
		Woche 120	51	84,44	16,848	0,0	86,67	100,0
		Woche 124	50	84,27	13,982	53,3	86,67	100,0
		Woche 128	45	83,41	14,258	46,7	80,00	100,0
		Woche 132	44	82,42	14,094	46,7	80,00	100,0
		Woche 136	39	81,71	14,806	46,7	80,00	100,0
		Woche 140	39	80,34	16,890	46,7	80,00	100,0
		Woche 144	35	82,67	14,480	53,3	80,00	100,0
		Woche 148	32	82,29	14,026	53,3	83,33	100,0
		Woche 152	33	83,43	13,857	53,3	80,00	100,0
		Woche 156	32	83,54	14,466	53,3	86,67	100,0
		Woche 160	31	81,94	15,415	53,3	80,00	100,0
		Woche 164	24	81,94	15,288	53,3	83,33	100,0
		Woche 168	28	82,62	16,263	40,0	83,33	100,0
		Woche 172	23	80,58	16,070	53,3	80,00	100,0
		Woche 176	21	80,00	17,127	46,7	80,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Körperfunktion	Placebo (N=266)	Woche 180	19	80,35	14,311	53,3	80,00	100,0
		Woche 184	20	81,00	14,872	60,0	80,00	100,0
		Woche 188	18	80,00	14,096	46,7	80,00	100,0
		Woche 192	16	79,17	14,782	46,7	80,00	100,0
		Woche 196	18	81,11	15,884	46,7	80,00	100,0
		Woche 200	19	82,81	15,286	46,7	80,00	100,0
		Woche 204	13	76,41	15,059	46,7	73,33	100,0
		Woche 208	12	83,33	10,050	73,3	80,00	100,0
		Woche 212	15	83,56	12,310	66,7	80,00	100,0
		Woche 216	12	80,56	15,429	46,7	80,00	100,0
		Woche 220	9	83,70	10,062	73,3	80,00	100,0
		Woche 224	11	84,85	10,787	66,7	80,00	100,0
		Woche 228	9	84,44	11,547	66,7	80,00	100,0
		Woche 232	5	88,00	11,926	73,3	86,67	100,0
		Woche 236	5	84,00	13,824	66,7	86,67	100,0
		Woche 240	5	82,67	13,824	66,7	80,00	100,0
		Woche 244	4	86,67	14,402	66,7	90,00	100,0
		Woche 248	2	96,67	4,714	93,3	96,67	100,0
		Woche 252	1	100,00	NC	100,0	100,00	100,0
		Woche 256	1	100,00	NC	100,0	100,00	100,0
Rollenfunktion	Durvalumab (N=264)	Baseline [a]	216	87,96	20,056	0,0	100,00	100,0
		Woche 4	236	86,51	20,001	0,0	100,00	100,0
		Woche 8	221	84,31	21,504	0,0	100,00	100,0
		Woche 12	202	82,43	23,346	0,0	100,00	100,0
		Woche 16	189	83,77	22,244	0,0	100,00	100,0
		Woche 20	179	83,52	22,898	0,0	100,00	100,0
		Woche 24	169	85,90	20,250	0,0	100,00	100,0
		Woche 28	163	84,66	22,527	0,0	100,00	100,0
		Woche 32	159	83,86	23,452	0,0	100,00	100,0
		Woche 36	149	85,46	19,306	33,3	100,00	100,0
		Woche 40	135	85,93	19,622	33,3	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Rollenfunktion	Durvalumab (N=264)	Woche 44	131	86,64	21,525	0,0	100,00	100,0
		Woche 48	123	84,01	22,624	0,0	100,00	100,0
		Woche 52	124	85,22	21,695	33,3	100,00	100,0
		Woche 56	121	84,16	21,821	16,7	100,00	100,0
		Woche 60	118	85,17	21,215	33,3	100,00	100,0
		Woche 64	113	84,22	22,695	0,0	100,00	100,0
		Woche 68	103	85,76	20,131	0,0	100,00	100,0
		Woche 72	100	85,67	19,963	0,0	100,00	100,0
		Woche 76	98	85,88	21,319	0,0	100,00	100,0
		Woche 80	97	83,33	24,296	0,0	100,00	100,0
		Woche 84	97	86,43	18,215	33,3	100,00	100,0
		Woche 88	91	86,08	20,071	33,3	100,00	100,0
		Woche 92	92	84,78	19,867	33,3	100,00	100,0
		Woche 96	87	84,87	20,433	33,3	100,00	100,0
		Woche 100	94	88,12	17,217	33,3	100,00	100,0
		Woche 104	80	84,38	19,905	33,3	100,00	100,0
		Woche 108	77	83,77	20,228	16,7	100,00	100,0
		Woche 112	73	83,79	20,967	33,3	100,00	100,0
		Woche 116	68	85,29	20,266	33,3	100,00	100,0
		Woche 120	63	83,33	22,200	16,7	100,00	100,0
		Woche 124	58	86,21	20,024	16,7	100,00	100,0
		Woche 128	59	87,57	19,474	33,3	100,00	100,0
		Woche 132	53	85,53	21,192	16,7	100,00	100,0
		Woche 136	52	87,18	23,013	33,3	100,00	100,0
		Woche 140	48	87,85	21,944	0,0	100,00	100,0
		Woche 144	39	85,90	22,794	16,7	100,00	100,0
		Woche 148	43	84,50	23,116	0,0	100,00	100,0
		Woche 152	41	86,59	21,480	33,3	100,00	100,0
		Woche 156	37	82,88	24,371	33,3	100,00	100,0
		Woche 160	33	84,34	24,629	33,3	100,00	100,0
		Woche 164	33	86,87	22,344	33,3	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Rollenfunktion	Durvalumab (N=264)	Woche 168	29	88,51	20,942	33,3	100,00	100,0
		Woche 172	32	88,02	21,683	33,3	100,00	100,0
		Woche 176	23	86,96	25,602	16,7	100,00	100,0
		Woche 180	21	85,71	27,531	0,0	100,00	100,0
		Woche 184	19	82,46	32,142	0,0	100,00	100,0
		Woche 188	17	81,37	29,393	0,0	100,00	100,0
		Woche 192	17	84,31	29,149	0,0	100,00	100,0
		Woche 196	14	88,10	24,832	33,3	100,00	100,0
		Woche 200	11	90,91	17,262	50,0	100,00	100,0
		Woche 204	7	100,00	0,000	100,0	100,00	100,0
		Woche 208	8	97,92	5,893	83,3	100,00	100,0
		Woche 212	7	100,00	0,000	100,0	100,00	100,0
		Woche 216	9	100,00	0,000	100,0	100,00	100,0
		Woche 220	7	100,00	0,000	100,0	100,00	100,0
		Woche 224	6	100,00	0,000	100,0	100,00	100,0
		Woche 228	6	97,22	6,804	83,3	100,00	100,0
		Woche 232	6	100,00	0,000	100,0	100,00	100,0
		Woche 236	4	95,83	8,333	83,3	100,00	100,0
		Woche 240	3	100,00	0,000	100,0	100,00	100,0
		Woche 244	2	91,67	11,785	83,3	91,67	100,0
		Woche 248	1	100,00	NC	100,0	100,00	100,0
		Woche 252	2	83,33	23,570	66,7	83,33	100,0
	Placebo (N=266)	Baseline [a]	212	88,68	18,149	16,7	100,00	100,0
		Woche 4	230	82,61	22,560	0,0	100,00	100,0
		Woche 8	209	80,38	24,032	0,0	83,33	100,0
		Woche 12	198	83,25	21,734	0,0	100,00	100,0
		Woche 16	197	83,67	21,623	16,7	100,00	100,0
		Woche 20	180	84,81	21,088	0,0	100,00	100,0
		Woche 24	172	84,79	20,300	16,7	100,00	100,0
		Woche 28	158	82,70	23,711	0,0	100,00	100,0
		Woche 32	150	82,67	24,492	0,0	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Rollenfunktion	Placebo (N=266)	Woche 36	141	82,98	22,313	0,0	100,00	100,0
		Woche 40	122	83,61	23,373	0,0	100,00	100,0
		Woche 44	124	84,95	22,332	0,0	100,00	100,0
		Woche 48	121	85,12	19,579	33,3	100,00	100,0
		Woche 52	118	84,89	21,460	0,0	100,00	100,0
		Woche 56	104	84,94	20,840	0,0	100,00	100,0
		Woche 60	98	86,22	18,848	33,3	100,00	100,0
		Woche 64	94	85,99	19,751	33,3	100,00	100,0
		Woche 68	91	86,26	19,018	16,7	100,00	100,0
		Woche 72	86	87,02	17,601	33,3	100,00	100,0
		Woche 76	77	85,06	23,506	0,0	100,00	100,0
		Woche 80	75	85,78	19,700	33,3	100,00	100,0
		Woche 84	75	84,00	22,667	0,0	100,00	100,0
		Woche 88	70	85,71	19,095	16,7	100,00	100,0
		Woche 92	69	86,23	17,840	33,3	100,00	100,0
		Woche 96	64	84,38	19,893	33,3	100,00	100,0
		Woche 100	66	86,62	17,836	33,3	100,00	100,0
		Woche 104	62	86,29	17,211	33,3	100,00	100,0
		Woche 108	59	84,46	19,784	16,7	100,00	100,0
		Woche 112	54	85,49	19,167	33,3	100,00	100,0
		Woche 116	56	84,52	21,756	0,0	100,00	100,0
		Woche 120	51	85,29	21,252	0,0	100,00	100,0
		Woche 124	50	85,33	18,332	33,3	100,00	100,0
		Woche 128	45	84,81	19,405	33,3	100,00	100,0
		Woche 132	44	84,09	21,251	16,7	100,00	100,0
		Woche 136	39	85,04	19,792	33,3	100,00	100,0
		Woche 140	39	87,18	17,296	33,3	100,00	100,0
		Woche 144	35	86,67	18,436	33,3	100,00	100,0
		Woche 148	32	87,50	17,454	33,3	100,00	100,0
		Woche 152	33	84,34	20,387	33,3	100,00	100,0
		Woche 156	32	83,85	20,515	33,3	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Rollenfunktion	Placebo (N=266)	Woche 160	31	83,33	18,758	50,0	100,00	100,0
		Woche 164	24	82,64	20,548	33,3	100,00	100,0
		Woche 168	28	86,31	18,732	33,3	100,00	100,0
		Woche 172	23	82,61	19,121	33,3	83,33	100,0
		Woche 176	21	81,75	19,653	33,3	83,33	100,0
		Woche 180	19	79,82	19,704	33,3	66,67	100,0
		Woche 184	20	80,83	20,430	33,3	83,33	100,0
		Woche 188	18	83,33	18,960	33,3	83,33	100,0
		Woche 192	16	77,08	23,472	33,3	83,33	100,0
		Woche 196	18	84,26	22,486	16,7	100,00	100,0
		Woche 200	19	81,58	22,149	16,7	83,33	100,0
		Woche 204	13	74,36	18,777	33,3	66,67	100,0
		Woche 208	12	81,94	19,408	50,0	83,33	100,0
		Woche 212	15	85,56	17,668	50,0	100,00	100,0
		Woche 216	12	76,39	18,060	50,0	66,67	100,0
		Woche 220	9	81,48	17,568	66,7	66,67	100,0
		Woche 224	11	87,88	15,076	66,7	100,00	100,0
		Woche 228	9	83,33	16,667	66,7	83,33	100,0
		Woche 232	5	83,33	16,667	66,7	83,33	100,0
		Woche 236	5	86,67	18,257	66,7	100,00	100,0
		Woche 240	5	83,33	23,570	50,0	100,00	100,0
		Woche 244	4	91,67	16,667	66,7	100,00	100,0
		Woche 248	2	100,00	0,000	100,0	100,00	100,0
		Woche 252	1	100,00	NC	100,0	100,00	100,0
		Woche 256	1	100,00	NC	100,0	100,00	100,0
Soziale Funktion	Durvalumab (N=264)	Baseline [a]	216	86,96	19,316	0,0	100,00	100,0
		Woche 4	236	87,01	19,035	0,0	100,00	100,0
		Woche 8	221	83,79	21,492	33,3	100,00	100,0
		Woche 12	202	85,23	21,561	0,0	100,00	100,0
		Woche 16	189	85,63	21,139	0,0	100,00	100,0
		Woche 20	179	84,36	20,000	16,7	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Soziale Funktion	Durvalumab (N=264)	Woche 24	169	87,48	19,053	0,0	100,00	100,0
		Woche 28	163	85,99	21,270	0,0	100,00	100,0
		Woche 32	159	86,37	20,357	0,0	100,00	100,0
		Woche 36	149	86,91	19,906	0,0	100,00	100,0
		Woche 40	135	87,41	19,473	0,0	100,00	100,0
		Woche 44	131	86,64	20,193	0,0	100,00	100,0
		Woche 48	123	84,82	20,690	0,0	100,00	100,0
		Woche 52	124	86,16	20,018	16,7	100,00	100,0
		Woche 56	121	84,16	20,052	0,0	100,00	100,0
		Woche 60	118	86,30	20,164	0,0	100,00	100,0
		Woche 64	113	84,37	22,634	0,0	100,00	100,0
		Woche 68	103	86,57	20,751	16,7	100,00	100,0
		Woche 72	100	86,00	20,749	0,0	100,00	100,0
		Woche 76	98	84,52	23,234	0,0	100,00	100,0
		Woche 80	97	84,54	22,598	0,0	100,00	100,0
		Woche 84	97	87,63	18,206	0,0	100,00	100,0
		Woche 88	91	85,71	21,165	0,0	100,00	100,0
		Woche 92	92	84,96	19,621	0,0	100,00	100,0
		Woche 96	87	86,40	19,445	0,0	100,00	100,0
		Woche 100	94	89,01	16,676	33,3	100,00	100,0
		Woche 104	80	86,04	21,616	0,0	100,00	100,0
		Woche 108	77	85,06	19,791	33,3	100,00	100,0
		Woche 112	73	86,53	19,771	33,3	100,00	100,0
		Woche 116	68	87,25	21,378	0,0	100,00	100,0
		Woche 120	63	85,71	21,136	16,7	100,00	100,0
		Woche 124	58	87,36	19,574	16,7	100,00	100,0
		Woche 128	59	88,98	19,478	33,3	100,00	100,0
		Woche 132	53	87,42	21,159	0,0	100,00	100,0
		Woche 136	52	91,35	16,987	33,3	100,00	100,0
		Woche 140	48	88,19	20,901	0,0	100,00	100,0
		Woche 144	39	86,75	22,025	33,3	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

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Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Soziale Funktion	Durvalumab (N=264)	Woche 148	43	85,66	20,760	33,3	100,00	100,0
		Woche 152	41	88,62	18,797	33,3	100,00	100,0
		Woche 156	37	86,04	21,341	33,3	100,00	100,0
		Woche 160	33	87,88	20,101	33,3	100,00	100,0
		Woche 164	33	89,39	17,588	33,3	100,00	100,0
		Woche 168	29	89,66	18,588	33,3	100,00	100,0
		Woche 172	32	92,71	15,804	33,3	100,00	100,0
		Woche 176	23	90,58	19,349	33,3	100,00	100,0
		Woche 180	21	91,27	20,829	33,3	100,00	100,0
		Woche 184	19	91,23	17,889	33,3	100,00	100,0
		Woche 188	17	82,35	29,739	0,0	100,00	100,0
		Woche 192	17	89,22	26,965	0,0	100,00	100,0
		Woche 196	14	91,67	19,337	33,3	100,00	100,0
		Woche 200	11	96,97	10,050	66,7	100,00	100,0
		Woche 204	7	100,00	0,000	100,0	100,00	100,0
		Woche 208	8	100,00	0,000	100,0	100,00	100,0
		Woche 212	7	97,62	6,299	83,3	100,00	100,0
		Woche 216	9	100,00	0,000	100,0	100,00	100,0
		Woche 220	7	100,00	0,000	100,0	100,00	100,0
		Woche 224	6	100,00	0,000	100,0	100,00	100,0
		Woche 228	6	100,00	0,000	100,0	100,00	100,0
		Woche 232	6	97,22	6,804	83,3	100,00	100,0
		Woche 236	4	100,00	0,000	100,0	100,00	100,0
		Woche 240	3	100,00	0,000	100,0	100,00	100,0
		Woche 244	2	100,00	0,000	100,0	100,00	100,0
		Woche 248	1	100,00	NC	100,0	100,00	100,0
		Woche 252	2	100,00	0,000	100,0	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Soziale Funktion	Placebo (N=266)	Baseline [a]	212	86,40	20,261	0,0	100,00	100,0
		Woche 4	230	85,29	21,465	0,0	100,00	100,0
		Woche 8	209	84,21	22,776	0,0	100,00	100,0
		Woche 12	198	84,43	21,313	0,0	100,00	100,0
		Woche 16	197	85,53	20,432	0,0	100,00	100,0
		Woche 20	180	86,57	20,325	0,0	100,00	100,0
		Woche 24	172	86,92	19,204	0,0	100,00	100,0
		Woche 28	158	86,18	21,215	0,0	100,00	100,0
		Woche 32	150	85,67	23,809	0,0	100,00	100,0
		Woche 36	141	85,82	21,076	0,0	100,00	100,0
		Woche 40	122	85,52	22,160	0,0	100,00	100,0
		Woche 44	124	87,23	21,264	0,0	100,00	100,0
		Woche 48	121	88,29	17,697	33,3	100,00	100,0
		Woche 52	118	87,01	19,014	33,3	100,00	100,0
		Woche 56	104	86,38	20,612	16,7	100,00	100,0
		Woche 60	98	86,90	18,882	33,3	100,00	100,0
		Woche 64	94	85,82	19,546	33,3	100,00	100,0
		Woche 68	91	88,10	17,085	33,3	100,00	100,0
		Woche 72	86	91,09	14,619	33,3	100,00	100,0
		Woche 76	77	87,45	21,316	0,0	100,00	100,0
		Woche 80	75	89,11	18,070	33,3	100,00	100,0
		Woche 84	75	88,00	22,185	0,0	100,00	100,0
		Woche 88	70	89,76	17,328	16,7	100,00	100,0
		Woche 92	69	90,82	16,798	16,7	100,00	100,0
		Woche 96	64	88,80	18,319	16,7	100,00	100,0
		Woche 100	66	89,90	15,436	33,3	100,00	100,0
		Woche 104	62	86,56	20,208	16,7	100,00	100,0
		Woche 108	59	87,57	19,227	16,7	100,00	100,0
		Woche 112	54	87,96	18,716	16,7	100,00	100,0
		Woche 116	56	88,10	19,775	33,3	100,00	100,0
		Woche 120	51	86,27	22,535	0,0	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Soziale Funktion	Placebo (N=266)	Woche 124	50	90,67	15,851	33,3	100,00	100,0
		Woche 128	45	88,89	19,784	16,7	100,00	100,0
		Woche 132	44	90,15	18,086	16,7	100,00	100,0
		Woche 136	39	88,46	18,792	33,3	100,00	100,0
		Woche 140	39	90,17	19,391	16,7	100,00	100,0
		Woche 144	35	89,52	17,660	33,3	100,00	100,0
		Woche 148	32	88,54	20,053	16,7	100,00	100,0
		Woche 152	33	88,89	17,010	33,3	100,00	100,0
		Woche 156	32	89,58	17,326	33,3	100,00	100,0
		Woche 160	31	87,63	18,742	33,3	100,00	100,0
		Woche 164	24	88,19	18,044	33,3	100,00	100,0
		Woche 168	28	86,31	22,705	16,7	100,00	100,0
		Woche 172	23	92,03	15,787	50,0	100,00	100,0
		Woche 176	21	90,48	13,511	66,7	100,00	100,0
		Woche 180	19	92,11	12,872	66,7	100,00	100,0
		Woche 184	20	91,67	19,118	33,3	100,00	100,0
		Woche 188	18	91,67	13,098	66,7	100,00	100,0
		Woche 192	16	84,38	17,710	50,0	91,67	100,0
		Woche 196	18	90,74	18,277	33,3	100,00	100,0
		Woche 200	19	92,11	12,872	66,7	100,00	100,0
		Woche 204	13	88,46	17,193	50,0	100,00	100,0
		Woche 208	12	94,44	10,856	66,7	100,00	100,0
		Woche 212	15	93,33	12,280	66,7	100,00	100,0
		Woche 216	12	88,89	17,885	50,0	100,00	100,0
		Woche 220	9	90,74	14,699	66,7	100,00	100,0
		Woche 224	11	95,45	10,778	66,7	100,00	100,0
		Woche 228	9	94,44	11,785	66,7	100,00	100,0
		Woche 232	5	80,00	18,257	66,7	66,67	100,0
		Woche 236	5	86,67	18,257	66,7	100,00	100,0
		Woche 240	5	86,67	18,257	66,7	100,00	100,0
		Woche 244	4	91,67	16,667	66,7	100,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Soziale Funktion	Placebo (N=266)	Woche 248	2	100,00	0,000	100,0	100,00	100,0
		Woche 252	1	100,00	NC	100,0	100,00	100,0
		Woche 256	1	100,00	NC	100,0	100,00	100,0
Fatigue	Durvalumab (N=264)	Baseline [a]	216	23,66	20,310	0,0	22,22	100,0
		Woche 4	236	26,60	22,532	0,0	22,22	100,0
		Woche 8	221	30,17	23,583	0,0	33,33	100,0
		Woche 12	202	26,62	23,253	0,0	22,22	100,0
		Woche 16	189	26,46	22,319	0,0	22,22	100,0
		Woche 20	179	26,01	21,301	0,0	22,22	88,9
		Woche 24	169	26,10	21,318	0,0	22,22	88,9
		Woche 28	163	25,02	21,253	0,0	22,22	100,0
		Woche 32	159	25,65	21,614	0,0	22,22	100,0
		Woche 36	149	23,71	19,870	0,0	22,22	88,9
		Woche 40	135	23,54	20,182	0,0	22,22	77,8
		Woche 44	131	24,43	23,647	0,0	22,22	100,0
		Woche 48	123	25,20	23,336	0,0	22,22	100,0
		Woche 52	124	22,58	22,038	0,0	22,22	88,9
		Woche 56	121	24,06	20,952	0,0	22,22	77,8
		Woche 60	118	23,45	21,780	0,0	22,22	77,8
		Woche 64	113	23,11	23,809	0,0	22,22	100,0
		Woche 68	103	24,06	21,732	0,0	22,22	77,8
		Woche 72	100	23,11	21,169	0,0	22,22	77,8
		Woche 76	98	22,68	23,606	0,0	22,22	100,0
		Woche 80	97	24,28	21,655	0,0	22,22	77,8
		Woche 84	97	21,08	21,783	0,0	11,11	88,9
		Woche 88	91	23,69	23,495	0,0	22,22	100,0
		Woche 92	92	22,34	21,318	0,0	22,22	66,7
		Woche 96	87	24,27	23,204	0,0	22,22	88,9
		Woche 100	94	24,47	22,257	0,0	22,22	88,9
		Woche 104	80	23,89	23,791	0,0	11,11	100,0
		Woche 108	77	24,82	22,288	0,0	22,22	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Fatigue	Durvalumab (N=264)	Woche 112	73	24,35	23,104	0,0	22,22	100,0
		Woche 116	68	25,49	22,392	0,0	27,78	88,9
		Woche 120	63	24,51	23,541	0,0	22,22	100,0
		Woche 124	58	20,88	21,131	0,0	22,22	100,0
		Woche 128	59	22,03	21,491	0,0	22,22	77,8
		Woche 132	53	20,55	21,834	0,0	22,22	100,0
		Woche 136	52	19,87	22,259	0,0	11,11	77,8
		Woche 140	48	21,30	24,347	0,0	11,11	100,0
		Woche 144	39	18,80	20,257	0,0	22,22	66,7
		Woche 148	43	21,19	21,931	0,0	22,22	77,8
		Woche 152	41	20,33	21,788	0,0	11,11	66,7
		Woche 156	37	22,82	23,707	0,0	11,11	66,7
		Woche 160	33	23,91	25,927	0,0	22,22	100,0
		Woche 164	33	21,55	22,385	0,0	11,11	66,7
		Woche 168	29	19,54	21,343	0,0	11,11	66,7
		Woche 172	32	17,71	23,249	0,0	5,56	66,7
		Woche 176	23	23,67	23,524	0,0	22,22	77,8
		Woche 180	21	21,16	24,822	0,0	11,11	66,7
		Woche 184	19	25,73	24,582	0,0	22,22	77,8
		Woche 188	17	26,14	26,915	0,0	22,22	66,7
		Woche 192	17	22,22	28,054	0,0	11,11	100,0
		Woche 196	14	17,46	22,100	0,0	11,11	66,7
		Woche 200	11	18,18	20,045	0,0	22,22	66,7
		Woche 204	7	7,94	13,929	0,0	0,00	33,3
		Woche 208	8	9,72	12,511	0,0	5,56	33,3
		Woche 212	7	15,87	14,138	0,0	11,11	33,3
		Woche 216	9	8,64	10,798	0,0	0,00	22,2
		Woche 220	7	6,35	10,843	0,0	0,00	22,2
		Woche 224	6	11,11	14,055	0,0	5,56	33,3
		Woche 228	6	11,11	14,055	0,0	5,56	33,3
		Woche 232	6	9,26	10,924	0,0	5,56	22,2

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Fatigue	Durvalumab (N=264)	Woche 236	4	11,11	12,830	0,0	11,11	22,2
		Woche 240	3	11,11	11,111	0,0	11,11	22,2
		Woche 244	2	11,11	15,713	0,0	11,11	22,2
		Woche 248	1	22,22	NC	22,2	22,22	22,2
		Woche 252	2	22,22	15,713	11,1	22,22	33,3
	Placebo (N=266)	Baseline [a]	212	25,21	20,117	0,0	22,22	100,0
		Woche 4	230	29,18	23,517	0,0	33,33	100,0
		Woche 8	209	33,39	23,658	0,0	33,33	100,0
		Woche 12	198	28,62	22,284	0,0	33,33	100,0
		Woche 16	197	28,31	21,920	0,0	33,33	100,0
		Woche 20	180	25,86	21,362	0,0	22,22	100,0
		Woche 24	172	26,81	22,282	0,0	33,33	100,0
		Woche 28	158	26,16	22,576	0,0	22,22	100,0
		Woche 32	150	27,19	23,860	0,0	22,22	100,0
		Woche 36	141	27,03	23,243	0,0	22,22	100,0
		Woche 40	122	26,32	23,131	0,0	22,22	100,0
		Woche 44	124	23,57	20,067	0,0	22,22	100,0
		Woche 48	121	23,51	19,626	0,0	22,22	88,9
		Woche 52	118	25,52	21,998	0,0	22,22	100,0
		Woche 56	104	24,89	21,144	0,0	22,22	100,0
		Woche 60	98	23,58	19,687	0,0	22,22	77,8
		Woche 64	94	25,06	20,542	0,0	22,22	77,8
		Woche 68	91	22,95	20,273	0,0	22,22	77,8
		Woche 72	86	24,94	22,153	0,0	22,22	88,9
		Woche 76	77	23,23	23,166	0,0	22,22	100,0
		Woche 80	75	25,33	21,031	0,0	22,22	77,8
		Woche 84	75	25,19	20,204	0,0	22,22	88,9
		Woche 88	70	24,60	20,540	0,0	22,22	88,9
		Woche 92	69	22,87	17,762	0,0	22,22	66,7
		Woche 96	64	25,69	19,181	0,0	33,33	77,8
		Woche 100	66	23,91	19,120	0,0	22,22	66,7

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Fatigue	Placebo (N=266)	Woche 104	62	24,91	18,515	0,0	22,22	66,7
		Woche 108	59	25,24	22,013	0,0	22,22	100,0
		Woche 112	54	26,34	19,934	0,0	22,22	66,7
		Woche 116	56	23,81	20,370	0,0	22,22	77,8
		Woche 120	51	24,40	22,446	0,0	22,22	100,0
		Woche 124	50	23,78	20,204	0,0	22,22	66,7
		Woche 128	45	24,44	20,323	0,0	22,22	66,7
		Woche 132	44	26,52	22,634	0,0	27,78	77,8
		Woche 136	39	24,79	19,154	0,0	22,22	66,7
		Woche 140	39	27,35	20,527	0,0	33,33	66,7
		Woche 144	35	21,90	18,765	0,0	22,22	66,7
		Woche 148	32	25,35	21,164	0,0	27,78	77,8
		Woche 152	33	24,58	22,525	0,0	22,22	66,7
		Woche 156	32	22,22	20,351	0,0	22,22	55,6
		Woche 160	31	27,24	23,975	0,0	33,33	66,7
		Woche 164	24	28,70	21,959	0,0	33,33	66,7
		Woche 168	28	25,40	21,986	0,0	27,78	66,7
		Woche 172	23	28,02	27,395	0,0	33,33	77,8
		Woche 176	21	30,16	23,608	0,0	33,33	66,7
		Woche 180	19	29,82	21,293	0,0	33,33	66,7
		Woche 184	20	27,22	22,361	0,0	22,22	66,7
		Woche 188	18	26,54	23,843	0,0	27,78	66,7
		Woche 192	16	29,17	22,176	0,0	33,33	66,7
		Woche 196	18	20,99	23,459	0,0	11,11	66,7
		Woche 200	19	25,15	24,242	0,0	22,22	77,8
		Woche 204	13	32,48	26,239	0,0	33,33	77,8
		Woche 208	12	25,93	27,761	0,0	16,67	77,8
		Woche 212	15	23,70	22,564	0,0	22,22	77,8
		Woche 216	12	25,93	21,883	0,0	27,78	66,7
		Woche 220	9	27,16	25,526	0,0	33,33	66,7
		Woche 224	11	25,25	24,890	0,0	22,22	77,8

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Fatigue	Placebo (N=266)	Woche 228	9	25,93	24,216	0,0	33,33	66,7
		Woche 232	5	22,22	20,787	0,0	33,33	44,4
		Woche 236	5	24,44	24,088	0,0	33,33	55,6
		Woche 240	5	28,89	27,889	0,0	33,33	55,6
		Woche 244	4	22,22	20,286	0,0	22,22	44,4
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Schmerzen	Durvalumab (N=264)	Baseline [a]	216	10,19	15,967	0,0	0,00	66,7
		Woche 4	236	14,55	18,457	0,0	0,00	66,7
		Woche 8	221	15,99	20,370	0,0	16,67	100,0
		Woche 12	202	14,27	21,253	0,0	0,00	100,0
		Woche 16	189	15,34	20,406	0,0	0,00	100,0
		Woche 20	179	14,34	18,339	0,0	0,00	83,3
		Woche 24	169	13,91	19,131	0,0	0,00	100,0
		Woche 28	163	14,52	18,532	0,0	0,00	83,3
		Woche 32	159	13,42	18,513	0,0	0,00	100,0
		Woche 36	149	14,77	19,134	0,0	0,00	83,3
		Woche 40	135	12,47	17,601	0,0	0,00	83,3
		Woche 44	131	13,87	19,519	0,0	0,00	100,0
		Woche 48	123	14,50	20,127	0,0	0,00	100,0
		Woche 52	124	13,71	19,484	0,0	0,00	83,3
		Woche 56	121	15,01	20,345	0,0	0,00	83,3
		Woche 60	118	13,70	17,787	0,0	8,33	83,3
		Woche 64	113	14,60	20,790	0,0	0,00	100,0
		Woche 68	103	11,17	16,066	0,0	0,00	66,7
		Woche 72	100	12,00	17,259	0,0	0,00	66,7
		Woche 76	98	12,41	20,067	0,0	0,00	83,3
		Woche 80	97	12,89	19,321	0,0	0,00	66,7
		Woche 84	97	10,31	16,217	0,0	0,00	66,7
		Woche 88	91	11,72	17,302	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen	Durvalumab (N=264)	Woche 92	92	11,05	15,874	0,0	0,00	66,7
		Woche 96	87	12,64	18,322	0,0	0,00	66,7
		Woche 100	94	10,82	15,784	0,0	0,00	66,7
		Woche 104	80	9,79	16,496	0,0	0,00	66,7
		Woche 108	77	12,77	18,515	0,0	0,00	66,7
		Woche 112	73	14,84	20,329	0,0	0,00	83,3
		Woche 116	68	12,25	20,487	0,0	0,00	83,3
		Woche 120	63	14,29	22,171	0,0	0,00	83,3
		Woche 124	58	10,92	19,384	0,0	0,00	100,0
		Woche 128	59	11,02	17,401	0,0	0,00	66,7
		Woche 132	53	10,06	19,973	0,0	0,00	100,0
		Woche 136	52	11,54	20,489	0,0	0,00	83,3
		Woche 140	48	10,07	19,672	0,0	0,00	83,3
		Woche 144	39	13,68	18,286	0,0	0,00	66,7
		Woche 148	43	11,63	19,428	0,0	0,00	66,7
		Woche 152	41	14,23	20,602	0,0	0,00	66,7
		Woche 156	37	14,41	19,310	0,0	0,00	66,7
		Woche 160	33	15,15	20,984	0,0	0,00	83,3
		Woche 164	33	11,11	18,002	0,0	0,00	66,7
		Woche 168	29	9,20	16,419	0,0	0,00	66,7
		Woche 172	32	12,50	21,167	0,0	0,00	66,7
		Woche 176	23	13,77	21,113	0,0	0,00	66,7
		Woche 180	21	7,94	16,346	0,0	0,00	66,7
		Woche 184	19	11,40	22,259	0,0	0,00	66,7
		Woche 188	17	17,65	25,325	0,0	0,00	66,7
		Woche 192	17	10,78	23,527	0,0	0,00	83,3
		Woche 196	14	10,71	18,030	0,0	0,00	66,7
		Woche 200	11	6,06	11,237	0,0	0,00	33,3
		Woche 204	7	2,38	6,299	0,0	0,00	16,7
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	7,14	13,113	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen	Durvalumab (N=264)	Woche 216	9	0,00	0,000	0,0	0,00	0,0
		Woche 220	7	2,38	6,299	0,0	0,00	16,7
		Woche 224	6	2,78	6,804	0,0	0,00	16,7
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	4,17	8,333	0,0	0,00	16,7
		Woche 240	3	5,56	9,623	0,0	0,00	16,7
		Woche 244	2	16,67	23,570	0,0	16,67	33,3
		Woche 248	1	16,67	NC	16,7	16,67	16,7
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	212	11,87	15,958	0,0	0,00	83,3
		Woche 4	230	18,33	20,917	0,0	16,67	83,3
		Woche 8	209	19,38	22,123	0,0	16,67	100,0
		Woche 12	198	18,27	20,401	0,0	16,67	83,3
		Woche 16	197	17,77	21,033	0,0	16,67	100,0
		Woche 20	180	17,22	21,060	0,0	16,67	100,0
		Woche 24	172	17,44	20,457	0,0	16,67	100,0
		Woche 28	158	19,41	22,951	0,0	16,67	100,0
		Woche 32	150	18,11	21,755	0,0	16,67	100,0
		Woche 36	141	17,38	21,901	0,0	16,67	100,0
		Woche 40	122	18,31	22,515	0,0	16,67	100,0
		Woche 44	124	18,41	21,965	0,0	16,67	100,0
		Woche 48	121	17,08	21,242	0,0	16,67	83,3
		Woche 52	118	16,67	19,612	0,0	16,67	100,0
		Woche 56	104	16,99	20,640	0,0	16,67	100,0
		Woche 60	98	18,03	20,119	0,0	16,67	83,3
		Woche 64	94	17,73	20,998	0,0	16,67	83,3
		Woche 68	91	15,20	18,864	0,0	0,00	83,3
		Woche 72	86	17,44	20,912	0,0	16,67	100,0
		Woche 76	77	17,10	22,126	0,0	16,67	100,0
		Woche 80	75	16,44	18,070	0,0	16,67	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen	Placebo (N=266)	Woche 84	75	19,56	20,389	0,0	16,67	83,3
		Woche 88	70	18,10	21,932	0,0	16,67	83,3
		Woche 92	69	15,46	16,499	0,0	16,67	66,7
		Woche 96	64	16,15	19,466	0,0	16,67	66,7
		Woche 100	66	15,66	19,802	0,0	8,33	66,7
		Woche 104	62	14,25	16,761	0,0	16,67	66,7
		Woche 108	59	17,51	24,841	0,0	0,00	100,0
		Woche 112	54	14,81	18,505	0,0	8,33	83,3
		Woche 116	56	17,26	19,583	0,0	16,67	66,7
		Woche 120	51	13,07	17,099	0,0	16,67	83,3
		Woche 124	50	15,33	16,782	0,0	16,67	50,0
		Woche 128	45	18,52	19,209	0,0	16,67	66,7
		Woche 132	44	14,77	18,404	0,0	8,33	66,7
		Woche 136	39	16,24	17,724	0,0	16,67	66,7
		Woche 140	39	13,25	16,303	0,0	0,00	50,0
		Woche 144	35	12,86	15,171	0,0	16,67	50,0
		Woche 148	32	12,50	14,665	0,0	8,33	50,0
		Woche 152	33	15,15	17,855	0,0	16,67	66,7
		Woche 156	32	14,06	18,984	0,0	0,00	66,7
		Woche 160	31	15,05	18,932	0,0	0,00	66,7
		Woche 164	24	15,97	18,701	0,0	16,67	66,7
		Woche 168	28	16,07	17,848	0,0	16,67	66,7
		Woche 172	23	15,94	20,399	0,0	0,00	66,7
		Woche 176	21	15,87	18,616	0,0	16,67	66,7
		Woche 180	19	14,91	19,160	0,0	16,67	66,7
		Woche 184	20	13,33	18,417	0,0	0,00	66,7
		Woche 188	18	11,11	18,960	0,0	0,00	66,7
		Woche 192	16	16,67	17,213	0,0	16,67	50,0
		Woche 196	18	11,11	19,803	0,0	0,00	66,7
		Woche 200	19	13,16	18,904	0,0	0,00	66,7
		Woche 204	13	16,67	20,412	0,0	0,00	50,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen	Placebo (N=266)	Woche 208	12	9,72	15,006	0,0	0,00	33,3
		Woche 212	15	8,89	12,387	0,0	0,00	33,3
		Woche 216	12	20,83	21,468	0,0	16,67	66,7
		Woche 220	9	12,96	18,215	0,0	0,00	50,0
		Woche 224	11	9,09	15,570	0,0	0,00	50,0
		Woche 228	9	11,11	18,634	0,0	0,00	50,0
		Woche 232	5	23,33	19,003	0,0	16,67	50,0
		Woche 236	5	20,00	13,944	0,0	16,67	33,3
		Woche 240	5	16,67	16,667	0,0	16,67	33,3
		Woche 244	4	12,50	15,957	0,0	8,33	33,3
		Woche 248	2	8,33	11,785	0,0	8,33	16,7
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	16,67	NC	16,7	16,67	16,7
Übelkeit und Erbrechen	Durvalumab (N=264)	Baseline [a]	216	6,25	13,286	0,0	0,00	100,0
		Woche 4	236	5,01	10,853	0,0	0,00	66,7
		Woche 8	221	7,92	16,249	0,0	0,00	83,3
		Woche 12	202	4,87	10,630	0,0	0,00	66,7
		Woche 16	189	5,82	13,257	0,0	0,00	100,0
		Woche 20	179	4,38	11,494	0,0	0,00	100,0
		Woche 24	169	4,24	9,454	0,0	0,00	50,0
		Woche 28	163	3,89	11,351	0,0	0,00	83,3
		Woche 32	159	4,09	10,888	0,0	0,00	66,7
		Woche 36	149	3,47	9,546	0,0	0,00	66,7
		Woche 40	135	2,47	8,276	0,0	0,00	66,7
		Woche 44	131	3,94	10,092	0,0	0,00	50,0
		Woche 48	123	4,47	11,307	0,0	0,00	66,7
		Woche 52	124	3,23	8,679	0,0	0,00	50,0
		Woche 56	121	2,48	8,515	0,0	0,00	66,7
		Woche 60	118	3,25	10,047	0,0	0,00	66,7
		Woche 64	113	4,13	10,092	0,0	0,00	50,0
		Woche 68	103	2,27	6,196	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Übelkeit und Erbrechen	Durvalumab (N=264)	Woche 72	100	1,83	5,752	0,0	0,00	33,3
		Woche 76	98	4,08	12,449	0,0	0,00	100,0
		Woche 80	97	2,75	6,667	0,0	0,00	33,3
		Woche 84	97	2,06	6,481	0,0	0,00	33,3
		Woche 88	91	1,65	8,261	0,0	0,00	66,7
		Woche 92	92	3,99	13,616	0,0	0,00	100,0
		Woche 96	87	3,26	9,791	0,0	0,00	66,7
		Woche 100	94	3,19	9,235	0,0	0,00	66,7
		Woche 104	80	2,50	8,835	0,0	0,00	66,7
		Woche 108	77	2,60	7,678	0,0	0,00	33,3
		Woche 112	73	2,74	7,863	0,0	0,00	33,3
		Woche 116	68	2,21	7,566	0,0	0,00	50,0
		Woche 120	63	3,44	12,033	0,0	0,00	83,3
		Woche 124	58	1,44	4,719	0,0	0,00	16,7
		Woche 128	59	2,54	6,790	0,0	0,00	33,3
		Woche 132	53	1,89	5,331	0,0	0,00	16,7
		Woche 136	52	2,24	8,104	0,0	0,00	50,0
		Woche 140	48	1,39	5,787	0,0	0,00	33,3
		Woche 144	39	0,85	3,724	0,0	0,00	16,7
		Woche 148	43	1,16	5,629	0,0	0,00	33,3
		Woche 152	41	2,44	5,964	0,0	0,00	16,7
		Woche 156	37	1,35	4,612	0,0	0,00	16,7
		Woche 160	33	1,01	4,038	0,0	0,00	16,7
		Woche 164	33	1,01	4,038	0,0	0,00	16,7
		Woche 168	29	0,57	3,095	0,0	0,00	16,7
		Woche 172	32	1,04	4,099	0,0	0,00	16,7
		Woche 176	23	0,72	3,475	0,0	0,00	16,7
		Woche 180	21	3,17	8,529	0,0	0,00	33,3
		Woche 184	19	1,75	5,255	0,0	0,00	16,7
		Woche 188	17	2,94	6,549	0,0	0,00	16,7
		Woche 192	17	2,94	6,549	0,0	0,00	16,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Übelkeit und Erbrechen	Durvalumab (N=264)	Woche 196	14	1,19	4,454	0,0	0,00	16,7
		Woche 200	11	1,52	5,025	0,0	0,00	16,7
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	0,00	0,000	0,0	0,00	0,0
		Woche 216	9	1,85	5,556	0,0	0,00	16,7
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	8,33	11,785	0,0	8,33	16,7
	Placebo (N=266)	Baseline [a]	212	6,45	11,259	0,0	0,00	50,0
		Woche 4	230	7,03	13,221	0,0	0,00	66,7
		Woche 8	209	8,21	17,837	0,0	0,00	83,3
		Woche 12	198	5,98	12,653	0,0	0,00	66,7
		Woche 16	197	5,16	11,426	0,0	0,00	83,3
		Woche 20	180	4,17	10,698	0,0	0,00	83,3
		Woche 24	172	4,17	9,893	0,0	0,00	66,7
		Woche 28	158	5,17	14,065	0,0	0,00	100,0
		Woche 32	150	3,78	11,769	0,0	0,00	100,0
		Woche 36	141	4,37	10,474	0,0	0,00	66,7
		Woche 40	122	4,92	13,668	0,0	0,00	83,3
		Woche 44	124	3,63	10,095	0,0	0,00	50,0
		Woche 48	121	3,17	9,456	0,0	0,00	66,7
		Woche 52	118	4,52	11,461	0,0	0,00	66,7
		Woche 56	104	4,33	10,642	0,0	0,00	50,0
		Woche 60	98	2,72	6,638	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Übelkeit und Erbrechen	Placebo (N=266)	Woche 64	94	3,01	6,449	0,0	0,00	16,7
		Woche 68	91	2,56	7,826	0,0	0,00	50,0
		Woche 72	86	2,33	7,304	0,0	0,00	33,3
		Woche 76	77	2,81	7,356	0,0	0,00	33,3
		Woche 80	75	1,78	5,860	0,0	0,00	33,3
		Woche 84	75	2,44	7,089	0,0	0,00	33,3
		Woche 88	70	2,86	9,818	0,0	0,00	66,7
		Woche 92	69	3,86	9,542	0,0	0,00	33,3
		Woche 96	64	2,34	6,551	0,0	0,00	33,3
		Woche 100	66	2,53	7,304	0,0	0,00	33,3
		Woche 104	62	2,15	6,390	0,0	0,00	33,3
		Woche 108	59	1,69	5,949	0,0	0,00	33,3
		Woche 112	54	2,47	8,195	0,0	0,00	50,0
		Woche 116	56	1,79	6,096	0,0	0,00	33,3
		Woche 120	51	2,29	10,011	0,0	0,00	66,7
		Woche 124	50	2,33	6,743	0,0	0,00	33,3
		Woche 128	45	2,96	8,172	0,0	0,00	33,3
		Woche 132	44	1,89	6,446	0,0	0,00	33,3
		Woche 136	39	1,28	4,499	0,0	0,00	16,7
		Woche 140	39	3,42	7,817	0,0	0,00	33,3
		Woche 144	35	0,95	3,925	0,0	0,00	16,7
		Woche 148	32	1,56	4,936	0,0	0,00	16,7
		Woche 152	33	1,01	4,038	0,0	0,00	16,7
		Woche 156	32	2,60	8,582	0,0	0,00	33,3
		Woche 160	31	2,15	7,126	0,0	0,00	33,3
		Woche 164	24	3,47	6,914	0,0	0,00	16,7
		Woche 168	28	3,57	8,311	0,0	0,00	33,3
		Woche 172	23	2,90	8,184	0,0	0,00	33,3
		Woche 176	21	3,17	8,529	0,0	0,00	33,3
		Woche 180	19	4,39	9,366	0,0	0,00	33,3
		Woche 184	20	0,83	3,727	0,0	0,00	16,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Übelkeit und Erbrechen	Placebo (N=266)	Woche 188	18	0,00	0,000	0,0	0,00	0,0
		Woche 192	16	1,04	4,167	0,0	0,00	16,7
		Woche 196	18	0,93	3,928	0,0	0,00	16,7
		Woche 200	19	0,88	3,824	0,0	0,00	16,7
		Woche 204	13	5,13	12,518	0,0	0,00	33,3
		Woche 208	12	4,17	10,360	0,0	0,00	33,3
		Woche 212	15	0,00	0,000	0,0	0,00	0,0
		Woche 216	12	0,00	0,000	0,0	0,00	0,0
		Woche 220	9	1,85	5,556	0,0	0,00	16,7
		Woche 224	11	0,00	0,000	0,0	0,00	0,0
		Woche 228	9	0,00	0,000	0,0	0,00	0,0
		Woche 232	5	0,00	0,000	0,0	0,00	0,0
		Woche 236	5	0,00	0,000	0,0	0,00	0,0
		Woche 240	5	0,00	0,000	0,0	0,00	0,0
		Woche 244	4	0,00	0,000	0,0	0,00	0,0
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Appetitverlust	Durvalumab (N=264)	Baseline [a]	216	18,98	25,412	0,0	0,00	100,0
		Woche 4	236	18,36	24,638	0,0	0,00	100,0
		Woche 8	221	26,40	30,685	0,0	33,33	100,0
		Woche 12	202	21,95	28,548	0,0	0,00	100,0
		Woche 16	189	19,22	26,646	0,0	0,00	100,0
		Woche 20	179	17,50	24,047	0,0	0,00	100,0
		Woche 24	169	15,58	21,833	0,0	0,00	100,0
		Woche 28	163	15,75	24,931	0,0	0,00	100,0
		Woche 32	159	16,56	23,977	0,0	0,00	100,0
		Woche 36	149	13,42	21,547	0,0	0,00	100,0
		Woche 40	135	9,88	19,981	0,0	0,00	100,0
		Woche 44	131	11,96	21,511	0,0	0,00	100,0
		Woche 48	123	13,28	22,478	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Appetitverlust	Durvalumab (N=264)	Woche 52	124	10,75	20,626	0,0	0,00	100,0
		Woche 56	121	13,22	20,852	0,0	0,00	100,0
		Woche 60	118	12,99	22,660	0,0	0,00	100,0
		Woche 64	113	12,09	21,391	0,0	0,00	100,0
		Woche 68	103	9,06	18,194	0,0	0,00	100,0
		Woche 72	100	10,67	16,330	0,0	0,00	66,7
		Woche 76	98	9,52	18,538	0,0	0,00	100,0
		Woche 80	97	10,31	18,857	0,0	0,00	100,0
		Woche 84	97	9,62	17,320	0,0	0,00	66,7
		Woche 88	91	12,45	24,164	0,0	0,00	100,0
		Woche 92	92	13,04	25,657	0,0	0,00	100,0
		Woche 96	87	8,81	21,840	0,0	0,00	100,0
		Woche 100	94	12,41	21,298	0,0	0,00	100,0
		Woche 104	80	8,33	19,487	0,0	0,00	100,0
		Woche 108	77	7,79	16,128	0,0	0,00	66,7
		Woche 112	73	8,68	19,267	0,0	0,00	100,0
		Woche 116	68	8,82	19,630	0,0	0,00	100,0
		Woche 120	63	7,94	18,660	0,0	0,00	66,7
		Woche 124	58	8,05	14,389	0,0	0,00	33,3
		Woche 128	59	5,65	14,050	0,0	0,00	66,7
		Woche 132	53	4,40	11,394	0,0	0,00	33,3
		Woche 136	52	3,21	11,918	0,0	0,00	66,7
		Woche 140	48	6,25	16,353	0,0	0,00	66,7
		Woche 144	39	3,42	10,245	0,0	0,00	33,3
		Woche 148	43	5,43	14,420	0,0	0,00	66,7
		Woche 152	41	5,69	14,724	0,0	0,00	66,7
		Woche 156	37	7,21	15,977	0,0	0,00	66,7
		Woche 160	33	9,09	20,871	0,0	0,00	100,0
		Woche 164	33	6,06	15,489	0,0	0,00	66,7
		Woche 168	29	4,60	11,698	0,0	0,00	33,3
		Woche 172	32	4,17	11,200	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Appetitverlust	Durvalumab (N=264)	Woche 176	23	5,80	16,368	0,0	0,00	66,7
		Woche 180	21	6,35	13,412	0,0	0,00	33,3
		Woche 184	19	8,77	18,732	0,0	0,00	66,7
		Woche 188	17	3,92	11,070	0,0	0,00	33,3
		Woche 192	17	3,92	16,169	0,0	0,00	66,7
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	3,03	10,050	0,0	0,00	33,3
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	4,17	11,785	0,0	0,00	33,3
		Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	11,11	17,213	0,0	0,00	33,3
		Woche 228	6	11,11	17,213	0,0	0,00	33,3
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	16,67	23,570	0,0	16,67	33,3
	Placebo (N=266)	Baseline [a]	212	16,67	23,289	0,0	0,00	100,0
		Woche 4	230	18,99	25,535	0,0	0,00	100,0
		Woche 8	209	23,60	29,885	0,0	0,00	100,0
		Woche 12	198	18,18	25,256	0,0	0,00	100,0
		Woche 16	197	16,58	23,720	0,0	0,00	100,0
		Woche 20	180	14,81	22,346	0,0	0,00	100,0
		Woche 24	172	12,40	20,101	0,0	0,00	100,0
		Woche 28	158	10,55	19,216	0,0	0,00	100,0
		Woche 32	150	12,44	20,992	0,0	0,00	100,0
		Woche 36	141	12,53	22,375	0,0	0,00	100,0
		Woche 40	122	10,93	22,037	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Appetitverlust	Placebo (N=266)	Woche 44	124	11,02	17,893	0,0	0,00	66,7
		Woche 48	121	8,26	16,822	0,0	0,00	100,0
		Woche 52	118	8,76	17,664	0,0	0,00	100,0
		Woche 56	104	10,26	20,812	0,0	0,00	100,0
		Woche 60	98	7,48	14,776	0,0	0,00	66,7
		Woche 64	94	6,38	14,063	0,0	0,00	66,7
		Woche 68	91	6,23	13,064	0,0	0,00	33,3
		Woche 72	86	5,81	13,712	0,0	0,00	66,7
		Woche 76	77	6,06	14,025	0,0	0,00	66,7
		Woche 80	75	8,00	16,293	0,0	0,00	66,7
		Woche 84	75	9,33	18,632	0,0	0,00	66,7
		Woche 88	70	7,14	15,944	0,0	0,00	66,7
		Woche 92	69	5,80	12,727	0,0	0,00	33,3
		Woche 96	64	5,21	12,199	0,0	0,00	33,3
		Woche 100	66	4,55	11,527	0,0	0,00	33,3
		Woche 104	62	5,91	12,838	0,0	0,00	33,3
		Woche 108	59	4,52	11,510	0,0	0,00	33,3
		Woche 112	54	4,32	11,302	0,0	0,00	33,3
		Woche 116	56	5,95	12,882	0,0	0,00	33,3
		Woche 120	51	4,58	11,585	0,0	0,00	33,3
		Woche 124	50	4,67	11,684	0,0	0,00	33,3
		Woche 128	45	7,41	14,015	0,0	0,00	33,3
		Woche 132	44	6,82	13,601	0,0	0,00	33,3
		Woche 136	39	5,13	12,184	0,0	0,00	33,3
		Woche 140	39	5,98	12,959	0,0	0,00	33,3
		Woche 144	35	4,76	11,835	0,0	0,00	33,3
		Woche 148	32	7,29	14,000	0,0	0,00	33,3
		Woche 152	33	5,05	12,137	0,0	0,00	33,3
		Woche 156	32	8,33	14,665	0,0	0,00	33,3
		Woche 160	31	7,53	16,577	0,0	0,00	66,7
		Woche 164	24	9,72	15,477	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Appetitverlust	Placebo (N=266)	Woche 168	28	7,14	16,623	0,0	0,00	66,7
		Woche 172	23	7,25	14,058	0,0	0,00	33,3
		Woche 176	21	4,76	11,952	0,0	0,00	33,3
		Woche 180	19	5,26	12,488	0,0	0,00	33,3
		Woche 184	20	5,00	12,212	0,0	0,00	33,3
		Woche 188	18	5,56	12,783	0,0	0,00	33,3
		Woche 192	16	2,08	8,333	0,0	0,00	33,3
		Woche 196	18	7,41	14,260	0,0	0,00	33,3
		Woche 200	19	7,02	13,962	0,0	0,00	33,3
		Woche 204	13	2,56	9,245	0,0	0,00	33,3
		Woche 208	12	13,89	17,164	0,0	0,00	33,3
		Woche 212	15	6,67	13,801	0,0	0,00	33,3
		Woche 216	12	13,89	17,164	0,0	0,00	33,3
		Woche 220	9	3,70	11,111	0,0	0,00	33,3
		Woche 224	11	12,12	16,817	0,0	0,00	33,3
		Woche 228	9	7,41	14,699	0,0	0,00	33,3
		Woche 232	5	13,33	18,257	0,0	0,00	33,3
		Woche 236	5	13,33	18,257	0,0	0,00	33,3
		Woche 240	5	13,33	18,257	0,0	0,00	33,3
		Woche 244	4	8,33	16,667	0,0	0,00	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Diarrhö	Durvalumab (N=264)	Baseline [a]	216	3,40	10,604	0,0	0,00	66,7
		Woche 4	236	5,79	14,403	0,0	0,00	66,7
		Woche 8	221	4,98	13,498	0,0	0,00	100,0
		Woche 12	202	6,11	15,635	0,0	0,00	100,0
		Woche 16	189	5,29	13,145	0,0	0,00	66,7
		Woche 20	179	6,33	14,470	0,0	0,00	66,7
		Woche 24	169	5,33	13,285	0,0	0,00	66,7
		Woche 28	163	6,13	13,976	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Diarrhö	Durvalumab (N=264)	Woche 32	159	6,71	15,362	0,0	0,00	66,7
		Woche 36	149	5,59	14,186	0,0	0,00	66,7
		Woche 40	135	5,93	14,028	0,0	0,00	66,7
		Woche 44	131	5,34	13,598	0,0	0,00	66,7
		Woche 48	123	4,88	13,281	0,0	0,00	66,7
		Woche 52	124	4,84	12,533	0,0	0,00	66,7
		Woche 56	121	3,86	12,315	0,0	0,00	66,7
		Woche 60	118	3,39	10,118	0,0	0,00	33,3
		Woche 64	113	4,42	12,990	0,0	0,00	66,7
		Woche 68	103	3,88	10,747	0,0	0,00	33,3
		Woche 72	100	2,67	9,089	0,0	0,00	33,3
		Woche 76	98	5,44	14,113	0,0	0,00	66,7
		Woche 80	97	4,81	13,600	0,0	0,00	66,7
		Woche 84	97	5,15	13,035	0,0	0,00	66,7
		Woche 88	91	2,93	9,491	0,0	0,00	33,3
		Woche 92	92	6,52	17,288	0,0	0,00	100,0
		Woche 96	87	4,60	12,629	0,0	0,00	66,7
		Woche 100	94	3,55	10,333	0,0	0,00	33,3
		Woche 104	80	4,17	12,296	0,0	0,00	66,7
		Woche 108	77	4,33	12,508	0,0	0,00	66,7
		Woche 112	73	3,65	10,485	0,0	0,00	33,3
		Woche 116	68	3,92	10,820	0,0	0,00	33,3
		Woche 120	63	4,76	14,489	0,0	0,00	66,7
		Woche 124	58	5,17	17,440	0,0	0,00	100,0
		Woche 128	59	4,52	13,069	0,0	0,00	66,7
		Woche 132	53	4,40	16,063	0,0	0,00	100,0
		Woche 136	52	2,56	8,969	0,0	0,00	33,3
		Woche 140	48	4,86	13,734	0,0	0,00	66,7
		Woche 144	39	2,56	8,998	0,0	0,00	33,3
		Woche 148	43	2,33	8,592	0,0	0,00	33,3
		Woche 152	41	2,44	8,788	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Diarrhö	Durvalumab (N=264)	Woche 156	37	3,60	10,493	0,0	0,00	33,3
		Woche 160	33	1,01	5,803	0,0	0,00	33,3
		Woche 164	33	2,02	8,077	0,0	0,00	33,3
		Woche 168	29	3,45	10,331	0,0	0,00	33,3
		Woche 172	32	2,08	8,198	0,0	0,00	33,3
		Woche 176	23	5,80	16,368	0,0	0,00	66,7
		Woche 180	21	1,59	7,274	0,0	0,00	33,3
		Woche 184	19	3,51	10,510	0,0	0,00	33,3
		Woche 188	17	1,96	8,085	0,0	0,00	33,3
		Woche 192	17	5,88	17,620	0,0	0,00	66,7
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	3,03	10,050	0,0	0,00	33,3
		Woche 204	7	4,76	12,599	0,0	0,00	33,3
		Woche 208	8	4,17	11,785	0,0	0,00	33,3
		Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	4,76	12,599	0,0	0,00	33,3
		Woche 224	6	5,56	13,608	0,0	0,00	33,3
		Woche 228	6	11,11	17,213	0,0	0,00	33,3
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	8,33	16,667	0,0	0,00	33,3
		Woche 240	3	11,11	19,245	0,0	0,00	33,3
		Woche 244	2	16,67	23,570	0,0	16,67	33,3
		Woche 248	1	33,33	NC	33,3	33,33	33,3
		Woche 252	2	16,67	23,570	0,0	16,67	33,3
	Placebo (N=266)	Baseline [a]	212	6,13	16,836	0,0	0,00	100,0
		Woche 4	230	7,54	18,722	0,0	0,00	100,0
		Woche 8	209	6,38	15,040	0,0	0,00	100,0
		Woche 12	198	6,06	13,736	0,0	0,00	66,7
		Woche 16	197	6,43	15,913	0,0	0,00	100,0
		Woche 20	180	6,11	13,405	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Diarrhö	Placebo (N=266)	Woche 24	172	7,17	17,107	0,0	0,00	100,0
		Woche 28	158	5,91	16,190	0,0	0,00	100,0
		Woche 32	150	6,00	15,481	0,0	0,00	100,0
		Woche 36	141	5,20	13,383	0,0	0,00	66,7
		Woche 40	122	6,28	15,049	0,0	0,00	66,7
		Woche 44	124	6,99	14,272	0,0	0,00	66,7
		Woche 48	121	5,79	14,062	0,0	0,00	66,7
		Woche 52	118	4,52	13,013	0,0	0,00	66,7
		Woche 56	104	6,41	14,745	0,0	0,00	66,7
		Woche 60	98	5,10	12,063	0,0	0,00	33,3
		Woche 64	94	6,38	14,063	0,0	0,00	66,7
		Woche 68	91	6,23	13,064	0,0	0,00	33,3
		Woche 72	86	3,88	10,748	0,0	0,00	33,3
		Woche 76	77	4,76	11,741	0,0	0,00	33,3
		Woche 80	75	5,78	13,834	0,0	0,00	66,7
		Woche 84	75	8,44	15,590	0,0	0,00	66,7
		Woche 88	70	5,24	13,472	0,0	0,00	66,7
		Woche 92	69	5,31	12,292	0,0	0,00	33,3
		Woche 96	64	7,29	15,105	0,0	0,00	66,7
		Woche 100	66	7,07	14,924	0,0	0,00	66,7
		Woche 104	62	6,99	13,680	0,0	0,00	33,3
		Woche 108	59	5,65	12,614	0,0	0,00	33,3
		Woche 112	54	4,94	11,953	0,0	0,00	33,3
		Woche 116	56	5,95	12,882	0,0	0,00	33,3
		Woche 120	51	5,23	12,243	0,0	0,00	33,3
		Woche 124	50	9,33	19,095	0,0	0,00	100,0
		Woche 128	45	8,89	16,514	0,0	0,00	66,7
		Woche 132	44	3,79	10,701	0,0	0,00	33,3
		Woche 136	39	5,13	14,385	0,0	0,00	66,7
		Woche 140	39	5,98	12,959	0,0	0,00	33,3
		Woche 144	35	1,90	7,850	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Diarrhö	Placebo (N=266)	Woche 148	32	5,21	12,297	0,0	0,00	33,3
		Woche 152	33	7,07	13,838	0,0	0,00	33,3
		Woche 156	32	6,25	13,219	0,0	0,00	33,3
		Woche 160	31	8,60	14,827	0,0	0,00	33,3
		Woche 164	24	11,11	18,822	0,0	0,00	66,7
		Woche 168	28	7,14	13,929	0,0	0,00	33,3
		Woche 172	23	5,80	12,918	0,0	0,00	33,3
		Woche 176	21	6,35	13,412	0,0	0,00	33,3
		Woche 180	19	5,26	12,488	0,0	0,00	33,3
		Woche 184	20	5,00	12,212	0,0	0,00	33,3
		Woche 188	18	7,41	14,260	0,0	0,00	33,3
		Woche 192	16	6,25	13,437	0,0	0,00	33,3
		Woche 196	18	5,56	12,783	0,0	0,00	33,3
		Woche 200	19	8,77	15,080	0,0	0,00	33,3
		Woche 204	13	7,69	14,618	0,0	0,00	33,3
		Woche 208	12	5,56	12,975	0,0	0,00	33,3
		Woche 212	15	6,67	13,801	0,0	0,00	33,3
		Woche 216	12	13,89	22,285	0,0	0,00	66,7
		Woche 220	9	18,52	24,216	0,0	0,00	66,7
		Woche 224	11	12,12	16,817	0,0	0,00	33,3
		Woche 228	9	14,81	17,568	0,0	0,00	33,3
		Woche 232	5	13,33	18,257	0,0	0,00	33,3
		Woche 236	5	26,67	14,907	0,0	33,33	33,3
		Woche 240	5	20,00	18,257	0,0	33,33	33,3
		Woche 244	4	33,33	27,217	0,0	33,33	66,7
		Woche 248	2	16,67	23,570	0,0	16,67	33,3
		Woche 252	1	33,33	NC	33,3	33,33	33,3
		Woche 256	1	0,00	NC	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Baseline [a]	216	14,81	19,991	0,0	0,00	100,0
		Woche 4	236	20,34	23,026	0,0	33,33	100,0
		Woche 8	221	23,23	24,892	0,0	33,33	100,0
		Woche 12	202	21,95	24,141	0,0	33,33	100,0
		Woche 16	189	20,81	23,360	0,0	33,33	100,0
		Woche 20	179	21,60	24,330	0,0	33,33	100,0
		Woche 24	169	20,32	23,034	0,0	33,33	100,0
		Woche 28	163	20,45	23,226	0,0	0,00	100,0
		Woche 32	159	22,43	24,734	0,0	33,33	100,0
		Woche 36	149	20,36	21,474	0,0	33,33	100,0
		Woche 40	135	20,00	22,006	0,0	33,33	66,7
		Woche 44	131	20,36	23,597	0,0	0,00	100,0
		Woche 48	123	20,05	22,880	0,0	0,00	66,7
		Woche 52	124	19,62	25,151	0,0	0,00	100,0
		Woche 56	121	22,04	23,787	0,0	33,33	100,0
		Woche 60	118	18,93	23,257	0,0	0,00	100,0
		Woche 64	113	19,47	24,691	0,0	0,00	100,0
		Woche 68	103	21,36	24,188	0,0	33,33	100,0
		Woche 72	100	19,00	22,847	0,0	0,00	100,0
		Woche 76	98	20,41	25,612	0,0	0,00	100,0
		Woche 80	97	19,93	24,372	0,0	0,00	100,0
		Woche 84	97	17,87	23,601	0,0	0,00	100,0
		Woche 88	91	20,15	24,282	0,0	0,00	100,0
		Woche 92	92	19,93	22,678	0,0	0,00	66,7
		Woche 96	87	19,54	25,695	0,0	0,00	100,0
		Woche 100	94	19,86	22,035	0,0	33,33	100,0
		Woche 104	80	20,42	24,010	0,0	0,00	100,0
		Woche 108	77	19,48	21,865	0,0	0,00	66,7
		Woche 112	73	24,20	24,381	0,0	33,33	100,0
		Woche 116	68	23,53	24,474	0,0	33,33	100,0
		Woche 120	63	24,87	27,414	0,0	33,33	100,0

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Woche 124	58	16,67	21,854	0,0	0,00	100,0
		Woche 128	59	19,77	21,548	0,0	33,33	66,7
		Woche 132	53	16,35	21,306	0,0	0,00	66,7
		Woche 136	52	18,59	24,176	0,0	0,00	100,0
		Woche 140	48	18,06	24,753	0,0	0,00	100,0
		Woche 144	39	16,24	22,778	0,0	0,00	100,0
		Woche 148	43	17,83	25,561	0,0	0,00	100,0
		Woche 152	41	17,89	22,482	0,0	0,00	66,7
		Woche 156	37	19,82	25,410	0,0	0,00	66,7
		Woche 160	33	21,21	24,746	0,0	0,00	66,7
		Woche 164	33	16,16	23,748	0,0	0,00	66,7
		Woche 168	29	17,24	26,157	0,0	0,00	100,0
		Woche 172	32	16,67	25,400	0,0	0,00	66,7
		Woche 176	23	23,19	27,404	0,0	0,00	66,7
		Woche 180	21	17,46	24,987	0,0	0,00	66,7
		Woche 184	19	26,32	30,589	0,0	33,33	100,0
		Woche 188	17	25,49	30,114	0,0	0,00	66,7
		Woche 192	17	23,53	30,652	0,0	0,00	100,0
		Woche 196	14	26,19	23,310	0,0	33,33	66,7
		Woche 200	11	24,24	21,556	0,0	33,33	66,7
		Woche 204	7	14,29	17,817	0,0	0,00	33,3
		Woche 208	8	20,83	24,801	0,0	16,67	66,7
		Woche 212	7	14,29	17,817	0,0	0,00	33,3
		Woche 216	9	18,52	17,568	0,0	33,33	33,3
		Woche 220	7	9,52	16,265	0,0	0,00	33,3
		Woche 224	6	11,11	17,213	0,0	0,00	33,3
		Woche 228	6	11,11	17,213	0,0	0,00	33,3
		Woche 232	6	11,11	17,213	0,0	0,00	33,3
		Woche 236	4	8,33	16,667	0,0	0,00	33,3
		Woche 240	3	11,11	19,245	0,0	0,00	33,3
		Woche 244	2	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	212	18,40	22,767	0,0	0,00	100,0
		Woche 4	230	23,33	24,160	0,0	33,33	100,0
		Woche 8	209	25,36	22,650	0,0	33,33	66,7
		Woche 12	198	24,92	24,837	0,0	33,33	100,0
		Woche 16	197	24,53	23,362	0,0	33,33	100,0
		Woche 20	180	23,15	23,398	0,0	33,33	100,0
		Woche 24	172	21,71	21,790	0,0	33,33	100,0
		Woche 28	158	21,31	22,008	0,0	33,33	100,0
		Woche 32	150	21,56	21,893	0,0	33,33	100,0
		Woche 36	141	21,51	21,133	0,0	33,33	100,0
		Woche 40	122	21,31	24,643	0,0	33,33	100,0
		Woche 44	124	21,51	23,740	0,0	33,33	100,0
		Woche 48	121	19,56	23,042	0,0	0,00	100,0
		Woche 52	118	19,77	23,565	0,0	0,00	100,0
		Woche 56	104	23,40	22,218	0,0	33,33	100,0
		Woche 60	98	21,43	23,570	0,0	33,33	100,0
		Woche 64	94	21,99	22,694	0,0	33,33	100,0
		Woche 68	91	19,41	21,120	0,0	33,33	100,0
		Woche 72	86	20,93	22,893	0,0	33,33	100,0
		Woche 76	77	21,65	22,792	0,0	33,33	100,0
		Woche 80	75	22,22	20,010	0,0	33,33	66,7
		Woche 84	75	22,22	19,245	0,0	33,33	66,7
		Woche 88	70	23,33	20,735	0,0	33,33	66,7
		Woche 92	69	22,71	20,999	0,0	33,33	100,0
		Woche 96	64	21,35	20,024	0,0	33,33	66,7
		Woche 100	66	21,21	20,785	0,0	33,33	66,7
		Woche 104	62	19,35	18,651	0,0	33,33	66,7
		Woche 108	59	21,47	22,963	0,0	33,33	100,0
		Woche 112	54	22,84	22,266	0,0	33,33	66,7

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Placebo (N=266)	Woche 116	56	22,02	21,345	0,0	33,33	66,7
		Woche 120	51	20,26	20,087	0,0	33,33	66,7
		Woche 124	50	22,67	21,759	0,0	33,33	66,7
		Woche 128	45	22,96	19,876	0,0	33,33	66,7
		Woche 132	44	26,52	22,250	0,0	33,33	66,7
		Woche 136	39	23,08	20,454	0,0	33,33	66,7
		Woche 140	39	24,79	21,245	0,0	33,33	66,7
		Woche 144	35	22,86	22,537	0,0	33,33	66,7
		Woche 148	32	26,04	18,422	0,0	33,33	66,7
		Woche 152	33	24,24	22,473	0,0	33,33	66,7
		Woche 156	32	26,04	21,972	0,0	33,33	66,7
		Woche 160	31	26,88	23,443	0,0	33,33	66,7
		Woche 164	24	27,78	21,234	0,0	33,33	66,7
		Woche 168	28	23,81	23,757	0,0	33,33	66,7
		Woche 172	23	27,54	23,894	0,0	33,33	66,7
		Woche 176	21	26,98	24,987	0,0	33,33	66,7
		Woche 180	19	29,82	26,977	0,0	33,33	66,7
		Woche 184	20	30,00	30,397	0,0	33,33	100,0
		Woche 188	18	24,07	25,063	0,0	33,33	66,7
		Woche 192	16	29,17	23,960	0,0	33,33	66,7
		Woche 196	18	24,07	25,063	0,0	33,33	66,7
		Woche 200	19	28,07	25,491	0,0	33,33	66,7
		Woche 204	13	35,90	25,318	0,0	33,33	66,7
		Woche 208	12	25,00	25,126	0,0	33,33	66,7
		Woche 212	15	26,67	25,820	0,0	33,33	66,7
		Woche 216	12	22,22	21,711	0,0	33,33	66,7
		Woche 220	9	33,33	28,868	0,0	33,33	66,7
		Woche 224	11	24,24	26,208	0,0	33,33	66,7
		Woche 228	9	29,63	26,058	0,0	33,33	66,7
		Woche 232	5	20,00	18,257	0,0	33,33	33,3
		Woche 236	5	33,33	23,570	0,0	33,33	66,7

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Placebo (N=266)	Woche 240	5	33,33	23,570	0,0	33,33	66,7
		Woche 244	4	16,67	19,245	0,0	16,67	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Finanzielle Schwierigkeiten	Durvalumab (N=264)	Baseline [a]	216	16,20	25,105	0,0	0,00	100,0
		Woche 4	236	11,86	22,816	0,0	0,00	100,0
		Woche 8	221	13,73	24,978	0,0	0,00	100,0
		Woche 12	202	14,03	24,119	0,0	0,00	100,0
		Woche 16	189	12,52	22,588	0,0	0,00	100,0
		Woche 20	179	14,53	24,735	0,0	0,00	100,0
		Woche 24	169	15,38	24,125	0,0	0,00	100,0
		Woche 28	163	15,54	25,735	0,0	0,00	100,0
		Woche 32	159	15,93	25,666	0,0	0,00	100,0
		Woche 36	149	15,66	26,154	0,0	0,00	100,0
		Woche 40	135	14,32	25,929	0,0	0,00	100,0
		Woche 44	131	12,47	23,871	0,0	0,00	100,0
		Woche 48	123	15,72	27,436	0,0	0,00	100,0
		Woche 52	124	13,71	24,789	0,0	0,00	100,0
		Woche 56	121	14,33	24,656	0,0	0,00	100,0
		Woche 60	118	14,97	25,634	0,0	0,00	100,0
		Woche 64	113	13,86	24,691	0,0	0,00	100,0
		Woche 68	103	12,62	23,392	0,0	0,00	100,0
		Woche 72	100	15,67	27,404	0,0	0,00	100,0
		Woche 76	98	15,65	26,305	0,0	0,00	100,0
		Woche 80	97	15,81	27,256	0,0	0,00	100,0
		Woche 84	97	13,40	23,892	0,0	0,00	100,0
		Woche 88	91	15,02	25,946	0,0	0,00	100,0
		Woche 92	92	14,49	24,858	0,0	0,00	100,0
		Woche 96	87	16,48	26,352	0,0	0,00	100,0
		Woche 100	94	11,35	21,055	0,0	0,00	100,0

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Finanzielle Schwierigkeiten	Durvalumab (N=264)	Woche 104	80	13,75	24,703	0,0	0,00	100,0
		Woche 108	77	14,72	24,479	0,0	0,00	100,0
		Woche 112	73	11,87	21,780	0,0	0,00	100,0
		Woche 116	68	11,76	22,129	0,0	0,00	100,0
		Woche 120	63	13,23	23,600	0,0	0,00	100,0
		Woche 124	58	10,34	19,948	0,0	0,00	66,7
		Woche 128	59	11,30	22,836	0,0	0,00	100,0
		Woche 132	53	11,95	18,599	0,0	0,00	66,7
		Woche 136	52	7,69	18,216	0,0	0,00	66,7
		Woche 140	48	11,81	23,308	0,0	0,00	100,0
		Woche 144	39	10,26	20,454	0,0	0,00	66,7
		Woche 148	43	10,85	20,212	0,0	0,00	66,7
		Woche 152	41	7,32	15,833	0,0	0,00	66,7
		Woche 156	37	13,51	22,851	0,0	0,00	66,7
		Woche 160	33	10,10	19,516	0,0	0,00	66,7
		Woche 164	33	8,08	18,690	0,0	0,00	66,7
		Woche 168	29	9,20	17,586	0,0	0,00	66,7
		Woche 172	32	7,29	16,361	0,0	0,00	66,7
		Woche 176	23	4,35	11,478	0,0	0,00	33,3
		Woche 180	21	4,76	11,952	0,0	0,00	33,3
		Woche 184	19	5,26	12,488	0,0	0,00	33,3
		Woche 188	17	9,80	25,725	0,0	0,00	100,0
		Woche 192	17	7,84	25,082	0,0	0,00	100,0
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	3,03	10,050	0,0	0,00	33,3
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	0,00	0,000	0,0	0,00	0,0
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Finanzielle Schwierigkeiten	Durvalumab (N=264)	Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	212	17,30	23,506	0,0	0,00	100,0
		Woche 4	230	16,38	24,278	0,0	0,00	100,0
		Woche 8	209	15,79	24,252	0,0	0,00	100,0
		Woche 12	198	15,49	24,365	0,0	0,00	100,0
		Woche 16	197	14,55	23,864	0,0	0,00	100,0
		Woche 20	180	13,89	21,684	0,0	0,00	100,0
		Woche 24	172	13,37	19,961	0,0	0,00	66,7
		Woche 28	158	14,56	21,754	0,0	0,00	100,0
		Woche 32	150	13,56	21,187	0,0	0,00	100,0
		Woche 36	141	13,00	18,590	0,0	0,00	66,7
		Woche 40	122	12,30	20,642	0,0	0,00	100,0
		Woche 44	124	12,37	20,591	0,0	0,00	100,0
		Woche 48	121	11,57	17,591	0,0	0,00	66,7
		Woche 52	118	11,58	17,637	0,0	0,00	66,7
		Woche 56	104	11,86	19,105	0,0	0,00	66,7
		Woche 60	98	13,27	20,160	0,0	0,00	66,7
		Woche 64	94	12,41	19,543	0,0	0,00	66,7
		Woche 68	91	10,99	19,910	0,0	0,00	100,0
		Woche 72	86	11,63	18,972	0,0	0,00	66,7
		Woche 76	77	12,55	21,656	0,0	0,00	66,7
		Woche 80	75	13,78	24,564	0,0	0,00	100,0
		Woche 84	75	12,44	22,443	0,0	0,00	100,0
		Woche 88	70	14,29	20,907	0,0	0,00	66,7
		Woche 92	69	10,14	19,220	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Finanzielle Schwierigkeiten	Placebo (N=266)	Woche 96	64	12,50	22,616	0,0	0,00	100,0
		Woche 100	66	14,65	21,978	0,0	0,00	100,0
		Woche 104	62	16,13	25,423	0,0	0,00	100,0
		Woche 108	59	13,56	23,258	0,0	0,00	100,0
		Woche 112	54	12,35	22,706	0,0	0,00	100,0
		Woche 116	56	11,90	22,409	0,0	0,00	100,0
		Woche 120	51	14,38	23,338	0,0	0,00	100,0
		Woche 124	50	11,33	21,936	0,0	0,00	100,0
		Woche 128	45	11,11	22,473	0,0	0,00	100,0
		Woche 132	44	13,64	24,185	0,0	0,00	100,0
		Woche 136	39	12,82	24,916	0,0	0,00	100,0
		Woche 140	39	11,97	23,554	0,0	0,00	100,0
		Woche 144	35	12,38	25,675	0,0	0,00	100,0
		Woche 148	32	12,50	23,570	0,0	0,00	100,0
		Woche 152	33	14,14	26,392	0,0	0,00	100,0
		Woche 156	32	14,58	28,001	0,0	0,00	100,0
		Woche 160	31	16,13	27,040	0,0	0,00	100,0
		Woche 164	24	15,28	27,766	0,0	0,00	100,0
		Woche 168	28	17,86	30,741	0,0	0,00	100,0
		Woche 172	23	13,04	21,879	0,0	0,00	66,7
		Woche 176	21	12,70	19,653	0,0	0,00	66,7
		Woche 180	19	12,28	19,909	0,0	0,00	66,7
		Woche 184	20	11,67	19,571	0,0	0,00	66,7
		Woche 188	18	11,11	19,803	0,0	0,00	66,7
		Woche 192	16	12,50	20,638	0,0	0,00	66,7
		Woche 196	18	9,26	19,150	0,0	0,00	66,7
		Woche 200	19	10,53	19,413	0,0	0,00	66,7
		Woche 204	13	12,82	16,879	0,0	0,00	33,3
		Woche 208	12	5,56	12,975	0,0	0,00	33,3
		Woche 212	15	8,89	15,258	0,0	0,00	33,3
		Woche 216	12	8,33	15,076	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Finanzielle Schwierigkeiten	Placebo (N=266)	Woche 220	9	18,52	24,216	0,0	0,00	66,7
		Woche 224	11	9,09	15,570	0,0	0,00	33,3
		Woche 228	9	3,70	11,111	0,0	0,00	33,3
		Woche 232	5	13,33	18,257	0,0	0,00	33,3
		Woche 236	5	6,67	14,907	0,0	0,00	33,3
		Woche 240	5	6,67	14,907	0,0	0,00	33,3
		Woche 244	4	8,33	16,667	0,0	0,00	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Schlaflosigkeit	Durvalumab (N=264)	Baseline [a]	216	16,05	24,051	0,0	0,00	100,0
		Woche 4	236	14,69	22,615	0,0	0,00	100,0
		Woche 8	221	18,85	25,256	0,0	0,00	100,0
		Woche 12	202	16,67	24,035	0,0	0,00	100,0
		Woche 16	189	16,58	23,726	0,0	0,00	100,0
		Woche 20	179	17,88	25,296	0,0	0,00	100,0
		Woche 24	169	19,53	24,802	0,0	0,00	100,0
		Woche 28	163	19,43	24,516	0,0	0,00	100,0
		Woche 32	159	17,61	23,958	0,0	0,00	100,0
		Woche 36	149	20,58	25,585	0,0	0,00	100,0
		Woche 40	135	15,80	22,242	0,0	0,00	100,0
		Woche 44	131	17,05	22,020	0,0	0,00	100,0
		Woche 48	123	20,05	25,515	0,0	0,00	100,0
		Woche 52	124	15,59	21,437	0,0	0,00	66,7
		Woche 56	121	19,83	24,562	0,0	0,00	100,0
		Woche 60	118	18,64	26,345	0,0	0,00	100,0
		Woche 64	113	17,70	23,600	0,0	0,00	100,0
		Woche 68	103	20,39	24,358	0,0	0,00	100,0
		Woche 72	100	17,00	22,471	0,0	0,00	66,7
		Woche 76	98	18,71	23,481	0,0	0,00	66,7
		Woche 80	97	18,56	25,445	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schlaflosigkeit	Durvalumab (N=264)	Woche 84	97	18,21	25,468	0,0	0,00	100,0
		Woche 88	91	16,48	24,532	0,0	0,00	100,0
		Woche 92	92	17,75	24,436	0,0	0,00	100,0
		Woche 96	87	17,62	26,821	0,0	0,00	100,0
		Woche 100	94	17,38	23,812	0,0	0,00	100,0
		Woche 104	80	16,25	23,715	0,0	0,00	100,0
		Woche 108	77	14,72	22,616	0,0	0,00	100,0
		Woche 112	73	16,89	24,922	0,0	0,00	100,0
		Woche 116	68	16,67	25,432	0,0	0,00	100,0
		Woche 120	63	16,93	27,352	0,0	0,00	100,0
		Woche 124	58	16,09	25,163	0,0	0,00	100,0
		Woche 128	59	15,25	25,007	0,0	0,00	100,0
		Woche 132	53	11,32	21,626	0,0	0,00	100,0
		Woche 136	52	16,03	25,127	0,0	0,00	100,0
		Woche 140	48	11,81	18,818	0,0	0,00	66,7
		Woche 144	39	14,53	23,933	0,0	0,00	100,0
		Woche 148	43	17,83	22,241	0,0	0,00	66,7
		Woche 152	41	15,45	21,210	0,0	0,00	66,7
		Woche 156	37	17,12	25,606	0,0	0,00	100,0
		Woche 160	33	19,19	26,392	0,0	0,00	100,0
		Woche 164	33	15,15	26,472	0,0	0,00	100,0
		Woche 168	29	11,49	16,124	0,0	0,00	33,3
		Woche 172	32	14,58	22,300	0,0	0,00	66,7
		Woche 176	23	14,49	24,259	0,0	0,00	66,7
		Woche 180	21	17,46	24,987	0,0	0,00	66,7
		Woche 184	19	10,53	15,919	0,0	0,00	33,3
		Woche 188	17	15,69	20,809	0,0	0,00	66,7
		Woche 192	17	15,69	29,149	0,0	0,00	100,0
		Woche 196	14	11,90	21,111	0,0	0,00	66,7
		Woche 200	11	15,15	22,918	0,0	0,00	66,7
		Woche 204	7	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schlaflosigkeit	Durvalumab (N=264)	Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	9,52	16,265	0,0	0,00	33,3
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	5,56	13,608	0,0	0,00	33,3
		Woche 228	6	5,56	13,608	0,0	0,00	33,3
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	212	17,45	24,809	0,0	0,00	100,0
		Woche 4	230	18,26	25,591	0,0	0,00	100,0
		Woche 8	209	20,89	25,412	0,0	0,00	100,0
		Woche 12	198	19,02	27,131	0,0	0,00	100,0
		Woche 16	197	20,30	26,610	0,0	0,00	100,0
		Woche 20	180	16,48	22,969	0,0	0,00	100,0
		Woche 24	172	17,25	24,310	0,0	0,00	100,0
		Woche 28	158	14,56	23,018	0,0	0,00	100,0
		Woche 32	150	19,56	25,671	0,0	0,00	100,0
		Woche 36	141	16,78	23,779	0,0	0,00	100,0
		Woche 40	122	18,03	22,329	0,0	0,00	100,0
		Woche 44	124	16,13	21,874	0,0	0,00	100,0
		Woche 48	121	17,63	23,204	0,0	0,00	100,0
		Woche 52	118	15,54	21,209	0,0	0,00	66,7
		Woche 56	104	17,63	22,735	0,0	0,00	100,0
		Woche 60	98	18,03	23,039	0,0	0,00	66,7
		Woche 64	94	16,31	21,721	0,0	0,00	100,0
		Woche 68	91	16,85	22,429	0,0	0,00	100,0
		Woche 72	86	13,95	21,368	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schlaflosigkeit	Placebo (N=266)	Woche 76	77	20,78	25,385	0,0	0,00	100,0
		Woche 80	75	20,44	24,442	0,0	0,00	100,0
		Woche 84	75	17,33	24,112	0,0	0,00	100,0
		Woche 88	70	18,10	24,531	0,0	0,00	100,0
		Woche 92	69	15,46	22,564	0,0	0,00	66,7
		Woche 96	64	15,10	20,513	0,0	0,00	66,7
		Woche 100	66	19,70	26,134	0,0	0,00	100,0
		Woche 104	62	14,52	20,575	0,0	0,00	100,0
		Woche 108	59	18,08	25,762	0,0	0,00	100,0
		Woche 112	54	19,14	25,577	0,0	0,00	100,0
		Woche 116	56	13,69	21,814	0,0	0,00	100,0
		Woche 120	51	18,30	23,394	0,0	0,00	100,0
		Woche 124	50	15,33	23,532	0,0	0,00	100,0
		Woche 128	45	18,52	26,165	0,0	0,00	100,0
		Woche 132	44	20,45	28,042	0,0	0,00	100,0
		Woche 136	39	14,53	26,263	0,0	0,00	100,0
		Woche 140	39	17,95	23,996	0,0	0,00	66,7
		Woche 144	35	10,48	17,660	0,0	0,00	66,7
		Woche 148	32	15,62	18,902	0,0	0,00	66,7
		Woche 152	33	14,14	22,096	0,0	0,00	66,7
		Woche 156	32	14,58	20,631	0,0	0,00	66,7
		Woche 160	31	11,83	18,355	0,0	0,00	66,7
		Woche 164	24	13,89	19,453	0,0	0,00	66,7
		Woche 168	28	9,52	19,994	0,0	0,00	66,7
		Woche 172	23	13,04	19,434	0,0	0,00	66,7
		Woche 176	21	11,11	19,245	0,0	0,00	66,7
		Woche 180	19	10,53	22,368	0,0	0,00	66,7
		Woche 184	20	8,33	18,337	0,0	0,00	66,7
		Woche 188	18	5,56	12,783	0,0	0,00	33,3
		Woche 192	16	8,33	14,907	0,0	0,00	33,3
		Woche 196	18	5,56	17,150	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schlaflosigkeit	Placebo (N=266)	Woche 200	19	8,77	18,732	0,0	0,00	66,7
		Woche 204	13	12,82	25,598	0,0	0,00	66,7
		Woche 208	12	16,67	22,473	0,0	0,00	66,7
		Woche 212	15	11,11	20,574	0,0	0,00	66,7
		Woche 216	12	13,89	26,432	0,0	0,00	66,7
		Woche 220	9	7,41	14,699	0,0	0,00	33,3
		Woche 224	11	6,06	20,101	0,0	0,00	66,7
		Woche 228	9	11,11	23,570	0,0	0,00	66,7
		Woche 232	5	20,00	29,814	0,0	0,00	66,7
		Woche 236	5	20,00	29,814	0,0	0,00	66,7
		Woche 240	5	20,00	29,814	0,0	0,00	66,7
		Woche 244	4	16,67	19,245	0,0	16,67	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Verstopfung	Durvalumab (N=264)	Baseline [a]	216	11,11	20,835	0,0	0,00	100,0
		Woche 4	236	10,03	17,883	0,0	0,00	66,7
		Woche 8	221	11,92	21,410	0,0	0,00	100,0
		Woche 12	202	12,87	21,014	0,0	0,00	100,0
		Woche 16	189	14,64	23,134	0,0	0,00	100,0
		Woche 20	179	13,04	21,583	0,0	0,00	100,0
		Woche 24	169	14,60	23,514	0,0	0,00	100,0
		Woche 28	163	11,66	20,798	0,0	0,00	66,7
		Woche 32	159	10,48	19,894	0,0	0,00	100,0
		Woche 36	149	12,75	20,722	0,0	0,00	100,0
		Woche 40	135	11,60	20,491	0,0	0,00	100,0
		Woche 44	131	12,98	22,484	0,0	0,00	100,0
		Woche 48	123	15,72	22,714	0,0	0,00	100,0
		Woche 52	124	13,71	24,049	0,0	0,00	100,0
		Woche 56	121	14,05	22,258	0,0	0,00	100,0
		Woche 60	118	12,15	18,317	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Verstopfung	Durvalumab (N=264)	Woche 64	113	13,57	22,110	0,0	0,00	100,0
		Woche 68	103	12,30	20,340	0,0	0,00	66,7
		Woche 72	100	12,00	20,932	0,0	0,00	100,0
		Woche 76	98	11,90	18,691	0,0	0,00	66,7
		Woche 80	97	13,75	19,692	0,0	0,00	66,7
		Woche 84	97	13,06	21,814	0,0	0,00	100,0
		Woche 88	91	12,09	19,574	0,0	0,00	100,0
		Woche 92	92	11,96	20,123	0,0	0,00	66,7
		Woche 96	87	11,49	19,574	0,0	0,00	66,7
		Woche 100	94	13,12	21,429	0,0	0,00	100,0
		Woche 104	80	12,08	22,024	0,0	0,00	100,0
		Woche 108	77	9,52	20,129	0,0	0,00	100,0
		Woche 112	73	13,24	20,593	0,0	0,00	100,0
		Woche 116	68	9,80	19,152	0,0	0,00	100,0
		Woche 120	63	12,17	19,215	0,0	0,00	66,7
		Woche 124	58	17,24	21,846	0,0	0,00	66,7
		Woche 128	59	10,17	20,765	0,0	0,00	100,0
		Woche 132	53	9,43	20,019	0,0	0,00	100,0
		Woche 136	52	10,90	17,113	0,0	0,00	66,7
		Woche 140	48	11,11	17,305	0,0	0,00	66,7
		Woche 144	39	17,95	27,409	0,0	0,00	100,0
		Woche 148	43	13,95	20,871	0,0	0,00	66,7
		Woche 152	41	16,26	23,714	0,0	0,00	100,0
		Woche 156	37	11,71	22,521	0,0	0,00	100,0
		Woche 160	33	12,12	18,292	0,0	0,00	66,7
		Woche 164	33	11,11	19,837	0,0	0,00	66,7
		Woche 168	29	9,20	17,586	0,0	0,00	66,7
		Woche 172	32	7,29	16,361	0,0	0,00	66,7
		Woche 176	23	13,04	19,434	0,0	0,00	66,7
		Woche 180	21	14,29	24,881	0,0	0,00	66,7
		Woche 184	19	7,02	13,962	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Verstopfung	Durvalumab (N=264)	Woche 188	17	15,69	20,809	0,0	0,00	66,7
		Woche 192	17	17,65	20,809	0,0	0,00	66,7
		Woche 196	14	9,52	15,627	0,0	0,00	33,3
		Woche 200	11	12,12	16,817	0,0	0,00	33,3
		Woche 204	7	9,52	16,265	0,0	0,00	33,3
		Woche 208	8	8,33	15,430	0,0	0,00	33,3
		Woche 212	7	9,52	16,265	0,0	0,00	33,3
		Woche 216	9	11,11	16,667	0,0	0,00	33,3
		Woche 220	7	4,76	12,599	0,0	0,00	33,3
		Woche 224	6	11,11	17,213	0,0	0,00	33,3
		Woche 228	6	11,11	17,213	0,0	0,00	33,3
		Woche 232	6	11,11	17,213	0,0	0,00	33,3
		Woche 236	4	16,67	19,245	0,0	16,67	33,3
		Woche 240	3	22,22	19,245	0,0	33,33	33,3
		Woche 244	2	33,33	0,000	33,3	33,33	33,3
		Woche 248	1	33,33	NC	33,3	33,33	33,3
		Woche 252	2	16,67	23,570	0,0	16,67	33,3
	Placebo (N=266)	Baseline [a]	212	11,48	21,753	0,0	0,00	100,0
		Woche 4	230	10,72	21,827	0,0	0,00	100,0
		Woche 8	209	11,32	21,041	0,0	0,00	100,0
		Woche 12	198	12,46	21,811	0,0	0,00	100,0
		Woche 16	197	13,20	21,178	0,0	0,00	100,0
		Woche 20	180	13,52	22,200	0,0	0,00	100,0
		Woche 24	172	11,82	19,640	0,0	0,00	66,7
		Woche 28	158	13,08	24,623	0,0	0,00	100,0
		Woche 32	150	13,78	24,175	0,0	0,00	100,0
		Woche 36	141	10,64	22,650	0,0	0,00	100,0
		Woche 40	122	10,93	21,187	0,0	0,00	100,0
		Woche 44	124	9,68	20,284	0,0	0,00	100,0
		Woche 48	121	12,40	18,823	0,0	0,00	66,7
		Woche 52	118	10,45	20,764	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Verstopfung	Placebo (N=266)	Woche 56	104	11,86	19,662	0,0	0,00	66,7
		Woche 60	98	9,18	19,014	0,0	0,00	100,0
		Woche 64	94	10,64	19,683	0,0	0,00	100,0
		Woche 68	91	10,62	19,801	0,0	0,00	100,0
		Woche 72	86	13,18	22,451	0,0	0,00	100,0
		Woche 76	77	11,26	20,669	0,0	0,00	100,0
		Woche 80	75	13,78	21,984	0,0	0,00	100,0
		Woche 84	75	12,89	19,677	0,0	0,00	66,7
		Woche 88	70	10,00	20,735	0,0	0,00	100,0
		Woche 92	69	10,63	20,999	0,0	0,00	100,0
		Woche 96	64	14,58	21,311	0,0	0,00	66,7
		Woche 100	66	14,14	21,131	0,0	0,00	66,7
		Woche 104	62	11,29	22,538	0,0	0,00	100,0
		Woche 108	59	12,99	20,545	0,0	0,00	66,7
		Woche 112	54	16,05	24,003	0,0	0,00	100,0
		Woche 116	56	8,93	16,195	0,0	0,00	66,7
		Woche 120	51	10,46	18,245	0,0	0,00	66,7
		Woche 124	50	6,67	13,469	0,0	0,00	33,3
		Woche 128	45	11,11	17,408	0,0	0,00	66,7
		Woche 132	44	14,39	23,181	0,0	0,00	66,7
		Woche 136	39	12,82	22,446	0,0	0,00	100,0
		Woche 140	39	13,68	21,245	0,0	0,00	66,7
		Woche 144	35	15,24	24,711	0,0	0,00	100,0
		Woche 148	32	12,50	21,997	0,0	0,00	100,0
		Woche 152	33	9,09	17,225	0,0	0,00	66,7
		Woche 156	32	10,42	19,743	0,0	0,00	66,7
		Woche 160	31	15,05	22,507	0,0	0,00	66,7
		Woche 164	24	8,33	14,744	0,0	0,00	33,3
		Woche 168	28	5,95	13,001	0,0	0,00	33,3
		Woche 172	23	11,59	19,092	0,0	0,00	66,7
		Woche 176	21	9,52	18,687	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.1 ADRIATIC: Summary of EORTC QLQ-C30 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Verstopfung	Placebo (N=266)	Woche 180	19	5,26	12,488	0,0	0,00	33,3
		Woche 184	20	8,33	14,809	0,0	0,00	33,3
		Woche 188	18	5,56	12,783	0,0	0,00	33,3
		Woche 192	16	8,33	14,907	0,0	0,00	33,3
		Woche 196	18	3,70	10,779	0,0	0,00	33,3
		Woche 200	19	5,26	12,488	0,0	0,00	33,3
		Woche 204	13	7,69	14,618	0,0	0,00	33,3
		Woche 208	12	11,11	16,412	0,0	0,00	33,3
		Woche 212	15	6,67	13,801	0,0	0,00	33,3
		Woche 216	12	8,33	15,076	0,0	0,00	33,3
		Woche 220	9	3,70	11,111	0,0	0,00	33,3
		Woche 224	11	6,06	13,484	0,0	0,00	33,3
		Woche 228	9	11,11	16,667	0,0	0,00	33,3
		Woche 232	5	13,33	18,257	0,0	0,00	33,3
		Woche 236	5	6,67	14,907	0,0	0,00	33,3
		Woche 240	5	0,00	0,000	0,0	0,00	0,0
		Woche 244	4	8,33	16,667	0,0	0,00	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanpra 10JUN2025:14:15

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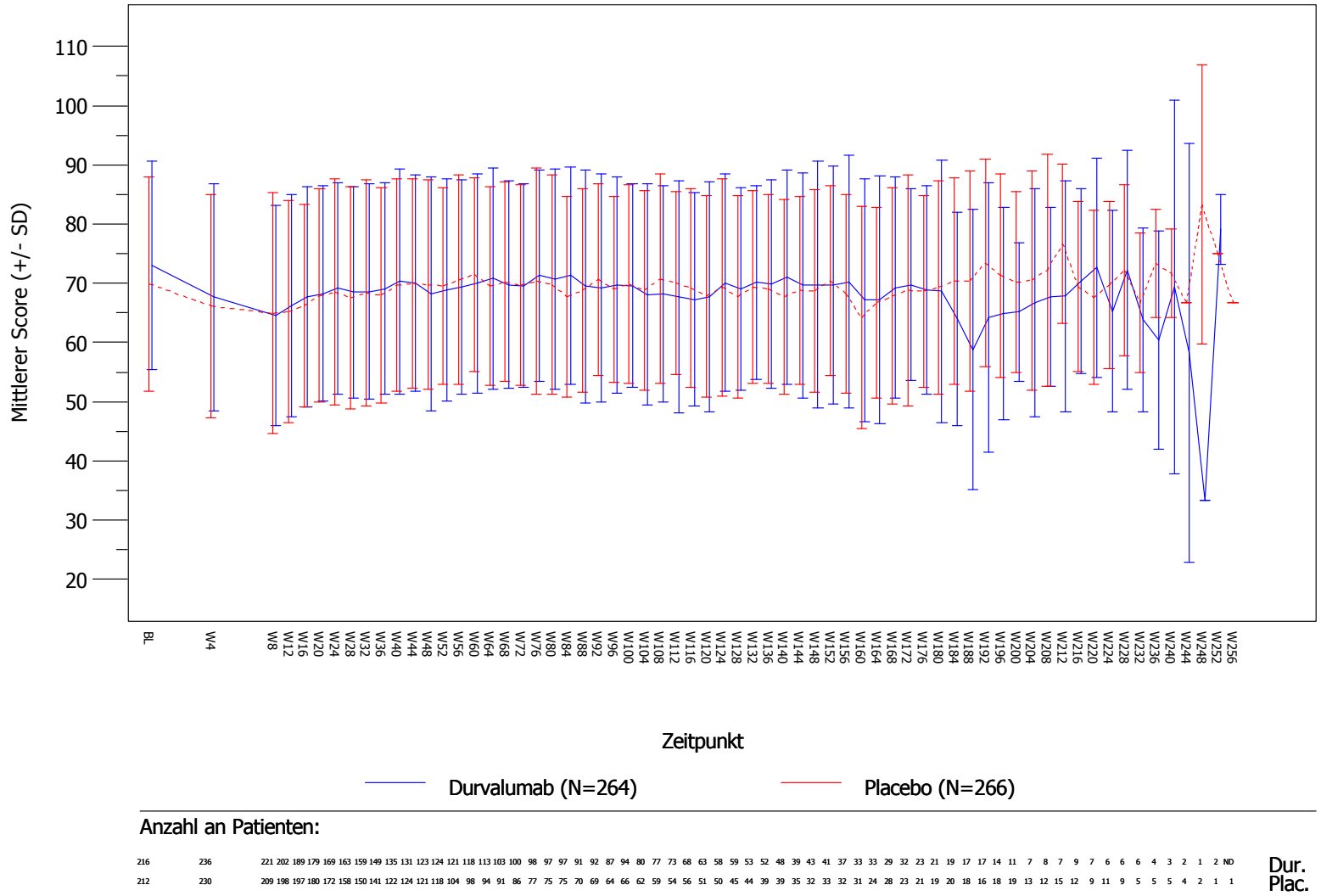
Figure 3.4.1.1 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Global QoL/health status across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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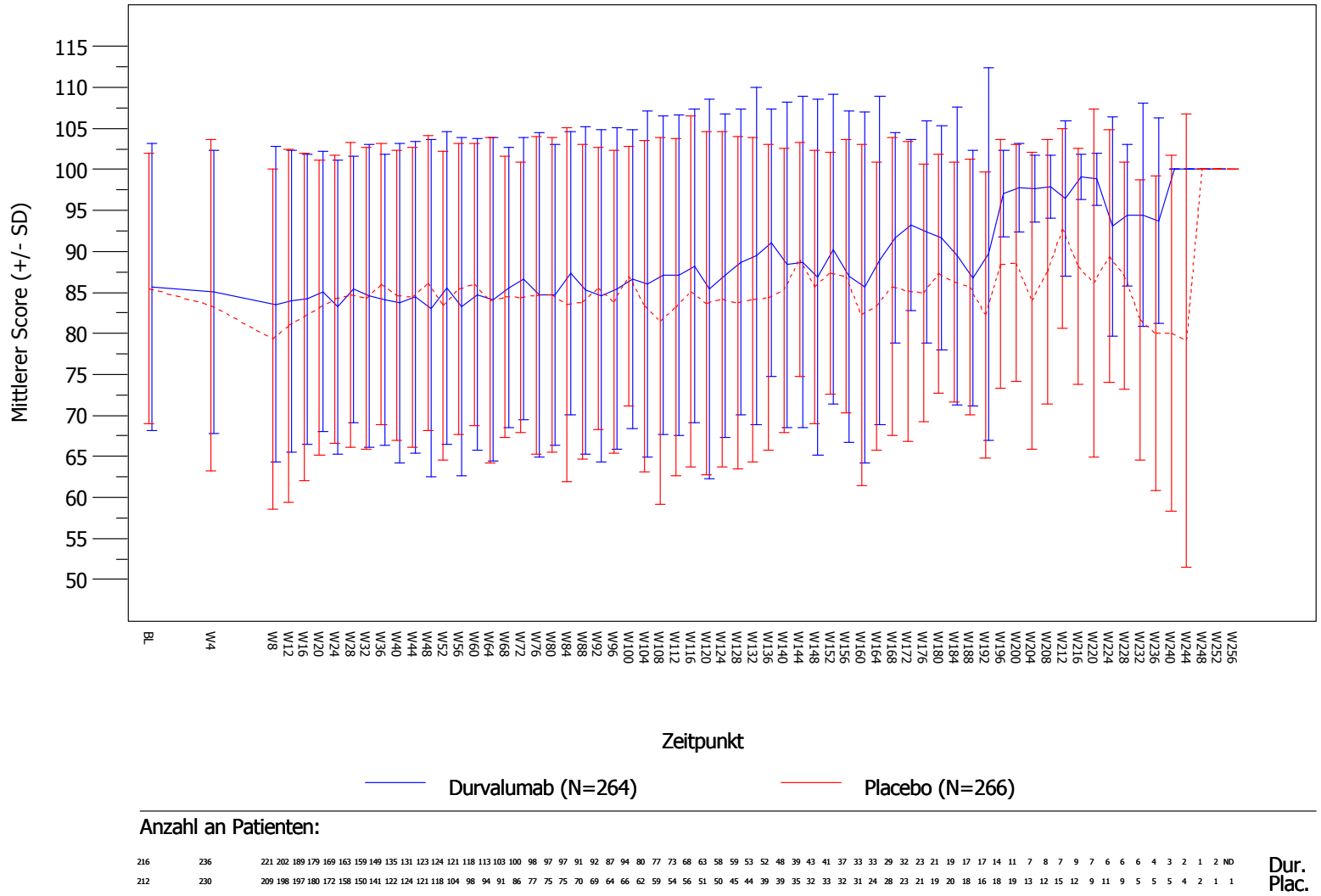
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.2 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Functional scale: Emotional across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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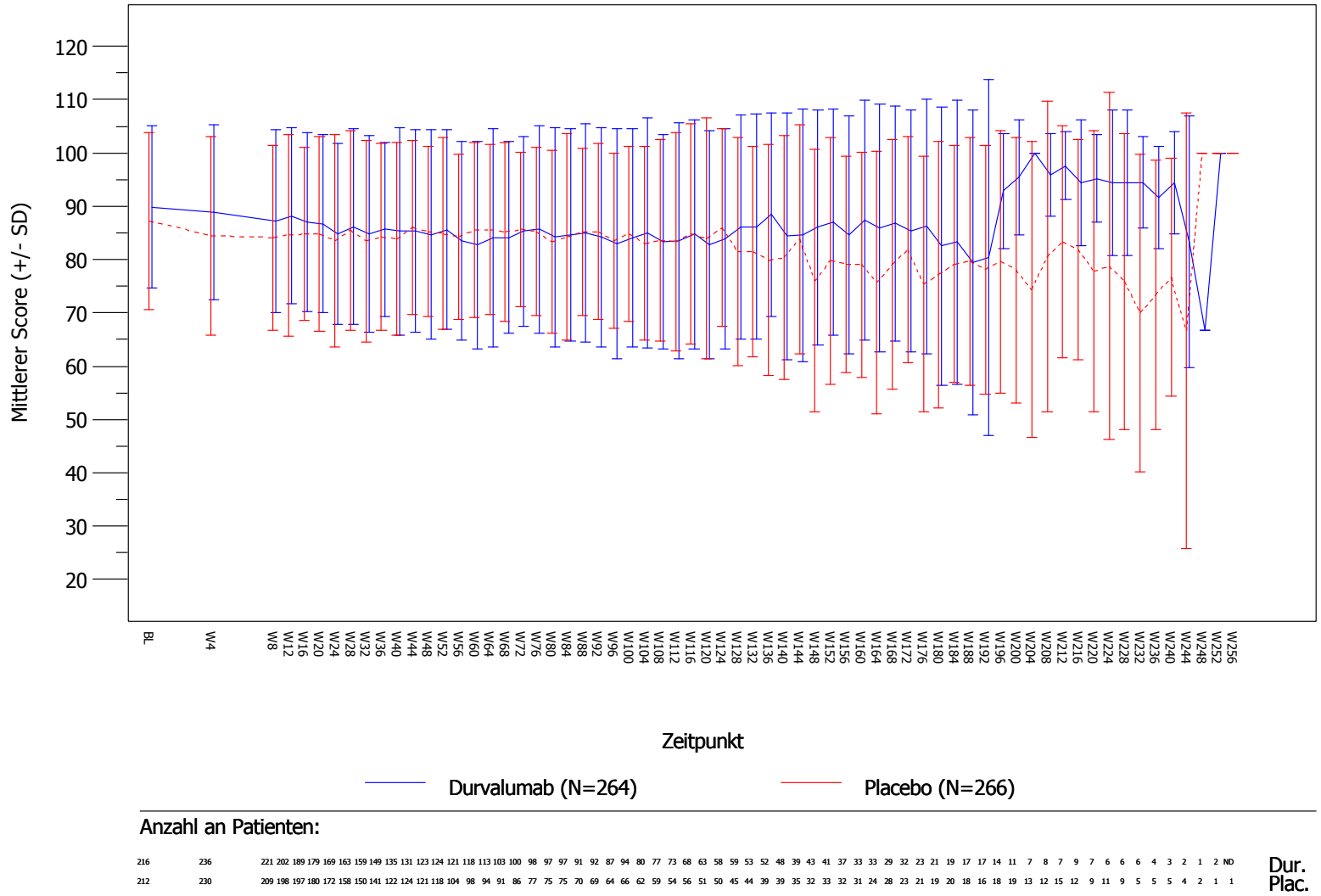
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.3 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Functional scale: Cognitive across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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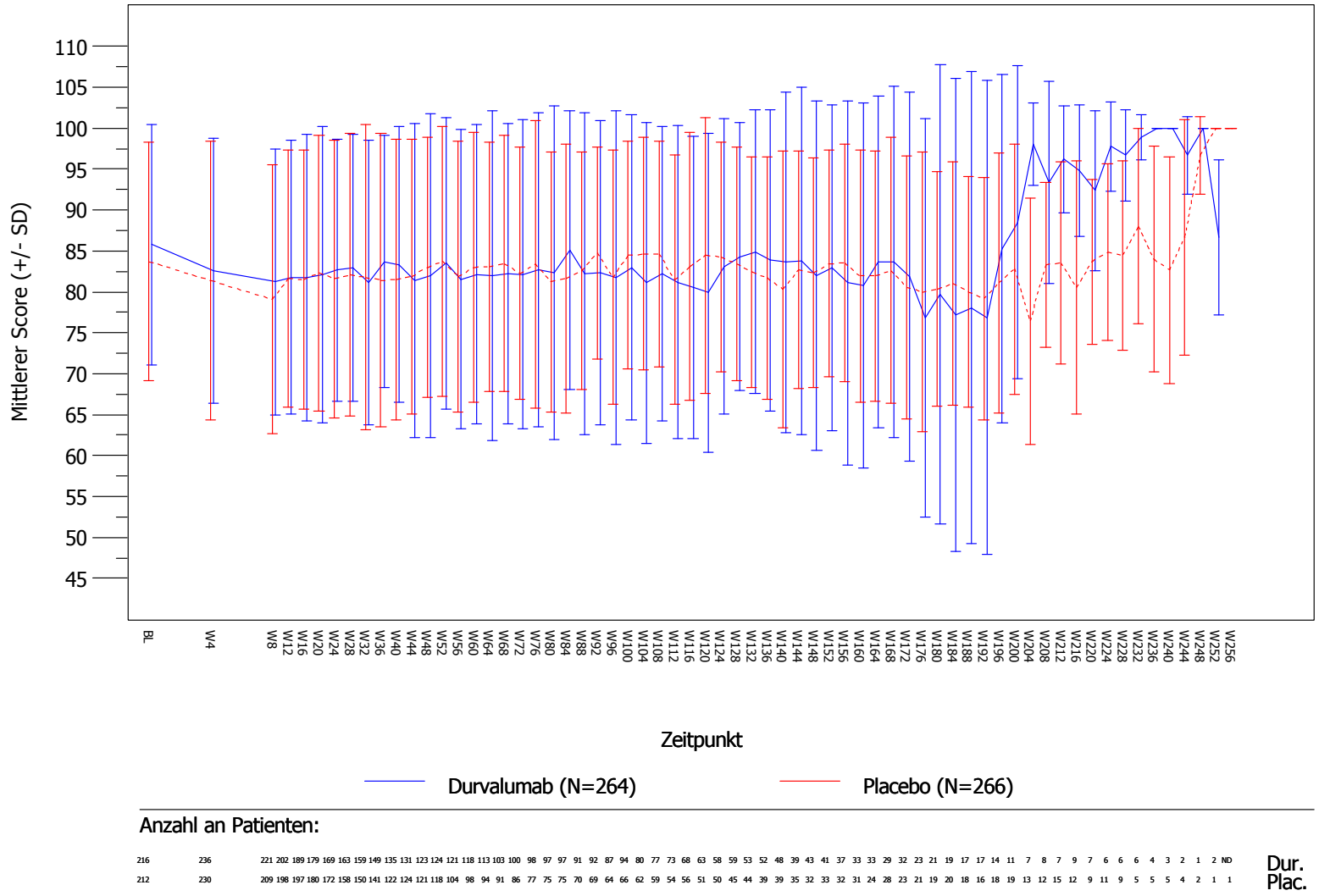
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.4 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Functional scale: Physical across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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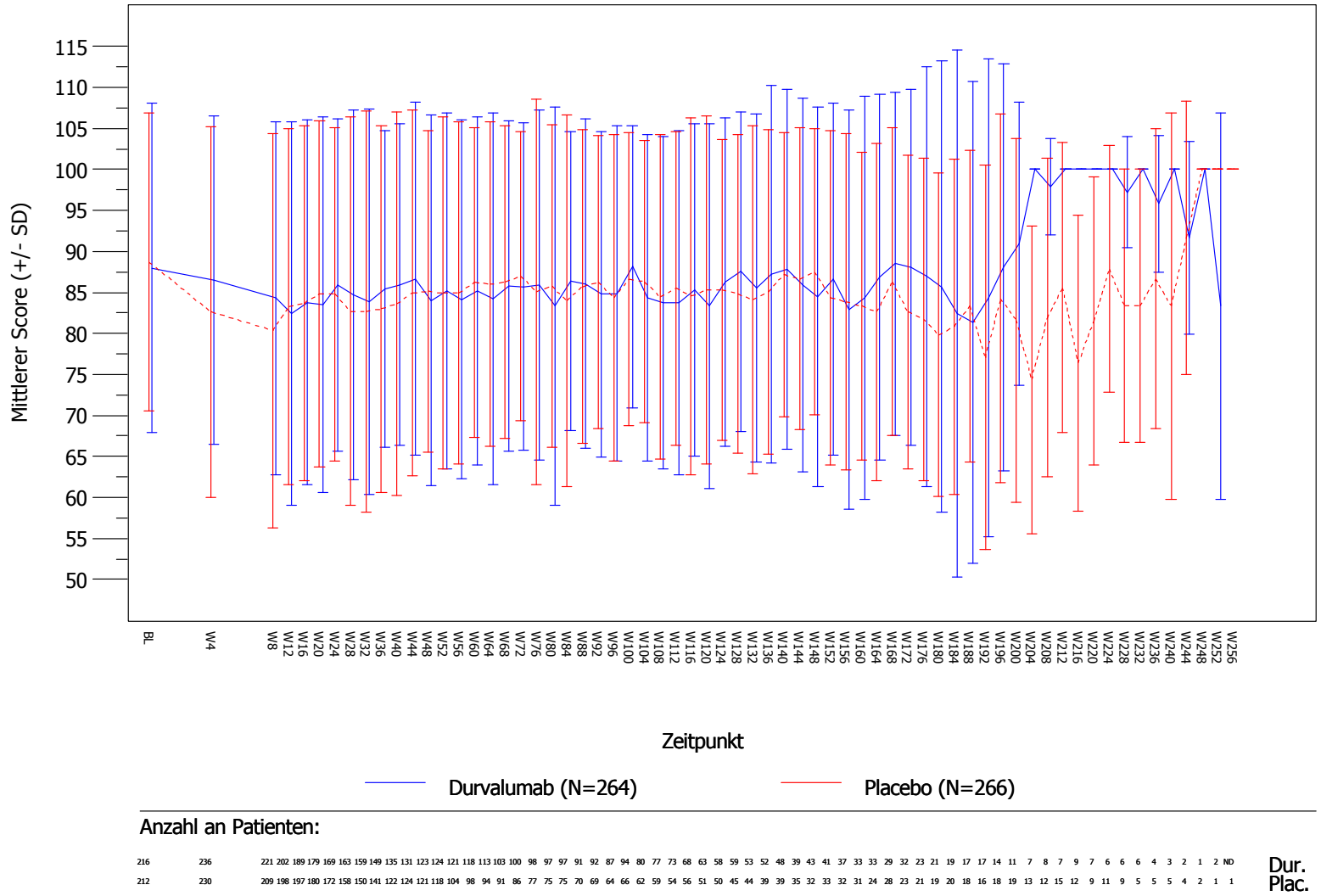
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.5 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Functional scale: Role across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.6 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Functional scale: Social across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

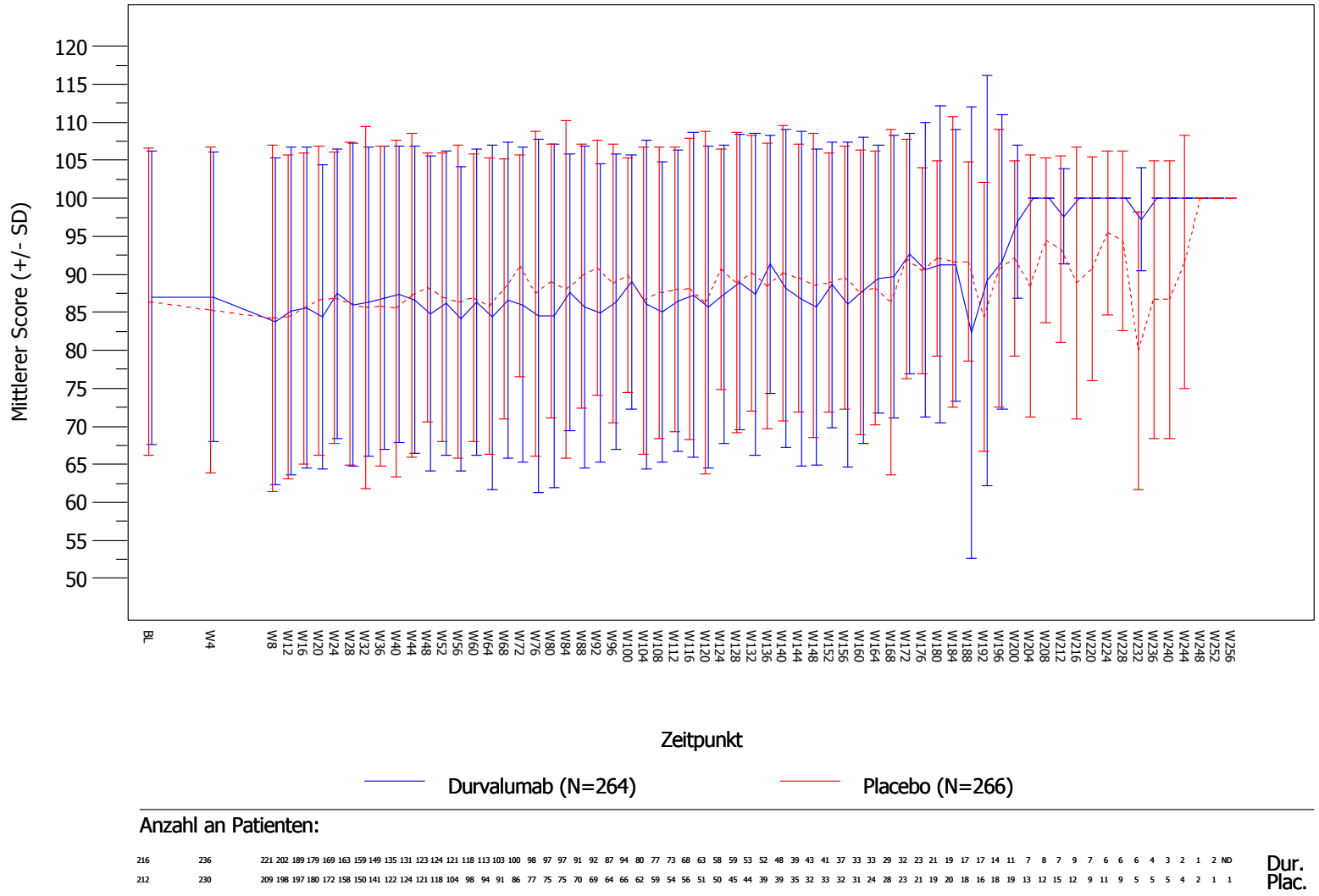

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Figure 3.4.1.7 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Symptom scale: Fatigue across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

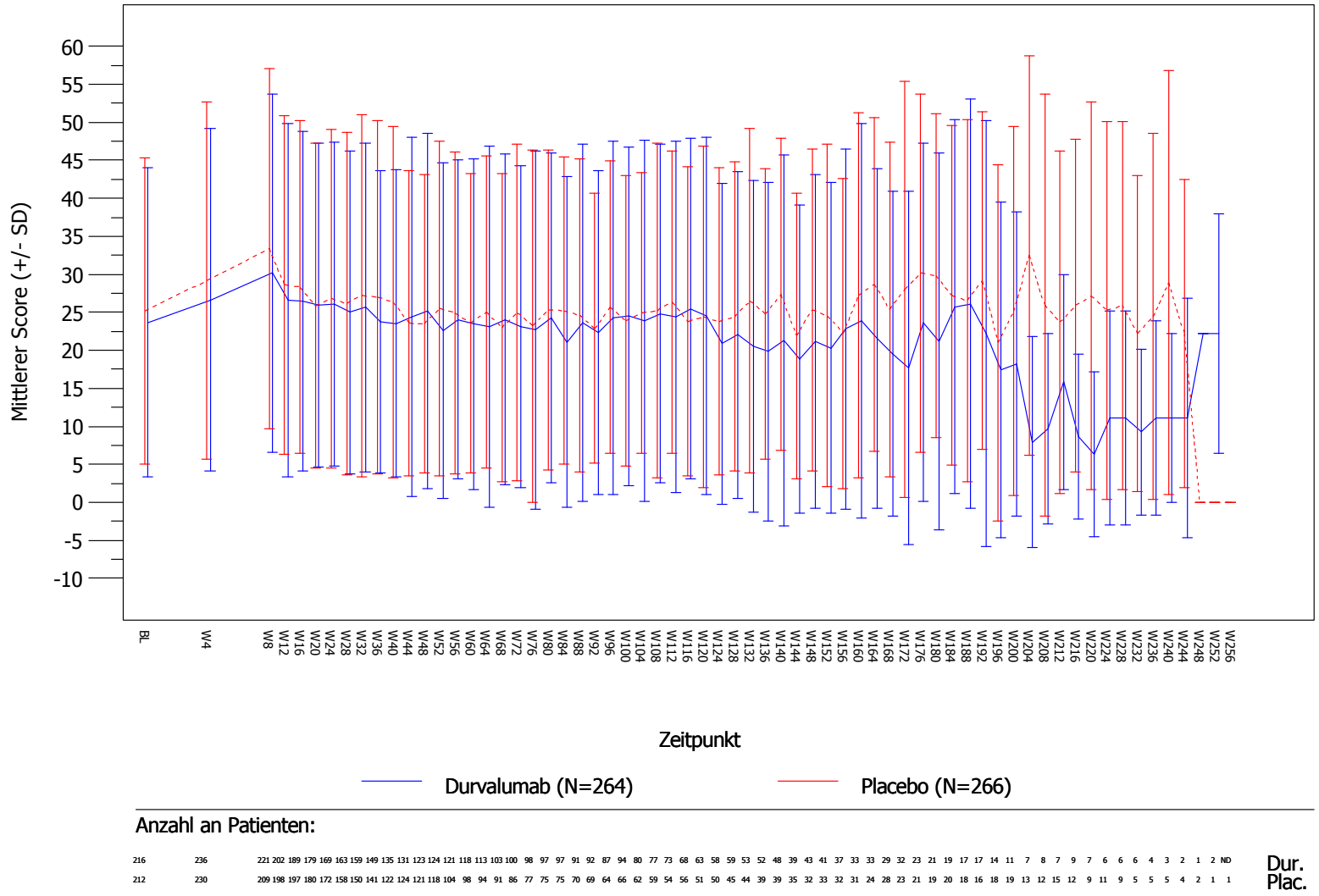

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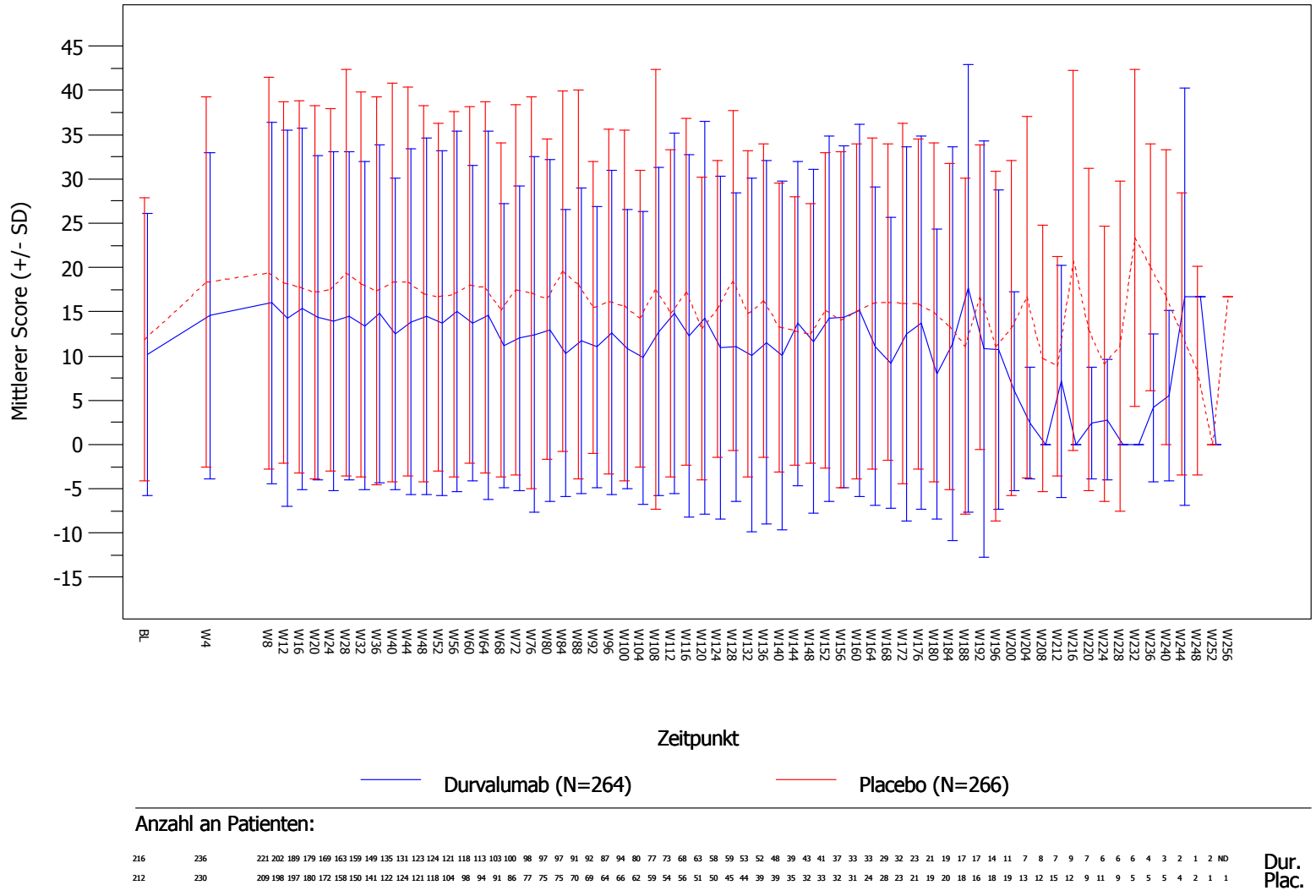
Figure 3.4.1.8 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Symptom scale: Pain across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten:

| | | |

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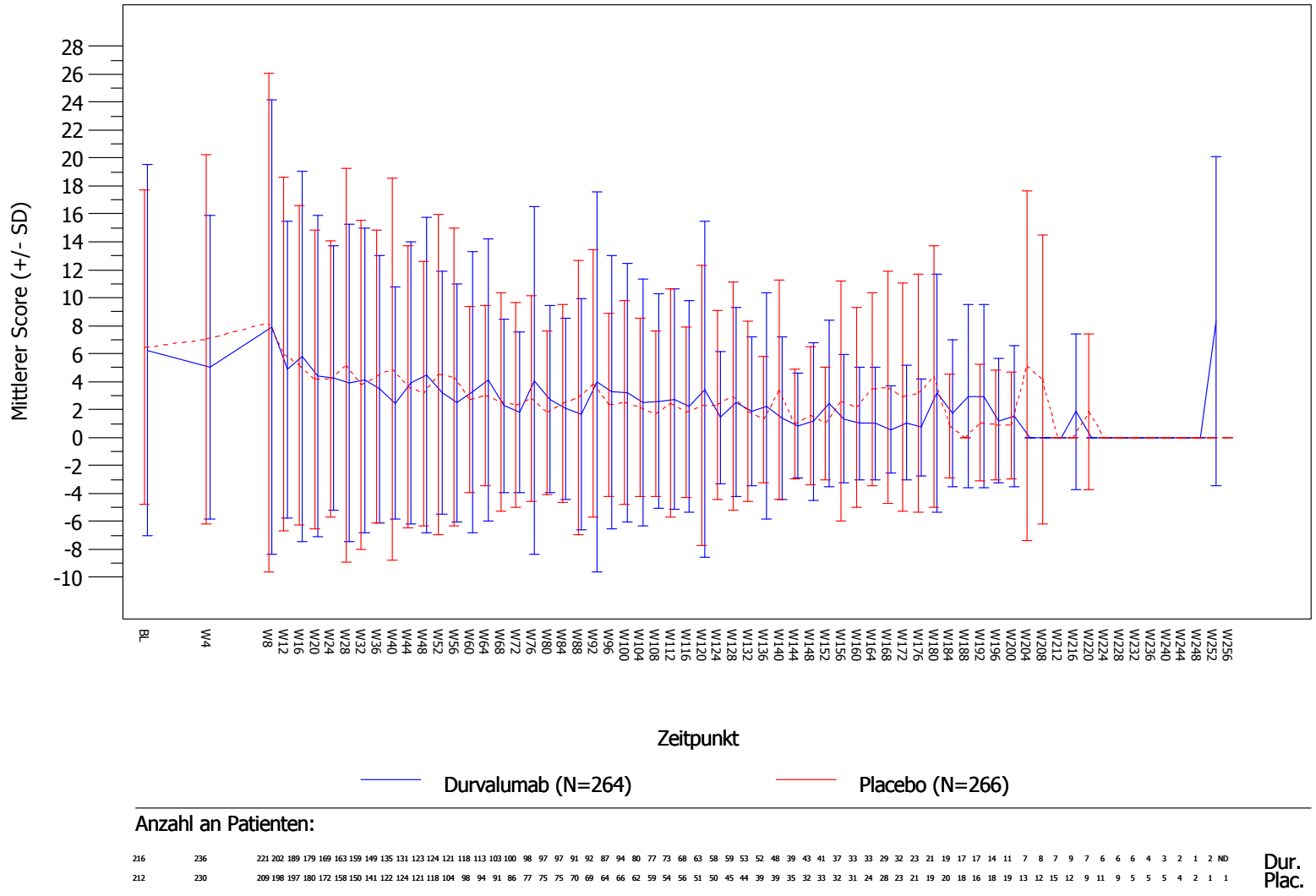
Figure 3.4.1.9 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Symptom scale: Nausea and vomiting across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten:

216	236	221 202 189 179 169 163 159 149 135 131 123 124 121 118 113 103 100 98 97 97 91 92 87 94 80 77 73 68 63 58 59 53 52 48 39 43 41 37 33 33 29 32 23 21 19 17 17 14 11 7 8 7 9 7 6 6 6 4 3 2 1 2 ND	Dur.
212	230	209 198 197 180 172 158 150 141 122 124 121 118 104 98 94 91 86 77 75 75 70 69 64 66 62 59 54 56 51 50 45 44 39 39 35 32 33 32 31 24 28 23 21 19 20 18 16 18 19 13 12 15 12 9 11 9 5 5 5 4 2 1 1	Plac.

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Figure 3.4.1.10 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Loss of appetite across timepoints, by treatment gr
Full Analysis Set, DCO 15JAN2024

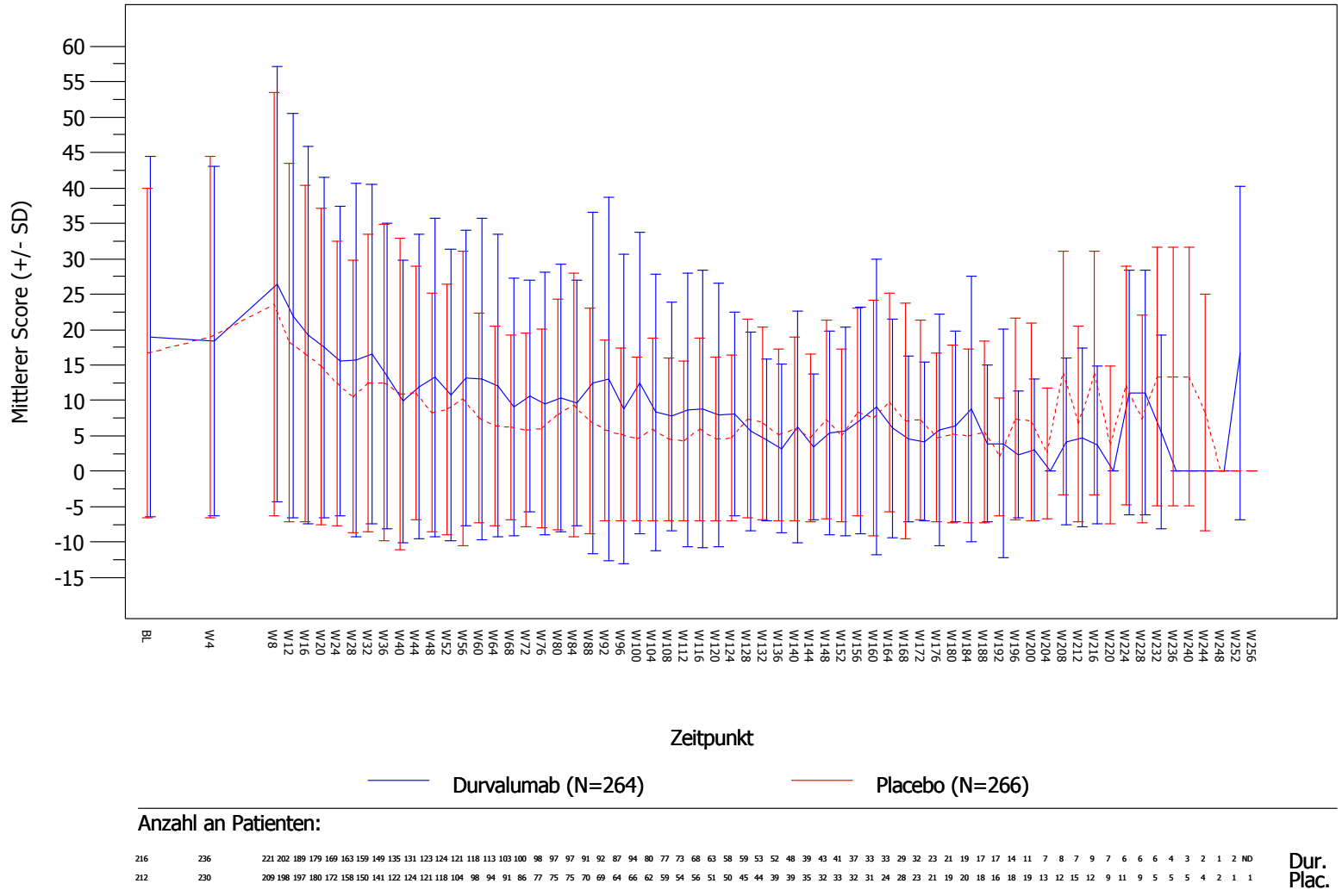

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Figure 3.4.1.11 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Diarrhoea across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

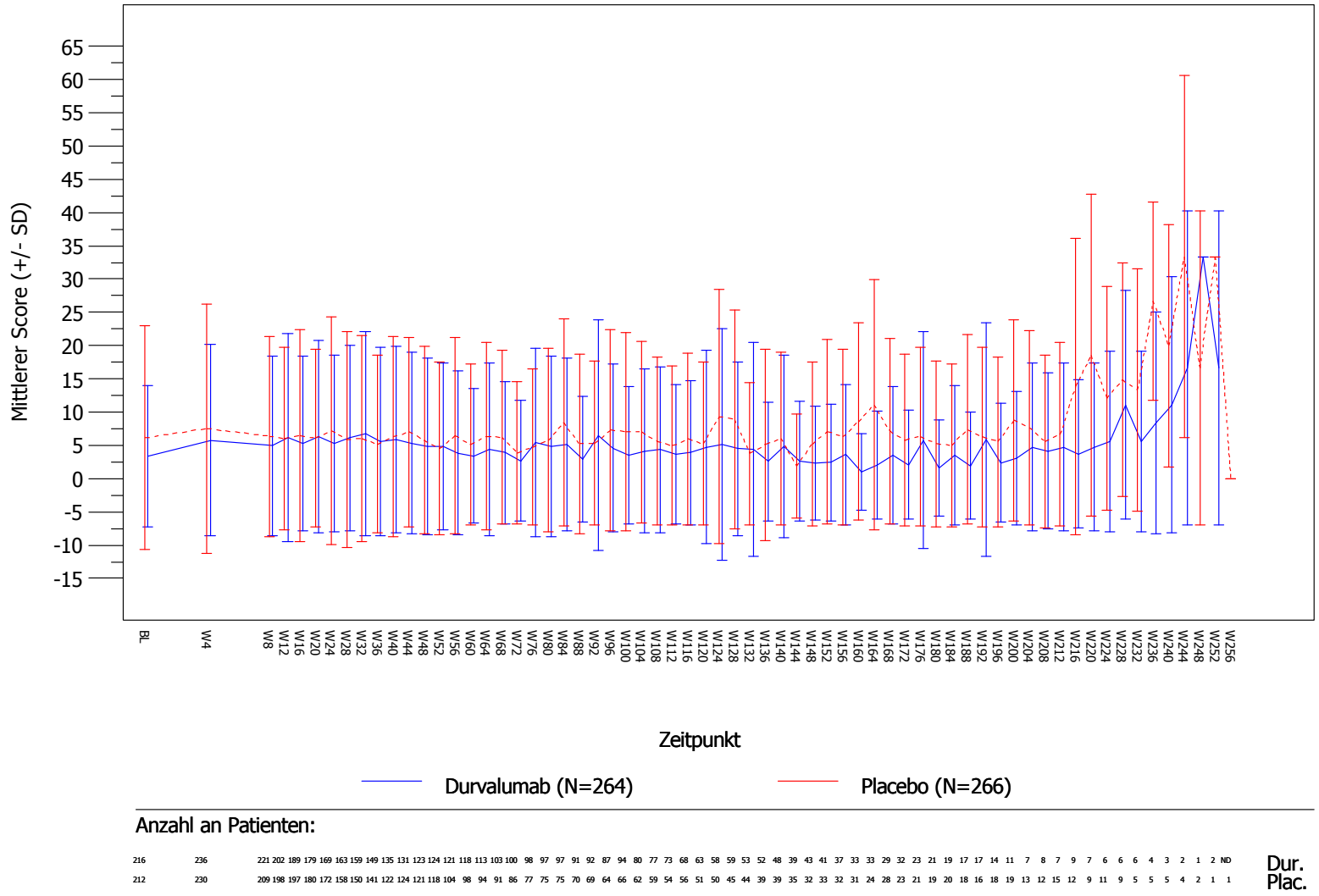

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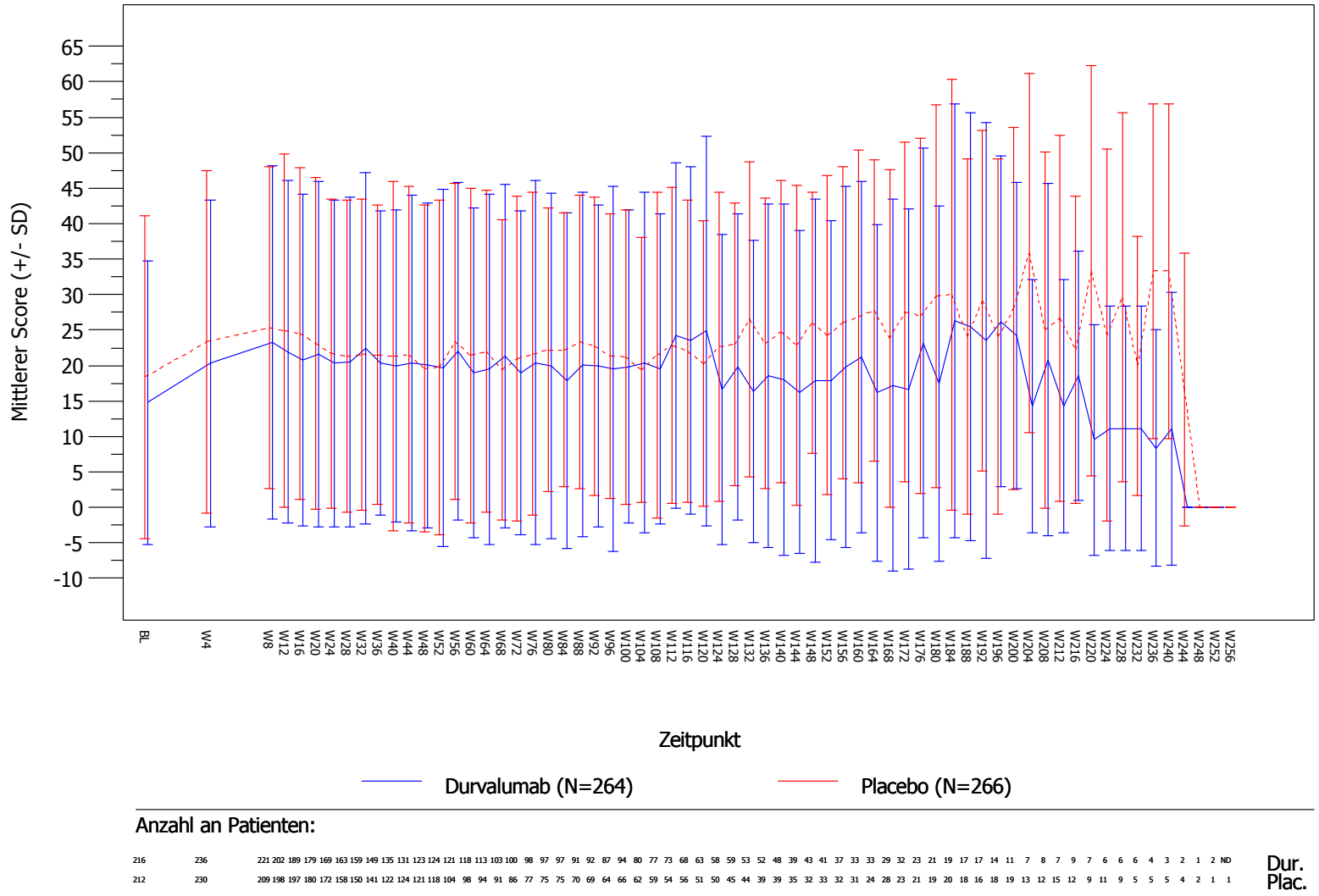
Figure 3.4.1.12 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Dyspnoea across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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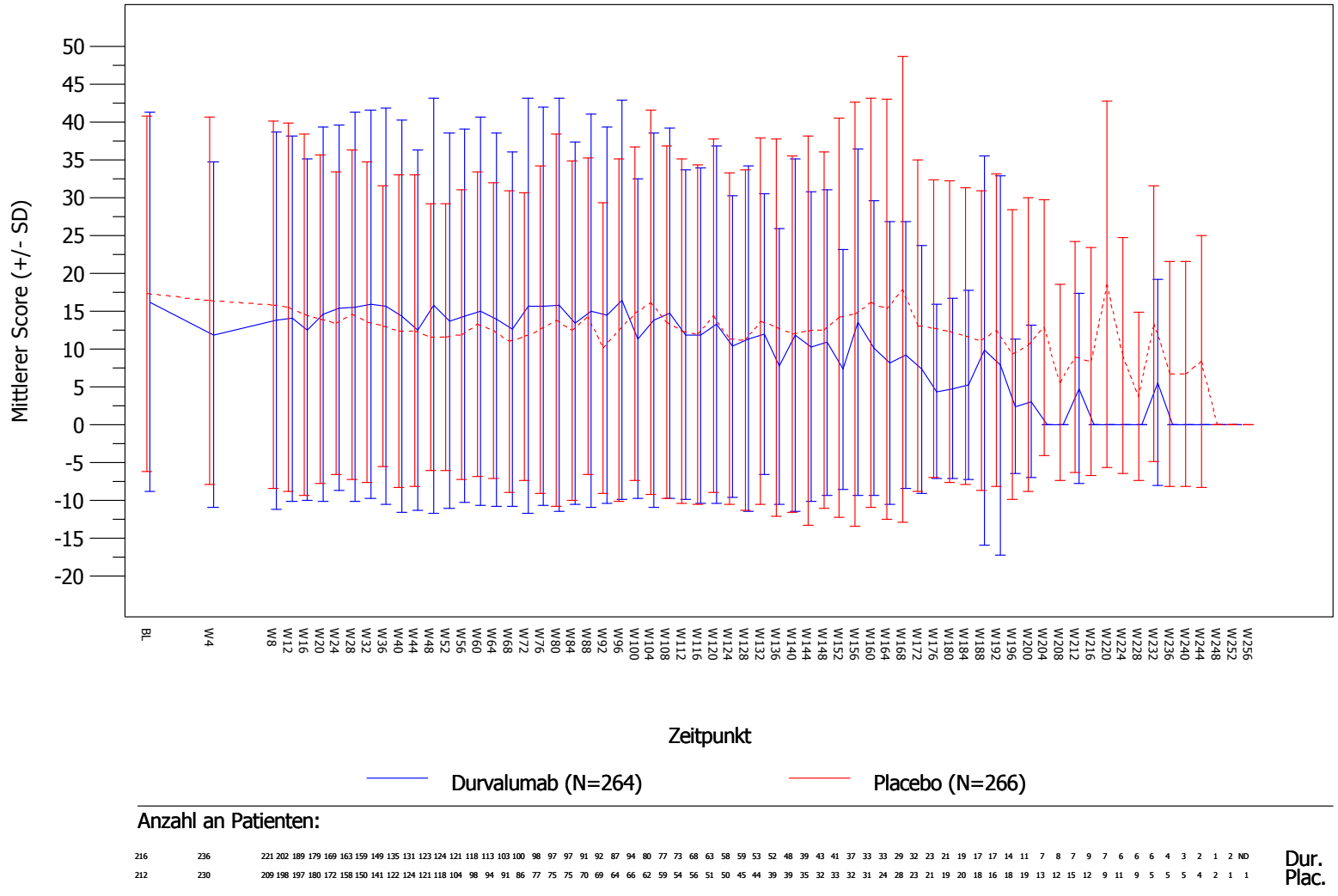
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.13 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Financial difficulties across timepoints, by treatm
Full Analysis Set, DCO 15JAN2024



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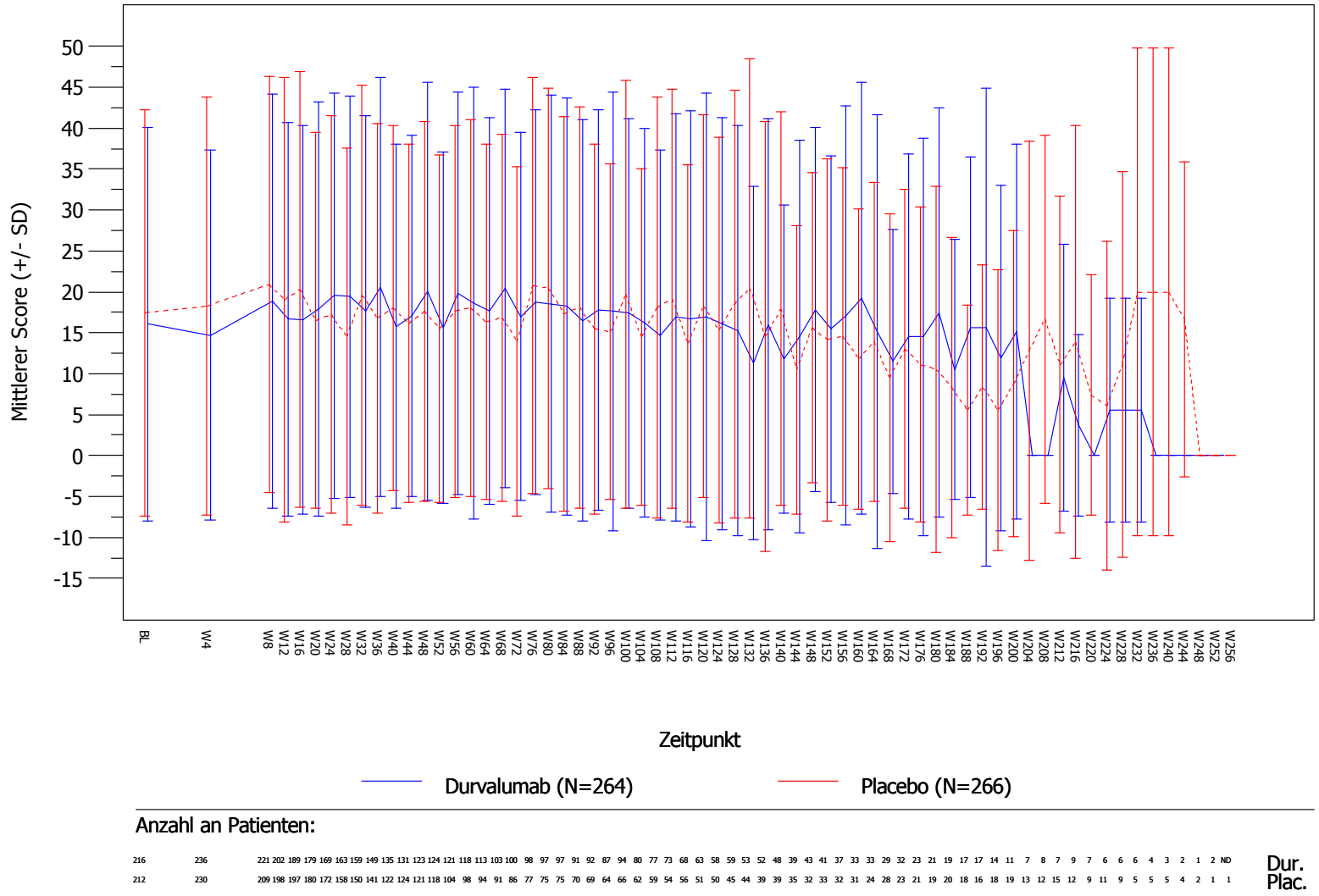
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.14 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Constipation across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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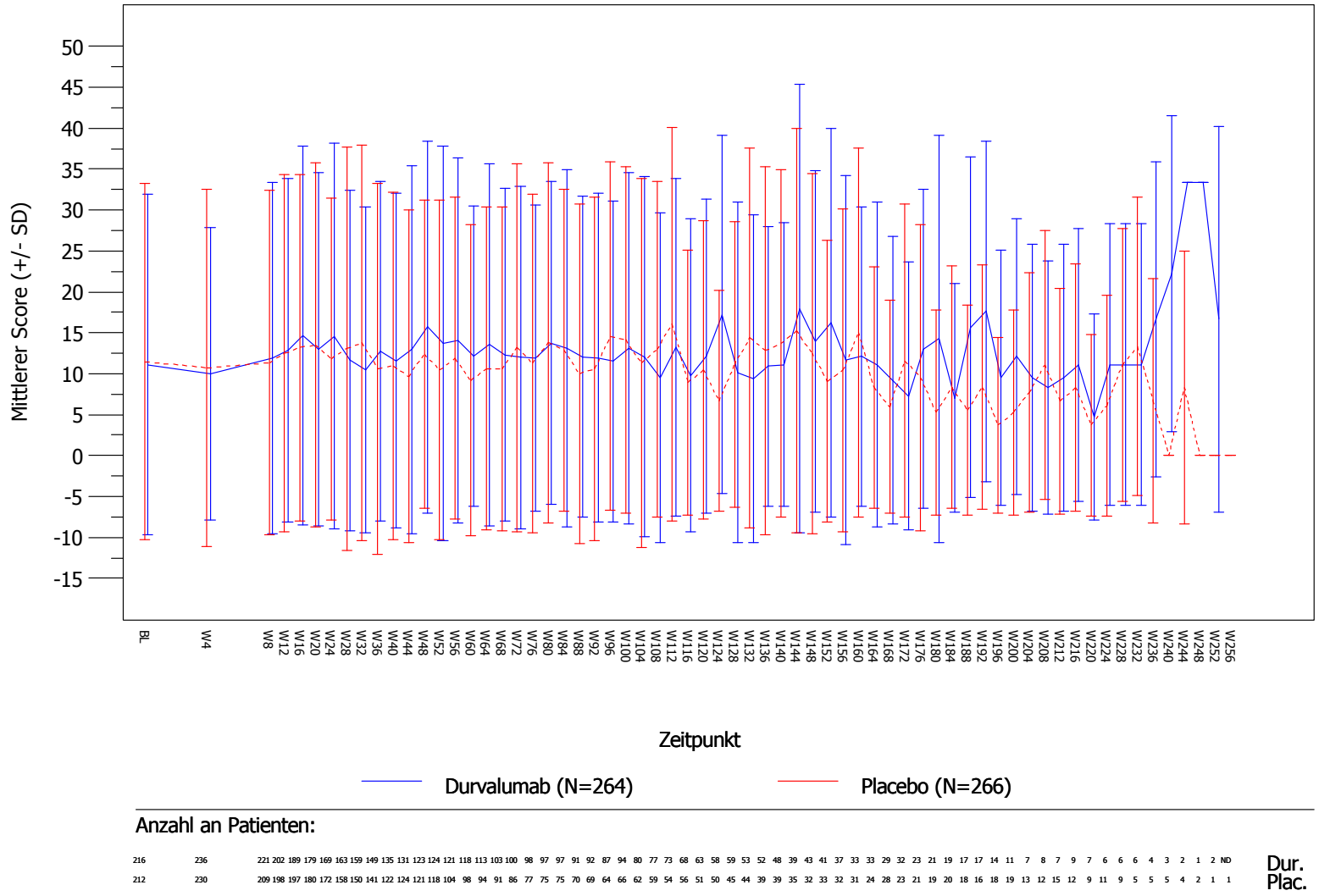
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.1.15 ADRIATIC: Mean (+/- SD) EORTC QLQ-C30 Single item symptom scale: Insomnia across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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Anhang 4-G7.3: EORTC QLQ-LC13 - MMRM-Analyse

Table 3.8.2.1 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	17,10 (16,205)	-0,67 (1,183)	180	21,42 (17,422)	-0,95 (1,183)	0,29 [-3,013; 3,584]	0,8649
Woche 2	185	17,84 (16,180)	0,33 (1,162)	186	21,15 (17,602)	0,75 (1,163)	-0,42 [-3,663; 2,815]	0,7971
Woche 3	185	18,08 (16,612)	1,37 (1,178)	179	21,04 (17,128)	0,55 (1,190)	0,82 [-2,475; 4,120]	0,6243
Woche 4	204	18,14 (16,643)	2,15 (1,225)	198	21,55 (17,900)	1,90 (1,238)	0,25 [-3,179; 3,681]	0,8856
Woche 5	183	17,55 (16,567)	3,27 (1,286)	190	21,87 (18,213)	3,53 (1,284)	-0,26 [-3,846; 3,317]	0,8847
Woche 6	184	17,57 (16,153)	3,94 (1,283)	176	22,16 (17,877)	1,20 (1,301)	2,74 [-0,861; 6,345]	0,1355
Woche 7	181	17,86 (16,587)	4,47 (1,402)	176	21,78 (17,713)	3,63 (1,419)	0,84 [-3,088; 4,771]	0,6741
Woche 8	192	17,59 (16,253)	5,17 (1,372)	183	21,80 (17,755)	4,68 (1,394)	0,49 [-3,361; 4,348]	0,8015
Woche 12	177	17,77 (16,208)	4,40 (1,374)	176	22,22 (18,014)	2,97 (1,386)	1,43 [-2,418; 5,276]	0,4658
Woche 16	168	18,06 (16,299)	4,61 (1,397)	170	22,68 (18,105)	3,87 (1,405)	0,75 [-3,161; 4,653]	0,7075
Woche 20	160	18,26 (16,548)	4,32 (1,409)	158	22,36 (17,601)	2,32 (1,424)	2,00 [-1,950; 5,949]	0,3203
Woche 24	147	18,14 (15,985)	3,94 (1,362)	151	22,59 (17,935)	3,31 (1,366)	0,63 [-3,173; 4,438]	0,7441
Woche 28	148	18,92 (16,620)	6,08 (1,489)	136	23,04 (18,277)	2,33 (1,530)	3,74 [-0,465; 7,952]	0,0811
Woche 32	141	18,75 (16,647)	5,10 (1,499)	131	21,80 (16,388)	2,13 (1,540)	2,97 [-1,265; 7,207]	0,1687
Woche 36	135	18,93 (16,237)	4,33 (1,366)	125	22,22 (18,290)	3,28 (1,408)	1,05 [-2,815; 4,918]	0,5932
Woche 40	120	18,24 (15,897)	2,45 (1,433)	107	22,43 (18,186)	5,72 (1,492)	-3,27 [-7,354; 0,808]	0,1156
Woche 44	117	18,61 (16,235)	3,71 (1,372)	109	21,92 (17,663)	2,18 (1,418)	1,53 [-2,360; 5,418]	0,4400

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.1 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	17,94 (15,707)	5,01 (1,512)	107	21,18 (17,964)	5,22 (1,544)	-0,21 [-4,467; 4,053]	0,9240
Woche 52	112	17,86 (15,309)	4,61 (1,491)	103	20,71 (16,322)	4,04 (1,543)	0,58 [-3,652; 4,803]	0,7891
Woche 56	107	18,69 (15,758)	4,82 (1,462)	92	20,89 (16,210)	8,25 (1,543)	-3,43 [-7,614; 0,763]	0,1086
Woche 60	103	19,09 (15,822)	2,58 (1,436)	86	21,83 (16,209)	4,05 (1,532)	-1,47 [-5,606; 2,669]	0,4857
Woche 64	101	18,70 (15,550)	5,30 (1,544)	84	21,69 (16,354)	5,29 (1,652)	0,01 [-4,448; 4,467]	0,9966
Woche 68	91	18,56 (14,727)	3,44 (1,625)	82	21,41 (16,635)	5,23 (1,710)	-1,79 [-6,439; 2,862]	0,4499
Woche 72	91	19,17 (14,635)	4,34 (1,519)	78	20,80 (16,053)	4,99 (1,619)	-0,65 [-5,020; 3,728]	0,7715
Woche 76	90	18,64 (13,718)	3,31 (1,523)	69	22,38 (16,882)	4,24 (1,680)	-0,94 [-5,408; 3,537]	0,6810
Woche 80	87	19,67 (14,743)	3,76 (1,468)	65	21,88 (17,007)	4,64 (1,640)	-0,88 [-5,216; 3,460]	0,6908
Woche 84	87	17,88 (14,903)	2,71 (1,445)	67	22,39 (16,806)	6,56 (1,608)	-3,85 [-8,115; 0,422]	0,0772
Woche 88	84	18,78 (14,734)	5,16 (1,549)	61	22,77 (17,024)	7,32 (1,757)	-2,16 [-6,785; 2,464]	0,3586
Woche 92	84	19,18 (14,872)	4,11 (1,403)	60	22,04 (17,053)	5,14 (1,604)	-1,02 [-5,225; 3,183]	0,6330
Woche 96	79	19,55 (15,224)	5,60 (1,548)	55	22,63 (17,498)	6,42 (1,796)	-0,82 [-5,497; 3,856]	0,7300
Woche 100	86	18,35 (15,222)	3,47 (1,353)	59	22,22 (17,139)	3,57 (1,575)	-0,10 [-4,197; 4,002]	0,9627
Woche 104	73	19,18 (15,522)	4,96 (1,552)	56	21,83 (17,596)	5,16 (1,767)	-0,19 [-4,833; 4,446]	0,9346
Woche 108	71	20,03 (15,329)	4,50 (1,593)	52	21,79 (17,870)	2,82 (1,832)	1,68 [-3,111; 6,464]	0,4909
Woche 112	68	19,77 (15,928)	6,40 (1,591)	47	22,46 (18,019)	3,98 (1,857)	2,42 [-2,399; 7,247]	0,3232
Woche 116	62	19,18 (15,606)	5,49 (1,994)	51	22,22 (18,459)	7,82 (2,233)	-2,33 [-8,242; 3,580]	0,4380

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.1 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	18,52 (15,478)	7,98 (2,026)	47	23,64 (18,333)	9,61 (2,272)	-1,63 [-7,649; 4,393]	0,5947
Woche 124	54	19,34 (16,322)	5,90 (1,800)	45	22,96 (18,257)	6,14 (2,013)	-0,24 [-5,579; 5,101]	0,9298
Woche 128	54	18,11 (15,155)	5,06 (1,709)	40	22,78 (17,423)	4,89 (1,968)	0,18 [-4,987; 5,338]	0,9466
Woche 132	50	17,11 (15,586)	5,07 (1,794)	39	23,36 (16,479)	7,78 (2,045)	-2,71 [-8,109; 2,689]	0,3235
Woche 136	48	18,29 (15,961)	4,40 (1,647)	34	22,22 (13,948)	3,98 (1,928)	0,42 [-4,603; 5,442]	0,8693
Woche 140	45	17,78 (16,817)	2,28 (1,758)	34	22,22 (13,948)	4,46 (2,021)	-2,18 [-7,489; 3,129]	0,4188
Woche 144	36	18,83 (16,970)	4,89 (1,867)	30	21,11 (12,499)	3,15 (2,093)	1,74 [-3,817; 7,297]	0,5370
Woche 148	40	18,61 (16,574)	2,84 (1,961)	27	22,22 (11,111)	5,05 (2,329)	-2,21 [-8,256; 3,828]	0,4700
Woche 152	38	17,25 (16,880)	3,40 (2,050)	28	21,83 (11,899)	4,02 (2,374)	-0,62 [-6,853; 5,618]	0,8450
Woche 156	35	18,10 (17,482)	6,54 (2,077)	28	21,83 (13,348)	2,19 (2,359)	4,35 [-1,893; 10,598]	0,1703
Woche 160	31	18,28 (17,580)	3,84 (2,213)	26	23,50 (13,082)	4,81 (2,488)	-0,97 [-7,599; 5,657]	0,7724
Woche 164	31	19,00 (17,730)	2,95 (2,239)	22	22,73 (12,112)	7,65 (2,613)	-4,70 [-11,541; 2,145]	0,1766
Woche 168	27	16,05 (17,792)	5,96 (2,501)	25	22,67 (13,410)	3,63 (2,703)	2,33 [-5,024; 9,692]	0,5310
Woche 172	30	17,41 (18,381)	4,06 (2,475)	20	23,89 (15,411)	4,27 (2,937)	-0,22 [-7,887; 7,453]	0,9554
Woche 176	22	19,70 (18,760)	8,14 (2,708)	18	21,60 (13,988)	4,73 (3,042)	3,41 [-4,719; 11,533]	0,4067
Woche 180	20	20,56 (19,169)	-0,80 (2,748)	16	20,83 (13,380)	10,64 (3,078)	-11,45 [-19,669; -3,226]	0,0069*
Woche 184	18	21,60 (19,235)	2,24 (3,045)	17	20,26 (13,168)	5,00 (3,245)	-2,76 [-11,630; 6,113]	0,5378

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.1 ADRIATIC: Summary of analysis of change from baseline over time in Dyspnoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	22,92 (19,655)	3,43 (3,491)	15	17,78 (10,951)	2,09 (3,694)	1,33 [-8,895; 11,560]	0,7953
Durchschnitt über alle Visiten	216	18,00 (16,373)	4,09 (0,937)	211	21,22 (17,806)	4,38 (1,015)	-0,29 [-3,013; 2,429]	0,8331
Hedges' g SMD							-0,02 [-0,210; 0,169]	0,8327

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.2 ADRIATIC: Summary of analysis of change from baseline over time in Alopezie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	17,04 (28,075)	-0,40 (2,260)	180	24,07 (33,437)	0,18 (2,276)	-0,58 [-6,899; 5,734]	0,8562
Woche 2	185	18,02 (28,862)	-5,61 (2,067)	186	24,55 (33,611)	-3,55 (2,083)	-2,06 [-7,837; 3,714]	0,4834
Woche 3	185	17,48 (29,297)	-5,63 (1,915)	179	24,02 (33,336)	-5,94 (1,945)	0,30 [-5,066; 5,674]	0,9114
Woche 4	204	18,63 (30,350)	-9,42 (1,679)	198	23,91 (33,262)	-7,05 (1,707)	-2,37 [-7,074; 2,337]	0,3233
Woche 5	183	16,94 (28,143)	-6,82 (1,659)	190	23,68 (33,340)	-9,39 (1,665)	2,57 [-2,055; 7,192]	0,2756
Woche 6	184	18,30 (29,524)	-8,30 (1,501)	176	24,62 (34,178)	-11,40 (1,535)	3,10 [-1,116; 7,325]	0,1491
Woche 7	181	18,23 (29,695)	-8,06 (1,534)	176	24,43 (33,660)	-11,70 (1,568)	3,65 [-0,668; 7,959]	0,0974
Woche 8	192	17,36 (28,733)	-9,73 (1,719)	183	24,23 (33,547)	-11,35 (1,763)	1,62 [-3,222; 6,469]	0,5107
Woche 12	177	18,64 (30,321)	-12,78 (1,270)	176	23,67 (32,487)	-16,90 (1,291)	4,12 [0,558; 7,684]	0,0235*
Woche 16	168	17,26 (28,948)	-13,73 (1,316)	170	22,55 (32,149)	-16,90 (1,329)	3,18 [-0,506; 6,858]	0,0907
Woche 20	160	17,29 (28,951)	-15,76 (1,371)	158	23,84 (32,602)	-16,00 (1,390)	0,24 [-3,603; 4,091]	0,9007
Woche 24	147	17,01 (28,766)	-13,99 (1,641)	151	23,40 (32,385)	-14,63 (1,649)	0,64 [-3,944; 5,221]	0,7843
Woche 28	148	17,57 (29,724)	-14,02 (1,593)	136	23,28 (32,029)	-13,55 (1,641)	-0,46 [-4,967; 4,042]	0,8402
Woche 32	141	18,20 (29,940)	-13,91 (1,554)	131	22,14 (32,715)	-12,10 (1,606)	-1,80 [-6,203; 2,594]	0,4203
Woche 36	135	18,02 (29,014)	-16,11 (1,480)	125	21,07 (31,548)	-11,81 (1,534)	-4,31 [-8,503; -0,107]	0,0444*
Woche 40	120	18,89 (29,856)	-13,58 (1,657)	107	22,74 (32,569)	-11,56 (1,738)	-2,01 [-6,742; 2,714]	0,4026
Woche 44	117	19,09 (30,424)	-13,20 (1,570)	109	22,63 (32,673)	-11,57 (1,638)	-1,63 [-6,094; 2,836]	0,4735

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.2 ADRIATIC: Summary of analysis of change from baseline over time in Alopezie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	19,27 (30,189)	-11,92 (1,713)	107	22,74 (32,890)	-11,81 (1,770)	-0,11 [-4,956; 4,740]	0,9650
Woche 52	112	16,96 (28,297)	-12,24 (1,679)	103	23,95 (33,793)	-13,20 (1,757)	0,96 [-3,833; 5,748]	0,6944
Woche 56	107	17,76 (28,710)	-12,69 (1,518)	92	22,83 (33,853)	-11,07 (1,617)	-1,61 [-5,984; 2,757]	0,4679
Woche 60	103	18,77 (30,130)	-14,63 (1,392)	86	22,09 (32,584)	-12,28 (1,501)	-2,35 [-6,380; 1,681]	0,2523
Woche 64	101	19,47 (31,008)	-12,05 (1,440)	84	21,03 (31,380)	-12,35 (1,556)	0,30 [-3,870; 4,478]	0,8861
Woche 68	91	19,41 (30,658)	-12,42 (1,849)	82	23,58 (34,142)	-9,89 (1,966)	-2,52 [-7,839; 2,790]	0,3506
Woche 72	91	18,32 (30,737)	-10,89 (1,724)	78	21,79 (33,475)	-10,51 (1,854)	-0,38 [-5,365; 4,606]	0,8809
Woche 76	90	17,04 (29,665)	-11,98 (1,633)	69	19,81 (31,477)	-10,40 (1,818)	-1,58 [-6,394; 3,231]	0,5183
Woche 80	87	17,62 (30,431)	-10,67 (1,550)	65	18,46 (30,636)	-12,80 (1,757)	2,13 [-2,485; 6,744]	0,3643
Woche 84	87	19,16 (31,183)	-10,72 (1,608)	67	17,41 (29,791)	-10,92 (1,823)	0,21 [-4,582; 4,994]	0,9327
Woche 88	84	17,46 (29,938)	-10,41 (1,523)	61	19,13 (30,707)	-13,33 (1,754)	2,92 [-1,661; 7,492]	0,2106
Woche 92	84	17,46 (29,487)	-10,77 (1,460)	60	15,00 (27,049)	-14,73 (1,703)	3,95 [-0,462; 8,367]	0,0790
Woche 96	79	18,99 (30,515)	-12,06 (1,576)	55	16,36 (27,869)	-12,65 (1,868)	0,59 [-4,222; 5,407]	0,8085
Woche 100	86	17,83 (29,681)	-14,36 (1,268)	59	16,38 (27,939)	-12,71 (1,515)	-1,65 [-5,538; 2,239]	0,4042
Woche 104	73	18,26 (29,939)	-13,94 (1,313)	56	16,07 (27,700)	-12,29 (1,526)	-1,64 [-5,608; 2,322]	0,4149
Woche 108	71	15,96 (28,092)	-13,73 (1,254)	52	14,74 (25,061)	-14,22 (1,466)	0,49 [-3,299; 4,281]	0,7986
Woche 112	68	17,65 (30,185)	-11,73 (1,483)	47	15,60 (26,785)	-13,44 (1,746)	1,70 [-2,807; 6,210]	0,4576
Woche 116	62	14,52 (25,336)	-11,00 (1,663)	51	11,11 (18,459)	-10,73 (1,886)	-0,28 [-5,186; 4,630]	0,9113

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.2 ADRIATIC: Summary of analysis of change from baseline over time in Alopezie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	16,37 (27,547)	-12,26 (1,310)	47	13,48 (22,693)	-14,93 (1,473)	2,67 [-1,197; 6,534]	0,1748
Woche 124	54	12,35 (24,483)	-11,71 (1,552)	45	13,33 (23,995)	-14,31 (1,728)	2,60 [-1,931; 7,131]	0,2590
Woche 128	54	15,43 (27,252)	-9,86 (1,682)	40	11,67 (23,327)	-12,81 (1,952)	2,95 [-2,088; 7,995]	0,2491
Woche 132	50	14,67 (26,221)	-13,00 (1,653)	39	13,68 (27,272)	-12,40 (1,899)	-0,59 [-5,529; 4,340]	0,8122
Woche 136	48	17,36 (29,165)	-14,34 (1,524)	34	16,67 (28,721)	-12,78 (1,797)	-1,56 [-6,200; 3,084]	0,5082
Woche 140	45	20,00 (30,484)	-11,48 (1,777)	34	15,69 (26,253)	-12,80 (2,065)	1,32 [-4,060; 6,699]	0,6284
Woche 144	36	16,67 (28,172)	-10,71 (2,349)	30	8,89 (17,361)	-10,82 (2,706)	0,10 [-6,951; 7,161]	0,9765
Woche 148	40	20,00 (30,940)	-8,65 (2,194)	27	13,58 (24,909)	-10,05 (2,629)	1,40 [-5,379; 8,183]	0,6829
Woche 152	38	14,91 (25,347)	-9,09 (2,268)	28	15,48 (24,816)	-9,33 (2,651)	0,24 [-6,631; 7,109]	0,9452
Woche 156	35	16,19 (29,563)	-9,64 (2,228)	28	11,90 (18,624)	-10,60 (2,561)	0,96 [-5,709; 7,628]	0,7766
Woche 160	31	17,20 (30,877)	-8,14 (2,088)	26	15,38 (25,352)	-14,32 (2,345)	6,18 [-0,010; 12,364]	0,0504
Woche 164	31	15,05 (28,335)	-10,42 (1,602)	22	18,18 (26,681)	-15,50 (1,833)	5,09 [0,287; 9,887]	0,0379*
Woche 168	27	17,28 (29,772)	-11,19 (1,917)	25	17,33 (25,676)	-13,80 (2,055)	2,61 [-2,939; 8,158]	0,3535
Woche 172	30	15,56 (28,679)	-11,54 (2,052)	20	13,33 (19,941)	-12,54 (2,378)	1,00 [-5,167; 7,175]	0,7479
Woche 176	22	7,58 (17,614)	-12,58 (2,506)	18	14,81 (20,523)	-13,48 (2,668)	0,89 [-6,241; 8,028]	0,8035
Woche 180	20	11,67 (22,361)	-15,08 (1,974)	16	16,67 (21,082)	-11,04 (2,161)	-4,03 [-9,816; 1,751]	0,1680
Woche 184	18	12,96 (23,260)	-10,25 (2,315)	17	15,69 (20,809)	-13,26 (2,421)	3,02 [-3,617; 9,651]	0,3656

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.2 ADRIATIC: Summary of analysis of change from baseline over time in Alopezie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	12,50 (23,960)	-12,08 (1,836)	15	13,33 (21,082)	-13,55 (1,918)	1,48 [-3,825; 6,775]	0,5753
Durchschnitt über alle Visiten	216	18,98 (30,917)	-11,34 (0,757)	211	23,06 (32,771)	-11,94 (0,822)	0,60 [-1,597; 2,791]	0,5930
Hedges' g SMD							0,05 [-0,138; 0,241]	0,5935

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.3 ADRIATIC: Summary of analysis of change from baseline over time in Dysphagie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	8,33 (17,573)	-1,41 (1,119)	180	10,19 (19,006)	-1,76 (1,124)	0,36 [-2,766; 3,476]	0,8231
Woche 2	185	7,75 (17,203)	-1,82 (1,114)	186	9,32 (17,581)	-0,96 (1,117)	-0,86 [-3,963; 2,241]	0,5857
Woche 3	185	7,39 (15,909)	-3,00 (1,069)	179	8,57 (16,978)	-0,30 (1,081)	-2,70 [-5,688; 0,289]	0,0765
Woche 4	204	7,84 (16,985)	-2,61 (1,106)	198	9,09 (17,656)	-0,34 (1,120)	-2,27 [-5,366; 0,823]	0,1498
Woche 5	183	7,83 (17,277)	-2,39 (1,070)	190	8,60 (16,862)	-0,96 (1,067)	-1,43 [-4,403; 1,539]	0,3440
Woche 6	184	7,79 (17,240)	-3,25 (1,039)	176	9,85 (17,930)	-0,37 (1,056)	-2,88 [-5,796; 0,032]	0,0525
Woche 7	181	7,92 (17,353)	-1,63 (1,130)	176	9,85 (17,930)	0,34 (1,146)	-1,97 [-5,137; 1,192]	0,2211
Woche 8	192	7,99 (17,221)	-0,86 (1,273)	183	9,29 (17,608)	0,51 (1,297)	-1,37 [-4,941; 2,204]	0,4519
Woche 12	177	7,72 (17,317)	-2,90 (1,142)	176	9,47 (18,134)	-0,09 (1,152)	-2,81 [-6,002; 0,381]	0,0842
Woche 16	168	8,73 (18,326)	-1,14 (1,206)	170	10,39 (19,608)	-0,35 (1,213)	-0,79 [-4,154; 2,574]	0,6445
Woche 20	160	7,92 (16,922)	-1,48 (1,222)	158	9,92 (18,626)	-1,64 (1,234)	0,16 [-3,257; 3,575]	0,9270
Woche 24	147	7,94 (17,154)	-1,23 (1,334)	151	9,27 (18,119)	-0,45 (1,334)	-0,78 [-4,492; 2,932]	0,6797
Woche 28	148	7,88 (17,544)	-2,10 (1,248)	136	9,56 (18,552)	-2,10 (1,283)	0,00 [-3,520; 3,523]	0,9993
Woche 32	141	8,04 (17,321)	-2,49 (1,264)	131	9,41 (17,675)	-1,16 (1,300)	-1,33 [-4,896; 2,240]	0,4646
Woche 36	135	9,63 (19,043)	-2,29 (1,170)	125	8,27 (17,277)	-1,61 (1,206)	-0,68 [-3,987; 2,629]	0,6865
Woche 40	120	8,89 (18,704)	-4,07 (0,982)	107	9,03 (18,067)	-2,62 (1,025)	-1,46 [-4,248; 1,338]	0,3061
Woche 44	117	9,12 (18,375)	-3,84 (1,092)	109	8,26 (17,659)	-2,73 (1,129)	-1,12 [-4,208; 1,974]	0,4777

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.3 ADRIATIC: Summary of analysis of change from baseline over time in Dysphagie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	9,48 (19,294)	-2,54 (1,235)	107	7,79 (17,483)	-0,76 (1,260)	-1,79 [-5,261; 1,686]	0,3120
Woche 52	112	9,23 (19,093)	-5,04 (1,093)	103	8,74 (18,054)	-2,16 (1,134)	-2,88 [-5,977; 0,225]	0,0689
Woche 56	107	9,66 (19,431)	-3,55 (1,133)	92	7,25 (15,490)	-1,15 (1,201)	-2,41 [-5,661; 0,844]	0,1460
Woche 60	103	9,06 (18,783)	-4,93 (0,895)	86	8,14 (16,117)	-3,05 (0,959)	-1,88 [-4,463; 0,701]	0,1526
Woche 64	101	9,57 (19,054)	-3,66 (1,035)	84	7,54 (15,823)	-3,39 (1,112)	-0,27 [-3,264; 2,724]	0,8593
Woche 68	91	8,42 (16,919)	-3,71 (1,155)	82	7,32 (15,735)	-2,55 (1,216)	-1,16 [-4,461; 2,146]	0,4908
Woche 72	91	9,52 (19,427)	-4,10 (1,152)	78	7,69 (15,122)	-1,13 (1,230)	-2,97 [-6,297; 0,347]	0,0790
Woche 76	90	10,00 (19,641)	-1,86 (1,248)	69	8,21 (16,574)	-2,14 (1,383)	0,28 [-3,392; 3,953]	0,8805
Woche 80	87	9,58 (19,627)	-3,28 (1,161)	65	9,23 (17,187)	-1,23 (1,303)	-2,04 [-5,480; 1,396]	0,2432
Woche 84	87	10,34 (19,890)	-2,98 (1,078)	67	8,96 (16,999)	-3,24 (1,203)	0,26 [-2,918; 3,446]	0,8704
Woche 88	84	10,71 (20,147)	-3,84 (1,013)	61	8,74 (17,107)	-2,59 (1,152)	-1,25 [-4,272; 1,773]	0,4163
Woche 92	84	9,92 (19,892)	-2,53 (1,061)	60	7,78 (16,657)	-3,27 (1,218)	0,73 [-2,448; 3,918]	0,6497
Woche 96	79	10,97 (20,480)	-3,12 (1,279)	55	8,48 (17,235)	0,55 (1,487)	-3,67 [-7,533; 0,197]	0,0628
Woche 100	86	9,69 (19,714)	-4,51 (0,987)	59	6,78 (16,117)	-2,50 (1,158)	-2,01 [-5,009; 0,992]	0,1885
Woche 104	73	9,59 (19,626)	-4,12 (1,218)	56	8,93 (17,397)	-2,69 (1,385)	-1,44 [-5,070; 2,200]	0,4373
Woche 108	71	8,45 (19,288)	-3,30 (1,328)	52	7,05 (15,249)	-0,93 (1,531)	-2,37 [-6,368; 1,627]	0,2437
Woche 112	68	9,31 (20,641)	-4,01 (1,296)	47	5,67 (12,663)	-1,30 (1,519)	-2,71 [-6,651; 1,232]	0,1768
Woche 116	62	8,60 (19,959)	-3,06 (1,380)	51	5,88 (14,462)	-0,95 (1,540)	-2,11 [-6,190; 1,978]	0,3101

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.3 ADRIATIC: Summary of analysis of change from baseline over time in Dysphagie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	8,77 (19,443)	-3,46 (1,317)	47	7,80 (17,324)	-3,44 (1,462)	-0,02 [-3,911; 3,870]	0,9915
Woche 124	54	9,26 (19,870)	-4,41 (1,269)	45	8,15 (16,136)	-1,89 (1,406)	-2,53 [-6,268; 1,212]	0,1839
Woche 128	54	6,17 (14,586)	-2,49 (1,351)	40	9,17 (18,471)	-1,47 (1,547)	-1,02 [-5,078; 3,047]	0,6220
Woche 132	50	8,67 (17,574)	-4,46 (1,166)	39	10,26 (18,970)	-2,68 (1,327)	-1,78 [-5,277; 1,712]	0,3148
Woche 136	48	5,56 (14,314)	-2,28 (1,488)	34	10,78 (19,627)	-1,84 (1,737)	-0,45 [-4,984; 4,090]	0,8459
Woche 140	45	5,93 (14,718)	-3,46 (1,474)	34	8,82 (17,034)	0,44 (1,685)	-3,89 [-8,317; 0,532]	0,0842
Woche 144	36	7,41 (16,156)	-5,36 (1,041)	30	7,78 (16,800)	-3,72 (1,160)	-1,64 [-4,726; 1,445]	0,2945
Woche 148	40	8,33 (16,452)	-4,92 (1,247)	27	8,64 (17,523)	-1,97 (1,487)	-2,94 [-6,789; 0,902]	0,1322
Woche 152	38	8,77 (16,773)	-0,77 (1,741)	28	7,14 (16,623)	-1,66 (2,026)	0,89 [-4,400; 6,186]	0,7388
Woche 156	35	10,48 (17,660)	-0,68 (1,746)	28	5,95 (13,001)	-3,91 (1,981)	3,22 [-2,022; 8,467]	0,2261
Woche 160	31	9,68 (17,625)	-4,37 (1,561)	26	7,69 (17,147)	-1,15 (1,738)	-3,21 [-7,843; 1,421]	0,1723
Woche 164	31	7,53 (16,577)	-2,81 (1,752)	22	7,58 (17,614)	-1,11 (2,045)	-1,70 [-7,043; 3,644]	0,5293
Woche 168	27	9,88 (18,057)	-4,52 (1,674)	25	9,33 (20,458)	-1,89 (1,796)	-2,64 [-7,509; 2,237]	0,2856
Woche 172	30	8,89 (17,361)	-3,68 (1,695)	20	8,33 (18,337)	-3,43 (2,010)	-0,25 [-5,487; 4,983]	0,9240
Woche 176	22	7,58 (14,298)	-3,05 (1,866)	18	9,26 (19,150)	-2,64 (2,081)	-0,41 [-5,991; 5,177]	0,8847
Woche 180	20	8,33 (18,337)	-2,63 (2,149)	16	8,33 (19,245)	-1,19 (2,410)	-1,44 [-7,906; 5,029]	0,6577
Woche 184	18	9,26 (19,150)	-4,52 (2,035)	17	7,84 (18,743)	0,20 (2,112)	-4,72 [-10,608; 1,176]	0,1142

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.3 ADRIATIC: Summary of analysis of change from baseline over time in Dysphagie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	6,25 (18,130)	-7,40 (1,860)	15	2,22 (8,607)	-3,06 (1,988)	-4,34 [-9,743; 1,062]	0,1126
Durchschnitt über alle Visiten	216	7,72 (17,077)	-3,17 (0,670)	211	9,48 (18,536)	-1,65 (0,719)	-1,52 [-3,449; 0,414]	0,1232
Hedges' g SMD							-0,15 [-0,339; 0,041]	0,1233

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.4 ADRIATIC: Summary of analysis of change from baseline over time in Hämoptoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	1,85 (8,428)	-0,40 (0,468)	180	2,22 (9,052)	-0,01 (0,468)	-0,39 [-1,686; 0,909]	0,5573
Woche 2	185	1,80 (8,319)	-0,98 (0,460)	186	1,97 (8,612)	-0,01 (0,461)	-0,98 [-2,253; 0,300]	0,1339
Woche 3	185	1,80 (8,319)	-0,85 (0,460)	179	1,68 (8,114)	-0,75 (0,468)	-0,10 [-1,387; 1,186]	0,8782
Woche 4	204	2,12 (8,807)	-1,41 (0,441)	198	1,85 (8,359)	-1,33 (0,448)	-0,08 [-1,311; 1,153]	0,8999
Woche 5	183	1,64 (8,028)	-0,90 (0,463)	190	1,93 (8,525)	-1,53 (0,456)	0,63 [-0,644; 1,902]	0,3330
Woche 6	184	1,81 (8,340)	-1,08 (0,462)	176	2,08 (8,842)	-0,90 (0,472)	-0,18 [-1,472; 1,116]	0,7875
Woche 7	181	1,66 (8,071)	-0,52 (0,465)	176	2,08 (8,842)	-0,16 (0,472)	-0,37 [-1,666; 0,934]	0,5808
Woche 8	192	1,91 (8,483)	-0,15 (0,454)	183	2,00 (8,679)	-0,90 (0,465)	0,75 [-0,524; 2,022]	0,2489
Woche 12	177	1,32 (7,421)	-0,46 (0,472)	176	2,27 (9,148)	-1,03 (0,473)	0,57 [-0,737; 1,883]	0,3912
Woche 16	168	1,39 (7,612)	-1,57 (0,483)	170	2,35 (9,299)	-1,02 (0,481)	-0,54 [-1,879; 0,797]	0,4277
Woche 20	160	1,46 (7,794)	-1,70 (0,495)	158	2,11 (8,969)	-1,19 (0,498)	-0,50 [-1,880; 0,874]	0,4738
Woche 24	147	1,59 (8,121)	-0,54 (0,515)	151	2,43 (9,506)	-1,50 (0,509)	0,96 [-0,461; 2,380]	0,1853
Woche 28	148	1,58 (8,095)	-0,98 (0,515)	136	1,96 (7,872)	-1,94 (0,535)	0,96 [-0,498; 2,411]	0,1975
Woche 32	141	1,42 (7,840)	-1,45 (0,527)	131	1,53 (6,995)	-1,74 (0,546)	0,29 [-1,197; 1,775]	0,7030
Woche 36	135	1,73 (8,463)	-1,18 (0,538)	125	1,87 (7,695)	-0,90 (0,559)	-0,27 [-1,795; 1,247]	0,7240
Woche 40	120	1,11 (7,401)	-0,35 (0,570)	107	2,18 (8,281)	-0,88 (0,601)	0,54 [-1,089; 2,160]	0,5182
Woche 44	117	1,71 (8,584)	-0,99 (0,577)	109	2,14 (8,209)	-0,50 (0,598)	-0,49 [-2,123; 1,134]	0,5518

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.4 ADRIATIC: Summary of analysis of change from baseline over time in Hämoptoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	1,53 (8,346)	-1,24 (0,596)	107	2,18 (8,281)	-0,18 (0,604)	-1,06 [-2,729; 0,601]	0,2106
Woche 52	112	1,49 (8,236)	-1,05 (0,591)	103	1,62 (7,199)	-1,61 (0,616)	0,56 [-1,112; 2,232]	0,5116
Woche 56	107	1,56 (8,422)	-1,59 (0,604)	92	2,54 (8,886)	-0,56 (0,650)	-1,03 [-2,773; 0,707]	0,2447
Woche 60	103	1,94 (9,129)	-1,12 (0,615)	86	2,71 (9,168)	-1,81 (0,672)	0,69 [-1,096; 2,474]	0,4491
Woche 64	101	1,65 (8,662)	-1,47 (0,622)	84	2,38 (8,636)	-1,18 (0,680)	-0,29 [-2,095; 1,519]	0,7548
Woche 68	91	1,83 (9,112)	-1,09 (0,653)	82	2,85 (9,371)	-1,08 (0,690)	0,00 [-1,865; 1,859]	0,9977
Woche 72	91	2,20 (9,689)	-0,80 (0,653)	78	2,56 (8,940)	-0,93 (0,704)	0,13 [-1,754; 2,009]	0,8946
Woche 76	90	2,22 (9,741)	-1,65 (0,656)	69	2,90 (9,461)	-0,12 (0,747)	-1,52 [-3,472; 0,426]	0,1255
Woche 80	87	2,30 (9,900)	-1,69 (0,667)	65	2,56 (8,951)	-1,64 (0,769)	-0,05 [-2,041; 1,949]	0,9641
Woche 84	87	1,92 (9,313)	-0,95 (0,668)	67	2,99 (9,590)	-1,24 (0,762)	0,29 [-1,696; 2,279]	0,7734
Woche 88	84	2,38 (10,068)	-1,05 (0,680)	61	3,28 (10,009)	-1,17 (0,797)	0,12 [-1,933; 2,170]	0,9099
Woche 92	84	2,38 (10,068)	-0,82 (0,680)	60	2,78 (9,291)	-2,02 (0,803)	1,21 [-0,855; 3,270]	0,2511
Woche 96	79	2,53 (10,367)	-1,37 (0,699)	55	3,64 (10,488)	-1,84 (0,840)	0,48 [-1,662; 2,616]	0,6619
Woche 100	86	2,33 (9,955)	-1,05 (0,673)	59	3,39 (10,161)	-0,99 (0,814)	-0,06 [-2,128; 2,011]	0,9558
Woche 104	73	2,28 (10,136)	-1,50 (0,726)	56	3,57 (10,403)	-1,25 (0,836)	-0,25 [-2,423; 1,915]	0,8185
Woche 108	71	2,35 (10,272)	-1,40 (0,739)	52	3,21 (9,923)	-2,04 (0,865)	0,64 [-1,584; 2,872]	0,5708
Woche 112	68	2,45 (10,488)	-0,75 (0,756)	47	3,55 (10,389)	-0,56 (0,908)	-0,19 [-2,503; 2,123]	0,8721
Woche 116	62	2,15 (10,227)	-0,93 (0,790)	51	2,61 (9,051)	-0,28 (0,874)	-0,65 [-2,960; 1,660]	0,5810

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.4 ADRIATIC: Summary of analysis of change from baseline over time in Hämoptoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	1,75 (9,802)	1,27 (0,823)	47	3,55 (10,389)	-1,19 (0,912)	2,46 [0,048; 4,868]	0,0456*
Woche 124	54	1,23 (6,354)	-1,64 (0,847)	45	3,70 (10,594)	-0,10 (0,936)	-1,53 [-4,019; 0,953]	0,2266
Woche 128	54	0,62 (4,536)	-0,18 (0,856)	40	3,33 (10,127)	1,45 (0,989)	-1,63 [-4,215; 0,954]	0,2162
Woche 132	50	0,67 (4,714)	-1,78 (0,887)	39	3,42 (10,245)	-0,52 (1,006)	-1,26 [-3,910; 1,390]	0,3513
Woche 136	48	0,69 (4,811)	-1,93 (0,905)	34	3,92 (10,901)	-0,47 (1,078)	-1,47 [-4,253; 1,320]	0,3024
Woche 140	45	0,74 (4,969)	-1,71 (0,935)	34	3,92 (10,901)	-1,28 (1,082)	-0,44 [-3,266; 2,395]	0,7630
Woche 144	36	0,93 (5,556)	-1,43 (1,040)	30	2,22 (8,457)	-1,97 (1,139)	0,55 [-2,482; 3,574]	0,7235
Woche 148	40	0,83 (5,270)	-0,71 (0,995)	27	3,70 (10,675)	-0,58 (1,209)	-0,12 [-3,217; 2,970]	0,9377
Woche 152	38	0,88 (5,407)	1,34 (1,022)	28	3,57 (10,499)	-1,46 (1,194)	2,80 [-0,301; 5,902]	0,0767
Woche 156	35	1,90 (7,850)	-0,63 (1,061)	28	2,38 (8,742)	-1,44 (1,193)	0,81 [-2,322; 3,941]	0,6122
Woche 160	31	1,08 (5,987)	-1,23 (1,132)	26	3,85 (10,860)	-1,20 (1,253)	-0,03 [-3,358; 3,301]	0,9866
Woche 164	31	1,08 (5,987)	-1,45 (1,085)	22	4,55 (11,708)	0,00 (1,285)	-1,45 [-4,782; 1,878]	0,3923
Woche 168	27	0,00 (0,000)	-1,77 (1,153)	25	4,00 (11,055)	-1,13 (1,195)	-0,64 [-3,943; 2,671]	0,7061
Woche 172	30	1,11 (6,086)	-2,41 (1,100)	20	3,33 (10,260)	-1,49 (1,309)	-0,92 [-4,290; 2,448]	0,5918
Woche 176	22	1,52 (7,107)	-1,22 (1,243)	18	3,70 (10,779)	-1,25 (1,393)	0,03 [-3,640; 3,708]	0,9855
Woche 180	20	1,67 (7,454)	-2,09 (1,325)	16	4,17 (11,386)	-0,91 (1,495)	-1,17 [-5,104; 2,755]	0,5575
Woche 184	18	1,85 (7,857)	-1,18 (1,418)	17	3,92 (11,070)	-1,80 (1,494)	0,62 [-3,422; 4,669]	0,7623

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.4 ADRIATIC: Summary of analysis of change from baseline over time in Hämoptoe (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	2,08 (8,333)	-0,17 (1,553)	15	2,22 (8,607)	-2,19 (1,608)	2,02 [-2,369; 6,410]	0,3666
Durchschnitt über alle Visiten	216	2,01 (8,572)	-1,06 (0,204)	211	1,90 (8,394)	-1,03 (0,227)	-0,03 [-0,631; 0,572]	0,9228
Hedges' g SMD							-0,01 [-0,199; 0,180]	0,9226

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.5 ADRIATIC: Summary of analysis of change from baseline over time in Husten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	23,33 (21,976)	0,35 (1,360)	180	25,56 (23,923)	-0,32 (1,365)	0,67 [-3,119; 4,462]	0,7280
Woche 2	185	22,88 (21,677)	0,87 (1,382)	186	25,81 (24,076)	2,07 (1,387)	-1,20 [-5,052; 2,650]	0,5402
Woche 3	185	23,60 (22,554)	2,09 (1,439)	179	24,77 (22,649)	1,55 (1,458)	0,54 [-3,486; 4,568]	0,7919
Woche 4	204	23,53 (21,991)	3,10 (1,384)	198	25,25 (23,313)	3,44 (1,404)	-0,34 [-4,218; 3,535]	0,8626
Woche 5	183	22,95 (21,995)	5,04 (1,549)	190	25,79 (24,400)	1,91 (1,546)	3,13 [-1,175; 7,434]	0,1537
Woche 6	184	23,01 (21,949)	5,03 (1,478)	176	26,33 (24,329)	0,54 (1,508)	4,49 [0,341; 8,645]	0,0340*
Woche 7	181	22,65 (21,860)	6,23 (1,616)	176	26,70 (24,435)	1,94 (1,644)	4,29 [-0,244; 8,828]	0,0636
Woche 8	192	22,92 (21,741)	7,23 (1,611)	183	26,05 (24,367)	3,21 (1,646)	4,01 [-0,519; 8,543]	0,0825
Woche 12	177	22,41 (21,467)	4,80 (1,675)	176	25,95 (24,990)	1,53 (1,692)	3,27 [-1,419; 7,953]	0,1713
Woche 16	168	22,62 (22,285)	3,18 (1,697)	170	27,06 (24,857)	4,57 (1,708)	-1,39 [-6,132; 3,349]	0,5643
Woche 20	160	22,08 (22,082)	1,92 (1,646)	158	26,79 (25,366)	3,14 (1,665)	-1,22 [-5,831; 3,392]	0,6034
Woche 24	147	22,45 (22,126)	3,44 (1,580)	151	26,49 (25,623)	2,49 (1,581)	0,96 [-3,446; 5,356]	0,6698
Woche 28	148	22,07 (22,184)	2,31 (1,725)	136	26,47 (25,698)	3,69 (1,780)	-1,37 [-6,257; 3,509]	0,5804
Woche 32	141	22,46 (22,002)	3,29 (1,663)	131	26,21 (24,810)	5,03 (1,716)	-1,74 [-6,449; 2,961]	0,4664
Woche 36	135	21,73 (21,285)	1,83 (1,645)	125	25,87 (25,352)	0,63 (1,700)	1,20 [-3,461; 5,862]	0,6128
Woche 40	120	19,72 (20,496)	2,98 (1,743)	107	26,79 (26,477)	4,22 (1,820)	-1,24 [-6,220; 3,735]	0,6236
Woche 44	117	20,51 (20,457)	3,13 (1,899)	109	26,91 (25,851)	2,13 (1,965)	1,00 [-4,395; 6,397]	0,7153

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.5 ADRIATIC: Summary of analysis of change from baseline over time in Husten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	21,10 (20,618)	3,53 (1,888)	107	27,10 (25,954)	2,48 (1,930)	1,05 [-4,279; 6,381]	0,6983
Woche 52	112	21,73 (20,362)	-0,30 (1,794)	103	25,89 (25,106)	1,33 (1,866)	-1,63 [-6,739; 3,471]	0,5293
Woche 56	107	21,18 (20,676)	4,66 (1,805)	92	25,36 (24,890)	2,16 (1,917)	2,50 [-2,693; 7,693]	0,3441
Woche 60	103	20,71 (20,408)	-0,40 (1,859)	86	26,36 (25,625)	-2,06 (1,996)	1,66 [-3,730; 7,044]	0,5453
Woche 64	101	20,46 (20,532)	4,61 (1,945)	84	26,19 (25,387)	0,83 (2,092)	3,78 [-1,864; 9,419]	0,1885
Woche 68	91	21,25 (20,797)	0,12 (2,041)	82	25,20 (25,424)	2,29 (2,147)	-2,18 [-8,022; 3,670]	0,4643
Woche 72	91	20,88 (20,875)	0,55 (1,868)	78	25,64 (25,721)	1,64 (1,996)	-1,09 [-6,487; 4,309]	0,6915
Woche 76	90	21,48 (20,790)	0,07 (2,049)	69	27,54 (26,787)	3,89 (2,286)	-3,82 [-9,886; 2,251]	0,2165
Woche 80	87	21,46 (20,945)	0,03 (1,765)	65	27,18 (26,934)	0,92 (1,994)	-0,89 [-6,148; 4,376]	0,7403
Woche 84	87	20,69 (20,486)	-1,57 (1,906)	67	27,36 (27,170)	3,50 (2,139)	-5,07 [-10,735; 0,598]	0,0794
Woche 88	84	20,63 (20,636)	0,51 (2,063)	61	27,32 (26,880)	1,47 (2,361)	-0,96 [-7,161; 5,251]	0,7619
Woche 92	84	19,05 (19,557)	-3,39 (2,032)	60	24,44 (26,657)	1,22 (2,328)	-4,61 [-10,712; 1,495]	0,1382
Woche 96	79	20,68 (20,187)	0,46 (2,114)	55	27,88 (26,265)	2,43 (2,474)	-1,97 [-8,415; 4,476]	0,5475
Woche 100	86	20,93 (21,111)	0,75 (1,788)	59	27,12 (26,605)	-0,86 (2,104)	1,60 [-3,859; 7,065]	0,5636
Woche 104	73	21,00 (20,418)	1,68 (2,134)	56	26,79 (25,757)	1,00 (2,433)	0,68 [-5,721; 7,083]	0,8342
Woche 108	71	21,60 (21,156)	0,49 (2,406)	52	25,00 (24,588)	1,16 (2,774)	-0,67 [-7,927; 6,589]	0,8560
Woche 112	68	21,08 (20,688)	0,08 (2,191)	47	25,53 (25,265)	2,07 (2,565)	-2,00 [-8,667; 4,676]	0,5560
Woche 116	62	20,97 (21,111)	0,65 (2,236)	51	23,53 (24,307)	1,56 (2,478)	-0,90 [-7,497; 5,688]	0,7868

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.5 ADRIATIC: Summary of analysis of change from baseline over time in Husten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	18,71 (20,909)	3,53 (2,475)	47	26,95 (26,593)	1,65 (2,732)	1,88 [-5,438; 9,194]	0,6130
Woche 124	54	19,75 (19,977)	2,59 (2,592)	45	24,44 (26,968)	4,41 (2,856)	-1,82 [-9,452; 5,818]	0,6389
Woche 128	54	20,37 (19,870)	0,21 (2,424)	40	24,17 (26,135)	2,34 (2,781)	-2,13 [-9,435; 5,168]	0,5646
Woche 132	50	18,67 (20,382)	-3,51 (2,150)	39	25,64 (26,995)	0,25 (2,428)	-3,76 [-10,192; 2,678]	0,2504
Woche 136	48	20,83 (21,333)	-1,81 (2,404)	34	27,45 (26,554)	-2,41 (2,827)	0,60 [-6,770; 7,979]	0,8714
Woche 140	45	20,74 (21,660)	-4,87 (2,401)	34	25,49 (24,699)	-0,06 (2,760)	-4,81 [-12,070; 2,452]	0,1924
Woche 144	36	19,44 (20,119)	-3,18 (2,740)	30	22,22 (20,216)	1,57 (3,034)	-4,75 [-12,850; 3,355]	0,2477
Woche 148	40	20,83 (20,929)	-6,42 (2,223)	27	24,69 (25,474)	0,10 (2,653)	-6,52 [-13,401; 0,355]	0,0628
Woche 152	38	20,18 (21,280)	-1,73 (2,692)	28	25,00 (26,644)	-0,88 (3,123)	-0,85 [-9,055; 7,352]	0,8373
Woche 156	35	20,95 (21,520)	-5,81 (2,451)	28	25,00 (25,051)	-1,41 (2,773)	-4,40 [-11,761; 2,965]	0,2388
Woche 160	31	22,58 (21,751)	4,83 (3,561)	26	28,21 (29,352)	2,18 (3,975)	2,65 [-7,990; 13,291]	0,6218
Woche 164	31	19,35 (18,805)	-4,89 (3,180)	22	24,24 (25,577)	4,85 (3,689)	-9,73 [-19,462; -0,007]	0,0498*
Woche 168	27	19,75 (19,080)	-0,38 (3,210)	25	24,00 (26,387)	-0,50 (3,415)	0,12 [-9,224; 9,470]	0,9791
Woche 172	30	22,22 (20,216)	-5,65 (2,729)	20	26,67 (25,592)	1,31 (3,269)	-6,96 [-15,473; 1,545]	0,1072
Woche 176	22	21,21 (19,370)	2,38 (3,285)	18	24,07 (19,150)	4,15 (3,660)	-1,77 [-11,648; 8,106]	0,7205
Woche 180	20	21,67 (19,571)	-1,69 (3,601)	16	25,00 (19,245)	2,24 (4,054)	-3,93 [-14,841; 6,976]	0,4725
Woche 184	18	22,22 (16,169)	-7,75 (4,833)	17	23,53 (19,596)	5,08 (5,106)	-12,83 [-26,991; 1,327]	0,0746

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.5 ADRIATIC: Summary of analysis of change from baseline over time in Husten (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	18,75 (17,078)	1,04 (5,840)	15	20,00 (21,082)	3,62 (6,118)	-2,58 [-19,531; 14,380]	0,7601
Durchschnitt über alle Visiten	216	22,99 (21,831)	0,68 (1,073)	211	25,91 (23,963)	1,84 (1,165)	-1,15 [-4,271; 1,968]	0,4685
Hedges' g SMD							-0,07 [-0,260; 0,119]	0,4677

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.6 ADRIATIC: Summary of analysis of change from baseline over time in Periphere Neuropathie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	7,41 (16,734)	1,10 (1,089)	180	8,89 (17,117)	0,26 (1,092)	0,84 [-2,191; 3,875]	0,5856
Woche 2	185	7,75 (16,486)	1,02 (1,134)	186	8,96 (17,426)	0,43 (1,137)	0,59 [-2,563; 3,753]	0,7114
Woche 3	185	7,57 (16,751)	2,16 (1,205)	179	9,12 (16,495)	3,29 (1,221)	-1,13 [-4,502; 2,242]	0,5106
Woche 4	204	7,03 (16,198)	1,54 (1,281)	198	8,59 (16,083)	4,65 (1,298)	-3,11 [-6,698; 0,472]	0,0886
Woche 5	183	6,92 (16,410)	3,03 (1,234)	190	8,95 (17,368)	5,09 (1,232)	-2,07 [-5,494; 1,363]	0,2371
Woche 6	184	6,88 (16,373)	3,11 (1,282)	176	8,71 (17,086)	6,63 (1,305)	-3,53 [-7,123; 0,071]	0,0547
Woche 7	181	6,81 (16,375)	4,16 (1,440)	176	9,66 (17,857)	7,87 (1,463)	-3,72 [-7,756; 0,320]	0,0710
Woche 8	192	6,42 (15,975)	5,42 (1,378)	183	8,93 (16,367)	7,51 (1,405)	-2,09 [-5,957; 1,785]	0,2901
Woche 12	177	6,78 (16,795)	4,65 (1,437)	176	9,85 (17,930)	6,40 (1,453)	-1,75 [-5,775; 2,267]	0,3916
Woche 16	168	6,75 (16,540)	5,18 (1,438)	170	9,80 (18,003)	6,20 (1,447)	-1,02 [-5,036; 2,992]	0,6171
Woche 20	160	6,25 (15,499)	6,29 (1,429)	158	10,13 (18,319)	5,59 (1,446)	0,70 [-3,307; 4,701]	0,7324
Woche 24	147	5,90 (14,958)	6,57 (1,466)	151	9,05 (17,611)	7,09 (1,465)	-0,52 [-4,603; 3,558]	0,8014
Woche 28	148	6,31 (15,234)	5,88 (1,437)	136	10,05 (18,734)	5,20 (1,481)	0,68 [-3,381; 4,750]	0,7410
Woche 32	141	6,15 (15,225)	4,74 (1,527)	131	8,91 (17,455)	6,13 (1,572)	-1,39 [-5,702; 2,930]	0,5282
Woche 36	135	5,68 (13,834)	5,47 (1,525)	125	9,07 (17,646)	4,90 (1,571)	0,56 [-3,751; 4,881]	0,7970
Woche 40	120	5,83 (14,111)	6,16 (1,554)	107	9,35 (18,197)	5,89 (1,621)	0,27 [-4,157; 4,702]	0,9036
Woche 44	117	5,70 (14,041)	4,88 (1,524)	109	9,79 (18,869)	6,54 (1,576)	-1,66 [-5,989; 2,665]	0,4503

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.6 ADRIATIC: Summary of analysis of change from baseline over time in Periphere Neuropathie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	6,42 (14,683)	6,09 (1,578)	107	9,35 (18,197)	4,44 (1,612)	1,65 [-2,800; 6,095]	0,4666
Woche 52	112	6,55 (14,731)	4,85 (1,414)	103	8,41 (15,978)	4,84 (1,468)	0,01 [-4,005; 4,030]	0,9950
Woche 56	107	6,54 (14,794)	6,29 (1,491)	92	10,14 (18,972)	7,90 (1,584)	-1,61 [-5,900; 2,683]	0,4613
Woche 60	103	6,15 (14,573)	5,78 (1,517)	86	9,69 (19,040)	5,70 (1,627)	0,08 [-4,308; 4,473]	0,9706
Woche 64	101	5,94 (14,450)	7,13 (1,513)	84	9,92 (16,989)	6,02 (1,627)	1,12 [-3,268; 5,506]	0,6160
Woche 68	91	6,59 (15,088)	4,91 (1,439)	82	9,76 (19,236)	4,80 (1,518)	0,11 [-4,018; 4,238]	0,9583
Woche 72	91	6,23 (14,834)	6,73 (1,539)	78	10,26 (19,597)	4,35 (1,649)	2,38 [-2,077; 6,832]	0,2943
Woche 76	90	6,67 (15,156)	6,97 (1,708)	69	9,66 (19,886)	4,35 (1,899)	2,61 [-2,426; 7,655]	0,3080
Woche 80	87	6,90 (15,366)	8,25 (1,626)	65	11,28 (20,647)	3,93 (1,838)	4,32 [-0,528; 9,163]	0,0805
Woche 84	87	5,75 (14,562)	6,61 (1,733)	67	10,95 (20,423)	6,16 (1,947)	0,44 [-4,713; 5,599]	0,8657
Woche 88	84	5,56 (14,482)	6,68 (1,751)	61	10,93 (20,836)	3,75 (2,005)	2,93 [-2,337; 8,200]	0,2741
Woche 92	84	6,75 (15,332)	4,46 (1,698)	60	10,56 (20,805)	6,65 (1,964)	-2,20 [-7,327; 2,934]	0,3998
Woche 96	79	6,33 (15,169)	6,31 (1,771)	55	10,30 (20,157)	5,89 (2,073)	0,42 [-4,971; 5,811]	0,8781
Woche 100	86	5,81 (14,634)	7,73 (1,669)	59	10,17 (19,821)	4,20 (1,964)	3,54 [-1,559; 8,634]	0,1728
Woche 104	73	5,48 (14,713)	7,10 (1,613)	56	11,31 (20,377)	5,42 (1,846)	1,68 [-3,178; 6,539]	0,4962
Woche 108	71	4,69 (12,966)	3,54 (1,578)	52	9,62 (20,170)	5,75 (1,814)	-2,21 [-6,976; 2,546]	0,3602
Woche 112	68	4,90 (14,415)	4,92 (1,574)	47	10,64 (20,974)	5,39 (1,840)	-0,47 [-5,276; 4,327]	0,8457

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.6 ADRIATIC: Summary of analysis of change from baseline over time in Periphere Neuropathie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 116	62	4,30 (12,781)	5,80 (1,732)	51	9,80 (18,005)	4,88 (1,915)	0,92 [-4,204; 6,044]	0,7236
Woche 120	57	4,09 (12,709)	7,38 (1,889)	47	10,64 (18,528)	4,31 (2,086)	3,07 [-2,530; 8,673]	0,2806
Woche 124	54	3,70 (12,399)	6,99 (1,756)	45	10,37 (21,108)	1,62 (1,932)	5,37 [0,173; 10,561]	0,0429*
Woche 128	54	3,70 (12,399)	5,77 (1,837)	40	9,17 (16,858)	3,08 (2,083)	2,69 [-2,830; 8,207]	0,3372
Woche 132	50	3,33 (12,141)	4,21 (1,740)	39	8,55 (16,610)	2,45 (1,944)	1,76 [-3,416; 6,935]	0,5029
Woche 136	48	5,56 (14,314)	4,55 (2,004)	34	7,84 (14,352)	6,01 (2,338)	-1,45 [-7,553; 4,645]	0,6382
Woche 140	45	5,93 (14,718)	4,52 (1,894)	34	10,78 (21,274)	1,38 (2,181)	3,14 [-2,598; 8,883]	0,2808
Woche 144	36	6,48 (15,573)	1,66 (2,197)	30	7,78 (14,339)	6,79 (2,446)	-5,13 [-11,662; 1,395]	0,1220
Woche 148	40	5,00 (14,222)	3,78 (2,136)	27	8,64 (14,886)	5,54 (2,528)	-1,76 [-8,335; 4,817]	0,5971
Woche 152	38	6,14 (15,217)	5,12 (2,382)	28	8,33 (14,699)	3,09 (2,756)	2,02 [-5,215; 9,264]	0,5802
Woche 156	35	6,67 (15,760)	4,84 (2,243)	28	8,33 (14,699)	3,31 (2,528)	1,52 [-5,184; 8,232]	0,6533
Woche 160	31	6,45 (15,915)	4,60 (2,234)	26	8,97 (15,078)	-0,71 (2,479)	5,31 [-1,324; 11,938]	0,1155
Woche 164	31	5,38 (15,146)	7,41 (2,541)	22	10,61 (15,891)	1,22 (2,956)	6,19 [-1,602; 13,991]	0,1179
Woche 168	27	4,94 (15,202)	3,54 (2,679)	25	10,67 (15,870)	1,29 (2,850)	2,25 [-5,580; 10,073]	0,5699
Woche 172	30	5,56 (15,371)	7,34 (2,213)	20	11,67 (16,312)	2,82 (2,624)	4,52 [-2,349; 11,394]	0,1942
Woche 176	22	6,06 (16,703)	6,07 (2,607)	18	12,96 (16,721)	2,60 (2,943)	3,47 [-4,429; 11,374]	0,3837
Woche 180	20	6,67 (17,438)	6,90 (3,262)	16	12,50 (16,667)	6,13 (3,711)	0,77 [-9,148; 10,695]	0,8767

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.6 ADRIATIC: Summary of analysis of change from baseline over time in Periphere Neuropathie (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 184	18	5,56 (17,150)	5,33 (3,361)	17	11,76 (16,420)	6,69 (3,551)	-1,36 [-11,258; 8,539]	0,7838
Woche 188	16	8,33 (19,245)	8,35 (3,549)	15	8,89 (15,258)	4,43 (3,699)	3,92 [-6,385; 14,219]	0,4485
Durchschnitt über alle Visiten	216	7,56 (16,687)	5,28 (0,900)	211	8,53 (16,931)	4,64 (0,967)	0,64 [-1,967; 3,238]	0,6314
Hedges' g SMD							0,05 [-0,143; 0,236]	0,6308

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.7 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen an anderen Stellen des Körpers (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	11,85 (18,180)	0,31 (1,415)	180	15,37 (20,953)	1,90 (1,422)	-1,59 [-5,537; 2,363]	0,4301
Woche 2	185	12,07 (18,510)	-0,49 (1,484)	186	15,23 (21,387)	4,96 (1,491)	-5,45 [-9,591; -1,310]	0,0100*
Woche 3	185	12,43 (18,918)	-0,34 (1,492)	179	15,64 (21,864)	5,01 (1,516)	-5,35 [-9,539; -1,167]	0,0123*
Woche 4	204	12,58 (18,997)	-0,33 (1,502)	198	15,49 (21,928)	4,18 (1,526)	-4,51 [-8,725; -0,300]	0,0358*
Woche 5	183	11,48 (18,376)	1,62 (1,476)	190	16,14 (22,414)	3,39 (1,474)	-1,77 [-5,879; 2,339]	0,3977
Woche 6	184	11,96 (18,493)	1,96 (1,494)	176	17,23 (22,810)	5,12 (1,530)	-3,17 [-7,380; 1,043]	0,1399
Woche 7	181	11,79 (18,488)	1,72 (1,488)	176	16,86 (22,817)	3,66 (1,516)	-1,94 [-6,125; 2,243]	0,3624
Woche 8	192	11,63 (18,308)	2,90 (1,556)	183	16,03 (22,331)	5,32 (1,592)	-2,42 [-6,801; 1,966]	0,2790
Woche 12	177	11,49 (17,763)	0,55 (1,641)	176	16,67 (22,817)	3,56 (1,662)	-3,02 [-7,619; 1,588]	0,1986
Woche 16	168	11,90 (18,343)	3,95 (1,568)	170	16,08 (22,998)	4,05 (1,578)	-0,10 [-4,478; 4,285]	0,9654
Woche 20	160	11,88 (18,064)	2,91 (1,564)	158	17,09 (23,112)	5,67 (1,587)	-2,76 [-7,147; 1,637]	0,2182
Woche 24	147	12,47 (18,387)	5,09 (1,703)	151	16,56 (22,069)	4,82 (1,709)	0,27 [-4,486; 5,018]	0,9124
Woche 28	148	11,94 (18,241)	2,54 (1,743)	136	17,16 (21,463)	6,94 (1,807)	-4,40 [-9,348; 0,553]	0,0815
Woche 32	141	11,82 (18,316)	4,41 (1,689)	131	16,54 (20,827)	5,52 (1,749)	-1,11 [-5,903; 3,684]	0,6492
Woche 36	135	11,36 (17,355)	3,40 (1,587)	125	16,27 (21,003)	5,01 (1,645)	-1,61 [-6,120; 2,901]	0,4834
Woche 40	120	11,67 (17,633)	2,47 (1,835)	107	16,51 (21,168)	9,28 (1,930)	-6,81 [-12,061; -1,551]	0,0113*
Woche 44	117	11,68 (17,680)	5,02 (1,834)	109	17,43 (22,497)	6,44 (1,911)	-1,42 [-6,647; 3,810]	0,5938

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.7 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen an anderen Stellen des Körpers (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	10,09 (17,276)	2,59 (1,846)	107	16,82 (22,136)	5,93 (1,887)	-3,35 [-8,572; 1,873]	0,2078
Woche 52	112	10,12 (17,236)	4,42 (2,011)	103	16,83 (21,830)	6,90 (2,095)	-2,49 [-8,232; 3,260]	0,3952
Woche 56	107	10,28 (17,382)	2,73 (1,774)	92	15,22 (21,205)	6,69 (1,883)	-3,96 [-9,070; 1,152]	0,1284
Woche 60	103	11,00 (17,705)	2,26 (1,609)	86	16,67 (21,542)	3,37 (1,735)	-1,11 [-5,789; 3,564]	0,6399
Woche 64	101	9,90 (16,696)	5,57 (1,939)	84	15,87 (21,003)	4,51 (2,087)	1,06 [-4,573; 6,702]	0,7104
Woche 68	91	10,62 (17,126)	3,37 (1,643)	82	15,45 (21,720)	4,39 (1,728)	-1,03 [-5,739; 3,683]	0,6678
Woche 72	91	10,26 (16,991)	1,94 (1,683)	78	15,81 (21,303)	6,01 (1,799)	-4,07 [-8,945; 0,805]	0,1014
Woche 76	90	9,26 (15,823)	0,78 (1,735)	69	17,39 (22,585)	5,92 (1,933)	-5,14 [-10,301; 0,015]	0,0507
Woche 80	87	9,58 (16,001)	2,69 (1,818)	65	15,90 (22,133)	5,60 (2,044)	-2,91 [-8,331; 2,515]	0,2917
Woche 84	87	8,05 (15,221)	0,36 (1,689)	67	17,41 (22,740)	5,47 (1,881)	-5,10 [-10,137; -0,065]	0,0471*
Woche 88	84	9,13 (15,823)	1,31 (1,841)	61	16,94 (22,462)	6,94 (2,098)	-5,63 [-11,181; -0,087]	0,0465*
Woche 92	84	8,73 (15,625)	1,22 (1,801)	60	15,00 (21,633)	4,45 (2,056)	-3,23 [-8,650; 2,186]	0,2409
Woche 96	79	8,86 (15,752)	4,92 (2,096)	55	14,55 (22,002)	2,75 (2,426)	2,17 [-4,178; 8,527]	0,5004
Woche 100	86	10,08 (16,225)	1,15 (1,742)	59	15,25 (21,728)	4,02 (2,040)	-2,87 [-8,181; 2,439]	0,2878
Woche 104	73	8,22 (15,497)	2,17 (1,981)	56	15,48 (21,986)	4,96 (2,226)	-2,80 [-8,714; 3,121]	0,3525
Woche 108	71	9,86 (16,324)	3,31 (1,861)	52	17,31 (22,376)	5,64 (2,145)	-2,33 [-7,973; 3,316]	0,4169
Woche 112	68	10,29 (16,549)	4,48 (2,115)	47	17,02 (21,839)	2,34 (2,482)	2,15 [-4,335; 8,629]	0,5141

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.7 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen an anderen Stellen des Körpers (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 116	62	9,14 (16,161)	2,51 (2,020)	51	15,69 (22,463)	3,12 (2,223)	-0,60 [-6,572; 5,363]	0,8417
Woche 120	57	6,43 (13,272)	7,87 (2,398)	47	17,02 (22,918)	2,59 (2,603)	5,29 [-1,802; 12,377]	0,1428
Woche 124	54	7,41 (15,414)	5,36 (2,383)	45	17,78 (23,138)	5,11 (2,605)	0,25 [-6,825; 7,325]	0,9444
Woche 128	54	7,41 (15,414)	3,46 (2,412)	40	16,67 (22,646)	8,41 (2,733)	-4,95 [-12,238; 2,347]	0,1821
Woche 132	50	6,67 (13,469)	3,46 (2,175)	39	16,24 (22,778)	3,93 (2,412)	-0,47 [-6,970; 6,035]	0,8872
Woche 136	48	9,03 (14,970)	2,27 (2,107)	34	10,78 (17,829)	7,72 (2,439)	-5,46 [-11,809; 0,898]	0,0917
Woche 140	45	7,41 (14,015)	2,01 (2,197)	34	12,75 (20,125)	0,66 (2,453)	1,35 [-5,175; 7,870]	0,6832
Woche 144	36	8,33 (14,639)	1,56 (2,559)	30	11,11 (18,222)	5,71 (2,782)	-4,15 [-11,610; 3,315]	0,2726
Woche 148	40	6,67 (13,503)	1,88 (2,238)	27	13,58 (19,080)	0,11 (2,573)	1,76 [-5,016; 8,542]	0,6072
Woche 152	38	8,77 (14,875)	3,28 (2,276)	28	13,10 (18,898)	0,74 (2,588)	2,54 [-4,300; 9,388]	0,4625
Woche 156	35	9,52 (15,278)	6,18 (3,002)	28	14,29 (19,092)	1,69 (3,337)	4,49 [-4,453; 13,434]	0,3214
Woche 160	31	9,68 (15,380)	2,56 (2,661)	26	12,82 (19,037)	-0,67 (2,901)	3,23 [-4,600; 11,052]	0,4148
Woche 164	31	8,60 (14,827)	2,45 (2,547)	22	12,12 (19,370)	1,29 (2,920)	1,16 [-6,535; 8,852]	0,7651
Woche 168	27	7,41 (14,122)	-0,22 (2,583)	25	13,33 (19,245)	4,73 (2,654)	-4,95 [-12,328; 2,426]	0,1855
Woche 172	30	7,78 (14,339)	3,91 (3,037)	20	13,33 (19,941)	2,54 (3,533)	1,38 [-7,894; 10,645]	0,7688
Woche 176	22	6,06 (13,159)	0,43 (2,684)	18	14,81 (20,523)	3,85 (2,853)	-3,41 [-11,296; 4,470]	0,3908
Woche 180	20	5,00 (12,212)	-2,02 (3,207)	16	12,50 (16,667)	0,89 (3,303)	-2,91 [-12,078; 6,264]	0,5281

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.7 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen an anderen Stellen des Körpers (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 184	18	7,41 (14,260)	-4,19 (3,189)	17	11,76 (16,420)	0,44 (3,180)	-4,63 [-13,578; 4,320]	0,3046
Woche 188	16	4,17 (11,386)	-5,51 (4,509)	15	11,11 (16,265)	2,76 (4,244)	-8,28 [-20,499; 3,946]	0,1790
Durchschnitt über alle Visiten	216	12,35 (18,797)	2,27 (1,000)	211	15,32 (21,871)	4,27 (1,061)	-2,00 [-4,875; 0,870]	0,1714
Hedges' g SMD							-0,13 [-0,323; 0,057]	0,1705

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen im Arm oder in der Schulter (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	9,07 (18,251)	-0,49 (1,120)	180	8,70 (16,286)	1,71 (1,123)	-2,20 [-5,318; 0,917]	0,1660
Woche 2	185	9,01 (18,139)	0,99 (1,268)	186	7,89 (15,805)	4,55 (1,271)	-3,56 [-7,089; -0,032]	0,0480*
Woche 3	185	9,19 (18,214)	0,90 (1,269)	179	8,19 (16,034)	5,08 (1,283)	-4,17 [-7,720; -0,627]	0,0212*
Woche 4	204	8,66 (17,699)	0,52 (1,353)	198	8,08 (15,818)	6,39 (1,369)	-5,88 [-9,659; -2,095]	0,0024*
Woche 5	183	8,56 (17,633)	0,32 (1,385)	190	8,25 (15,968)	5,19 (1,381)	-4,87 [-8,712; -1,023]	0,0132*
Woche 6	184	8,70 (17,679)	2,65 (1,446)	176	8,33 (15,736)	6,89 (1,471)	-4,24 [-8,297; -0,189]	0,0403*
Woche 7	181	8,84 (17,790)	4,03 (1,511)	176	8,33 (16,134)	6,68 (1,533)	-2,65 [-6,880; 1,579]	0,2187
Woche 8	192	8,16 (17,641)	4,38 (1,425)	183	8,38 (16,096)	6,93 (1,454)	-2,55 [-6,551; 1,451]	0,2110
Woche 12	177	8,47 (17,688)	1,81 (1,484)	176	8,52 (16,231)	4,63 (1,498)	-2,82 [-6,966; 1,324]	0,1818
Woche 16	168	8,13 (17,302)	4,87 (1,545)	170	8,43 (16,242)	8,29 (1,552)	-3,42 [-7,722; 0,887]	0,1194
Woche 20	160	8,33 (17,132)	3,75 (1,475)	158	8,44 (16,372)	6,51 (1,490)	-2,76 [-6,882; 1,358]	0,1883
Woche 24	147	8,39 (17,379)	4,93 (1,774)	151	8,17 (15,854)	10,63 (1,774)	-5,70 [-10,631; -0,768]	0,0236*
Woche 28	148	8,33 (17,334)	5,18 (1,637)	136	9,07 (16,464)	7,31 (1,685)	-2,14 [-6,756; 2,479]	0,3631
Woche 32	141	8,98 (17,764)	6,89 (1,756)	131	8,40 (15,658)	9,79 (1,809)	-2,90 [-7,858; 2,058]	0,2508
Woche 36	135	9,14 (17,950)	8,35 (1,807)	125	8,53 (15,785)	9,42 (1,866)	-1,07 [-6,176; 4,041]	0,6812
Woche 40	120	8,06 (17,283)	7,20 (1,784)	107	7,48 (15,397)	8,46 (1,865)	-1,26 [-6,337; 3,814]	0,6253
Woche 44	117	8,55 (17,591)	7,68 (1,728)	109	7,65 (15,471)	7,64 (1,791)	0,04 [-4,855; 4,937]	0,9869

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen im Arm oder in der Schulter (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	7,95 (16,911)	10,69 (2,069)	107	7,48 (15,397)	10,06 (2,119)	0,64 [-5,188; 6,463]	0,8297
Woche 52	112	7,44 (17,161)	8,08 (1,825)	103	6,47 (14,048)	8,98 (1,901)	-0,91 [-6,088; 4,276]	0,7312
Woche 56	107	8,10 (17,639)	9,06 (1,865)	92	7,97 (15,913)	7,80 (1,981)	1,26 [-4,098; 6,609]	0,6449
Woche 60	103	7,12 (16,601)	5,65 (1,785)	86	8,14 (16,117)	9,45 (1,916)	-3,80 [-8,954; 1,355]	0,1479
Woche 64	101	7,26 (16,736)	7,63 (1,845)	84	7,14 (15,584)	9,69 (1,987)	-2,07 [-7,400; 3,268]	0,4465
Woche 68	91	6,23 (15,644)	7,14 (1,831)	82	8,13 (16,196)	9,27 (1,928)	-2,13 [-7,362; 3,109]	0,4245
Woche 72	91	6,23 (15,644)	7,41 (2,030)	78	7,69 (16,047)	10,47 (2,171)	-3,06 [-8,912; 2,786]	0,3035
Woche 76	90	8,52 (18,401)	6,71 (1,822)	69	8,21 (16,574)	8,41 (2,029)	-1,70 [-7,067; 3,669]	0,5338
Woche 80	87	7,66 (16,629)	5,93 (1,861)	65	8,21 (16,699)	10,99 (2,100)	-5,05 [-10,580; 0,470]	0,0728
Woche 84	87	6,90 (16,185)	6,05 (1,997)	67	7,96 (16,504)	13,88 (2,242)	-7,83 [-13,743; -1,920]	0,0096*
Woche 88	84	6,35 (15,065)	5,95 (1,872)	61	8,20 (16,839)	10,67 (2,141)	-4,72 [-10,315; 0,885]	0,0985
Woche 92	84	7,54 (16,648)	6,66 (1,788)	60	7,22 (16,343)	10,17 (2,068)	-3,51 [-8,890; 1,873]	0,2003
Woche 96	79	7,59 (15,968)	6,30 (1,986)	55	6,67 (14,907)	9,12 (2,332)	-2,82 [-8,854; 3,206]	0,3573
Woche 100	86	7,75 (16,705)	3,53 (1,674)	59	6,78 (14,881)	7,85 (1,978)	-4,32 [-9,420; 0,780]	0,0965
Woche 104	73	7,31 (15,954)	4,18 (1,784)	56	7,14 (15,195)	10,48 (2,043)	-6,30 [-11,636; -0,957]	0,0210*
Woche 108	71	7,04 (15,852)	5,42 (1,880)	52	7,69 (15,642)	8,79 (2,176)	-3,37 [-9,037; 2,298]	0,2425
Woche 112	68	6,37 (14,406)	6,57 (2,099)	47	7,80 (15,869)	11,92 (2,458)	-5,35 [-11,723; 1,021]	0,0993

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen im Arm oder in der Schulter (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 116	62	5,38 (13,755)	4,74 (2,183)	51	8,50 (17,440)	11,20 (2,423)	-6,46 [-12,898; -0,025]	0,0491*
Woche 120	57	6,43 (15,984)	7,04 (2,272)	47	9,22 (17,994)	10,97 (2,524)	-3,93 [-10,638; 2,777]	0,2491
Woche 124	54	8,02 (15,775)	3,53 (2,202)	45	8,15 (17,632)	11,99 (2,444)	-8,46 [-14,958; -1,965]	0,0110*
Woche 128	54	8,02 (18,240)	4,94 (2,305)	40	9,17 (18,471)	10,57 (2,655)	-5,63 [-12,581; 1,314]	0,1112
Woche 132	50	6,67 (15,058)	5,00 (2,044)	39	8,55 (18,286)	9,00 (2,325)	-4,00 [-10,122; 2,114]	0,1980
Woche 136	48	7,64 (17,176)	6,31 (2,309)	34	7,84 (16,532)	12,74 (2,712)	-6,43 [-13,466; 0,611]	0,0732
Woche 140	45	11,11 (20,101)	4,74 (2,144)	34	8,82 (17,034)	7,41 (2,459)	-2,67 [-9,117; 3,778]	0,4143
Woche 144	36	10,19 (19,222)	9,05 (2,726)	30	8,89 (17,361)	9,40 (3,039)	-0,35 [-8,441; 7,744]	0,9321
Woche 148	40	9,17 (16,858)	3,13 (2,477)	27	8,64 (17,523)	5,39 (2,953)	-2,26 [-9,904; 5,388]	0,5592
Woche 152	38	11,40 (19,415)	10,82 (3,079)	28	8,33 (17,273)	8,53 (3,560)	2,30 [-7,041; 11,632]	0,6268
Woche 156	35	12,38 (19,944)	7,28 (2,565)	28	8,33 (17,273)	5,82 (2,877)	1,45 [-6,185; 9,095]	0,7065
Woche 160	31	8,60 (17,144)	9,01 (2,852)	26	8,97 (17,783)	8,42 (3,170)	0,59 [-7,870; 9,052]	0,8901
Woche 164	31	7,53 (16,577)	5,05 (2,540)	22	9,09 (18,349)	4,44 (2,950)	0,61 [-7,135; 8,354]	0,8760
Woche 168	27	6,17 (16,111)	6,47 (2,655)	25	9,33 (18,053)	7,78 (2,840)	-1,32 [-9,048; 6,417]	0,7362
Woche 172	30	6,67 (16,141)	5,83 (2,754)	20	11,67 (19,571)	5,32 (3,252)	0,51 [-7,980; 9,001]	0,9051
Woche 176	22	4,55 (15,585)	3,52 (2,805)	18	11,11 (19,803)	8,57 (3,110)	-5,05 [-13,449; 3,352]	0,2347
Woche 180	20	6,67 (17,438)	4,73 (3,023)	16	10,42 (20,069)	9,83 (3,382)	-5,11 [-14,187; 3,974]	0,2655

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.8 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen im Arm oder in der Schulter (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 184	18	5,56 (17,150)	9,85 (4,680)	17	9,80 (19,596)	12,94 (4,902)	-3,09 [-16,723; 10,546]	0,6514
Woche 188	16	8,33 (19,245)	-0,44 (3,286)	15	6,67 (18,687)	4,24 (3,393)	-4,67 [-14,245; 4,897]	0,3289
Durchschnitt über alle Visiten	216	8,64 (17,825)	5,42 (1,003)	211	8,06 (15,715)	8,47 (1,080)	-3,04 [-5,937; -0,144]	0,0397*
Hedges' g SMD							-0,20 [-0,390; -0,009]	0,0398*

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.9 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen in der Brust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	8,70 (15,900)	-0,92 (1,091)	180	11,48 (16,647)	1,02 (1,100)	-1,94 [-4,988; 1,107]	0,2114
Woche 2	185	9,01 (16,018)	0,86 (1,281)	186	10,93 (16,439)	5,16 (1,288)	-4,30 [-7,874; -0,731]	0,0184*
Woche 3	185	8,83 (15,930)	0,95 (1,287)	179	10,61 (16,355)	3,81 (1,308)	-2,86 [-6,469; 0,749]	0,1200
Woche 4	204	8,66 (15,734)	2,46 (1,390)	198	11,45 (16,564)	6,35 (1,416)	-3,89 [-7,791; 0,013]	0,0508
Woche 5	183	8,20 (15,614)	1,90 (1,308)	190	11,05 (16,464)	3,57 (1,307)	-1,67 [-5,309; 1,969]	0,3677
Woche 6	184	8,15 (15,583)	2,61 (1,330)	176	10,80 (16,044)	5,74 (1,359)	-3,13 [-6,873; 0,609]	0,1006
Woche 7	181	8,10 (15,576)	4,67 (1,424)	176	12,12 (16,852)	5,98 (1,455)	-1,31 [-5,324; 2,694]	0,5196
Woche 8	192	8,51 (15,723)	5,53 (1,414)	183	11,48 (16,632)	7,79 (1,451)	-2,26 [-6,248; 1,723]	0,2652
Woche 12	177	7,53 (15,275)	3,39 (1,396)	176	11,74 (16,744)	6,06 (1,415)	-2,67 [-6,584; 1,250]	0,1815
Woche 16	168	8,13 (15,689)	4,59 (1,364)	170	11,76 (16,779)	5,75 (1,377)	-1,16 [-4,979; 2,654]	0,5496
Woche 20	160	8,33 (15,861)	4,15 (1,452)	158	11,39 (16,729)	4,18 (1,473)	-0,02 [-4,094; 4,046]	0,9908
Woche 24	147	7,94 (15,277)	4,37 (1,502)	151	10,15 (16,327)	4,60 (1,502)	-0,23 [-4,409; 3,953]	0,9147
Woche 28	148	8,56 (15,611)	5,11 (1,439)	136	11,52 (16,914)	3,45 (1,492)	1,66 [-2,419; 5,740]	0,4239
Woche 32	141	8,27 (15,510)	2,71 (1,386)	131	11,45 (16,932)	3,19 (1,436)	-0,47 [-4,401; 3,459]	0,8138
Woche 36	135	9,14 (15,996)	0,33 (1,225)	125	10,93 (16,814)	0,84 (1,271)	-0,51 [-3,985; 2,962]	0,7722
Woche 40	120	7,78 (14,802)	2,28 (1,381)	107	10,28 (16,768)	3,48 (1,450)	-1,20 [-5,147; 2,745]	0,5496
Woche 44	117	8,26 (15,724)	0,21 (1,423)	109	11,01 (16,390)	3,43 (1,480)	-3,22 [-7,270; 0,821]	0,1178

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.9 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen in der Brust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	7,95 (15,647)	3,13 (1,583)	107	9,97 (16,002)	3,04 (1,618)	0,09 [-4,367; 4,552]	0,9675
Woche 52	112	8,04 (15,657)	0,41 (1,342)	103	10,68 (16,312)	1,34 (1,400)	-0,93 [-4,754; 2,887]	0,6310
Woche 56	107	8,41 (15,923)	3,64 (1,466)	92	9,42 (15,880)	1,97 (1,562)	1,66 [-2,556; 5,885]	0,4382
Woche 60	103	8,09 (15,100)	-0,46 (1,277)	86	8,91 (15,697)	1,94 (1,376)	-2,39 [-6,087; 1,306]	0,2040
Woche 64	101	6,93 (14,389)	0,81 (1,293)	84	8,73 (15,625)	0,13 (1,392)	0,68 [-3,064; 4,416]	0,7223
Woche 68	91	7,33 (14,742)	0,24 (1,347)	82	8,94 (15,756)	1,01 (1,418)	-0,77 [-4,623; 3,085]	0,6945
Woche 72	91	7,33 (14,742)	1,27 (1,392)	78	8,97 (15,821)	1,84 (1,489)	-0,57 [-4,582; 3,451]	0,7817
Woche 76	90	7,78 (15,032)	-0,37 (1,232)	69	8,70 (15,814)	1,78 (1,375)	-2,15 [-5,787; 1,486]	0,2451
Woche 80	87	8,05 (15,221)	0,18 (1,477)	65	8,72 (15,896)	0,72 (1,670)	-0,54 [-4,938; 3,851]	0,8076
Woche 84	87	5,36 (12,320)	0,57 (1,479)	67	8,96 (15,978)	3,50 (1,644)	-2,93 [-7,288; 1,427]	0,1864
Woche 88	84	5,56 (12,497)	2,61 (1,639)	61	8,74 (15,988)	6,51 (1,861)	-3,90 [-8,785; 0,985]	0,1171
Woche 92	84	5,95 (12,843)	0,29 (1,491)	60	8,89 (16,082)	2,63 (1,712)	-2,34 [-6,811; 2,138]	0,3047
Woche 96	79	5,91 (12,810)	-0,34 (1,479)	55	8,48 (15,997)	2,66 (1,721)	-3,01 [-7,477; 1,463]	0,1862
Woche 100	86	6,98 (14,567)	-0,84 (1,299)	59	9,04 (16,177)	1,75 (1,530)	-2,59 [-6,540; 1,367]	0,1987
Woche 104	73	5,02 (12,007)	0,93 (1,468)	56	8,33 (15,891)	2,76 (1,653)	-1,84 [-6,189; 2,515]	0,4062
Woche 108	71	5,63 (13,785)	-1,64 (1,399)	52	8,33 (16,000)	2,41 (1,603)	-4,05 [-8,238; 0,143]	0,0583
Woche 112	68	6,86 (13,578)	-0,54 (1,632)	47	9,93 (16,904)	5,58 (1,912)	-6,12 [-11,092; -1,156]	0,0160*

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.2.9 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen in der Brust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 116	62	4,84 (11,838)	-1,59 (1,629)	51	8,50 (16,115)	2,00 (1,783)	-3,59 [-8,349; 1,176]	0,1389
Woche 120	57	3,51 (10,321)	-0,83 (1,673)	47	9,93 (16,904)	2,94 (1,806)	-3,78 [-8,664; 1,109]	0,1288
Woche 124	54	4,94 (11,953)	-0,72 (1,630)	45	10,37 (17,148)	1,94 (1,781)	-2,66 [-7,453; 2,137]	0,2750
Woche 128	54	4,32 (11,302)	-0,42 (1,917)	40	8,33 (16,452)	2,28 (2,162)	-2,69 [-8,401; 3,012]	0,3519
Woche 132	50	4,67 (11,684)	0,47 (1,707)	39	8,55 (16,610)	-0,40 (1,907)	0,88 [-4,176; 5,933]	0,7316
Woche 136	48	5,56 (14,314)	-0,53 (1,762)	34	7,84 (16,532)	2,77 (2,051)	-3,30 [-8,630; 2,039]	0,2240
Woche 140	45	5,93 (14,718)	-2,20 (1,631)	34	8,82 (17,034)	1,14 (1,862)	-3,34 [-8,243; 1,565]	0,1801
Woche 144	36	5,56 (12,599)	-0,97 (1,843)	30	10,00 (17,833)	2,26 (2,031)	-3,22 [-8,677; 2,233]	0,2442
Woche 148	40	4,17 (11,164)	-0,05 (1,812)	27	12,35 (18,829)	-1,64 (2,137)	1,59 [-4,033; 7,219]	0,5755
Woche 152	38	7,89 (16,319)	1,28 (2,223)	28	11,90 (18,624)	2,35 (2,593)	-1,06 [-7,857; 5,735]	0,7573
Woche 156	35	8,57 (16,848)	-1,02 (1,986)	28	9,52 (17,817)	1,42 (2,246)	-2,44 [-8,397; 3,517]	0,4181
Woche 160	31	6,45 (15,915)	3,05 (2,437)	26	11,54 (18,720)	2,14 (2,705)	0,90 [-6,369; 8,174]	0,8057
Woche 164	31	7,53 (16,577)	0,35 (2,773)	22	12,12 (19,370)	2,56 (3,247)	-2,22 [-10,755; 6,324]	0,6065
Woche 168	27	4,94 (12,067)	-0,67 (2,490)	25	10,67 (18,559)	1,75 (2,631)	-2,41 [-9,658; 4,830]	0,5092
Woche 172	30	6,67 (16,141)	-1,08 (2,180)	20	11,67 (19,571)	0,00 (2,594)	-1,08 [-7,864; 5,707]	0,7522
Woche 176	22	4,55 (11,708)	3,47 (3,141)	18	11,11 (19,803)	3,13 (3,459)	0,35 [-9,099; 9,792]	0,9415
Woche 180	20	5,00 (12,212)	-1,88 (2,697)	16	8,33 (14,907)	-0,11 (2,972)	-1,77 [-9,822; 6,285]	0,6608

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.9 ADRIATIC: Summary of analysis of change from baseline over time in Schmerzen in der Brust (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 184	18	5,56 (12,783)	2,07 (2,891)	17	7,84 (14,575)	3,05 (3,024)	-0,98 [-9,348; 7,390]	0,8153
Woche 188	16	6,25 (13,437)	2,68 (3,379)	15	6,67 (13,801)	1,77 (3,528)	0,91 [-8,849; 10,677]	0,8515
Durchschnitt über alle Visiten	216	8,49 (15,584)	1,07 (0,768)	211	11,06 (16,391)	2,78 (0,834)	-1,71 [-3,943; 0,517]	0,1318
Hedges' g SMD							-0,15 [-0,336; 0,044]	0,1318

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.10 ADRIATIC: Summary of analysis of change from baseline over time in Wunder Mund (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 1	180	5,74 (14,455)	-0,59 (0,971)	180	5,74 (13,569)	-0,46 (0,973)	-0,12 [-2,826; 2,580]	0,9286
Woche 2	185	5,77 (14,426)	0,51 (1,057)	186	6,27 (13,953)	-0,05 (1,059)	0,55 [-2,385; 3,494]	0,7108
Woche 3	185	5,77 (14,426)	-0,63 (0,928)	179	5,59 (12,976)	-0,13 (0,941)	-0,51 [-3,103; 2,092]	0,7022
Woche 4	204	5,72 (14,610)	-1,63 (0,795)	198	5,39 (12,751)	-0,34 (0,805)	-1,30 [-3,520; 0,926]	0,2523
Woche 5	183	5,46 (14,211)	-1,59 (0,808)	190	5,61 (13,415)	-0,14 (0,802)	-1,44 [-3,677; 0,796]	0,2062
Woche 6	184	5,98 (14,595)	-0,53 (0,964)	176	6,06 (13,843)	0,88 (0,982)	-1,41 [-4,112; 1,296]	0,3066
Woche 7	181	5,71 (14,421)	-0,79 (0,900)	176	6,06 (13,843)	1,21 (0,913)	-2,01 [-4,526; 0,511]	0,1179
Woche 8	192	5,56 (14,201)	-0,62 (0,877)	183	5,10 (12,530)	0,72 (0,895)	-1,35 [-3,809; 1,116]	0,2832
Woche 12	177	5,65 (14,415)	-0,35 (0,916)	176	5,49 (13,386)	0,23 (0,922)	-0,58 [-3,134; 1,975]	0,6559
Woche 16	168	5,36 (13,809)	0,42 (1,109)	170	6,08 (13,890)	2,70 (1,110)	-2,27 [-5,356; 0,811]	0,1482
Woche 20	160	5,21 (13,760)	2,60 (1,191)	158	5,91 (13,833)	1,89 (1,201)	0,72 [-2,610; 4,040]	0,6727
Woche 24	147	5,44 (14,089)	0,63 (1,291)	151	6,40 (14,254)	2,88 (1,286)	-2,25 [-5,836; 1,330]	0,2171
Woche 28	148	4,95 (13,672)	0,78 (1,265)	136	5,88 (13,986)	0,75 (1,308)	0,03 [-3,549; 3,609]	0,9869
Woche 32	141	5,20 (13,963)	0,74 (1,169)	131	6,11 (14,203)	2,06 (1,208)	-1,32 [-4,626; 1,989]	0,4335
Woche 36	135	5,68 (14,985)	0,39 (1,157)	125	5,87 (14,081)	2,16 (1,197)	-1,76 [-5,040; 1,510]	0,2899
Woche 40	120	4,72 (13,866)	-0,20 (1,021)	107	5,30 (13,071)	-0,26 (1,072)	0,06 [-2,854; 2,977]	0,9670
Woche 44	117	5,41 (15,135)	-1,37 (0,970)	109	4,89 (13,476)	-0,09 (1,005)	-1,27 [-4,022; 1,476]	0,3629

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.10 ADRIATIC: Summary of analysis of change from baseline over time in Wunder Mund (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 48	109	4,89 (14,219)	0,96 (1,207)	107	4,67 (13,309)	0,35 (1,228)	0,61 [-2,777; 4,003]	0,7221
Woche 52	112	4,46 (13,788)	-1,59 (0,976)	103	4,21 (12,063)	-1,24 (1,016)	-0,35 [-3,122; 2,423]	0,8041
Woche 56	107	4,98 (14,336)	-0,55 (1,185)	92	3,99 (11,945)	1,62 (1,266)	-2,18 [-5,592; 1,239]	0,2105
Woche 60	103	5,83 (15,778)	-1,66 (0,968)	86	4,65 (12,693)	-2,17 (1,046)	0,52 [-2,293; 3,326]	0,7176
Woche 64	101	4,95 (14,442)	-0,98 (1,045)	84	3,57 (10,372)	-0,15 (1,134)	-0,83 [-3,868; 2,208]	0,5909
Woche 68	91	5,86 (15,391)	1,19 (1,255)	82	2,44 (10,184)	0,23 (1,331)	0,96 [-2,653; 4,574]	0,6009
Woche 72	91	6,23 (16,414)	-1,11 (1,258)	78	4,27 (12,436)	2,10 (1,349)	-3,20 [-6,844; 0,435]	0,0841
Woche 76	90	6,30 (16,493)	-0,57 (1,188)	69	3,38 (11,639)	0,38 (1,336)	-0,95 [-4,480; 2,583]	0,5969
Woche 80	87	6,51 (16,736)	-0,08 (1,266)	65	4,10 (12,511)	1,32 (1,439)	-1,40 [-5,184; 2,387]	0,4670
Woche 84	87	4,98 (14,845)	-2,61 (1,137)	67	3,48 (11,798)	1,30 (1,285)	-3,91 [-7,288; -0,523]	0,0239*
Woche 88	84	5,95 (16,494)	-1,96 (0,990)	61	3,83 (12,320)	-0,50 (1,144)	-1,46 [-4,443; 1,531]	0,3374
Woche 92	84	5,95 (16,494)	0,09 (1,343)	60	3,89 (12,414)	-0,33 (1,563)	0,41 [-3,654; 4,484]	0,8409
Woche 96	79	6,33 (16,943)	-0,78 (1,358)	55	4,24 (12,917)	2,39 (1,602)	-3,17 [-7,318; 0,981]	0,1336
Woche 100	86	6,20 (16,578)	-1,19 (1,211)	59	4,52 (13,069)	0,93 (1,436)	-2,12 [-5,831; 1,585]	0,2601
Woche 104	73	5,48 (16,679)	-2,72 (1,244)	56	4,76 (13,377)	1,88 (1,417)	-4,61 [-8,330; -0,883]	0,0156*
Woche 108	71	5,16 (16,569)	-2,36 (1,064)	52	5,13 (13,822)	-0,21 (1,232)	-2,15 [-5,359; 1,067]	0,1892
Woche 112	68	5,88 (17,221)	-0,30 (1,320)	47	5,67 (14,445)	-0,32 (1,559)	0,02 [-4,013; 4,059]	0,9911
Woche 116	62	4,30 (15,369)	0,04 (1,295)	51	3,92 (10,847)	-0,85 (1,435)	0,90 [-2,921; 4,713]	0,6432

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.10 ADRIATIC: Summary of analysis of change from baseline over time in Wunder Mund (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 120	57	3,51 (15,019)	-0,88 (1,378)	47	4,26 (11,244)	0,59 (1,518)	-1,46 [-5,516; 2,586]	0,4755
Woche 124	54	4,94 (17,623)	-0,04 (1,447)	45	4,44 (13,484)	0,03 (1,593)	-0,07 [-4,332; 4,186]	0,9730
Woche 128	54	3,70 (15,414)	-0,83 (1,534)	40	3,33 (10,127)	0,27 (1,770)	-1,10 [-5,725; 3,525]	0,6386
Woche 132	50	4,67 (16,509)	0,05 (1,486)	39	2,56 (8,998)	0,19 (1,695)	-0,15 [-4,610; 4,317]	0,9483
Woche 136	48	4,17 (16,308)	-0,42 (1,510)	34	2,94 (9,597)	-0,71 (1,785)	0,29 [-4,333; 4,919]	0,9002
Woche 140	45	4,44 (16,817)	-2,35 (1,605)	34	3,92 (13,645)	3,01 (1,843)	-5,36 [-10,200; -0,520]	0,0303*
Woche 144	36	4,63 (18,088)	-2,73 (1,395)	30	4,44 (11,525)	-0,28 (1,542)	-2,45 [-6,584; 1,685]	0,2419
Woche 148	40	4,17 (17,193)	-2,69 (1,293)	27	3,70 (10,675)	-0,34 (1,554)	-2,35 [-6,363; 1,661]	0,2472
Woche 152	38	5,26 (18,218)	1,85 (1,844)	28	3,57 (10,499)	-2,17 (2,146)	4,02 [-1,613; 9,649]	0,1595
Woche 156	35	6,67 (21,082)	-0,53 (1,452)	28	3,57 (10,499)	-2,88 (1,635)	2,35 [-2,003; 6,702]	0,2864
Woche 160	31	5,38 (19,430)	-0,69 (2,376)	26	3,85 (10,860)	3,18 (2,626)	-3,87 [-10,924; 3,177]	0,2775
Woche 164	31	4,30 (18,742)	-0,09 (2,424)	22	4,55 (11,708)	6,06 (2,847)	-6,15 [-13,605; 1,302]	0,1042
Woche 168	27	3,70 (19,245)	-3,56 (1,222)	25	4,00 (11,055)	-2,50 (1,290)	-1,07 [-4,607; 2,472]	0,5494
Woche 172	30	4,44 (19,045)	0,35 (2,069)	20	5,00 (12,212)	0,73 (2,482)	-0,37 [-6,822; 6,075]	0,9083
Woche 176	22	0,00 (0,000)	0,81 (2,637)	18	5,56 (12,783)	-1,22 (2,713)	2,03 [-5,612; 9,666]	0,5960
Woche 180	20	5,00 (22,361)	2,02 (3,435)	16	6,25 (13,437)	3,40 (3,854)	-1,38 [-11,794; 9,037]	0,7907
Woche 184	18	5,56 (23,570)	-3,43 (2,150)	17	5,88 (13,098)	-0,57 (2,251)	-2,85 [-9,136; 3,426]	0,3643

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Table 3.8.2.10 ADRIATIC: Summary of analysis of change from baseline over time in Wunder Mund (mixed model for repeated measures)
Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 188	16	6,25 (25,000)	4,31 (3,796)	15	6,67 (13,801)	5,72 (3,920)	-1,40 [-12,448; 9,642]	0,7983
Durchschnitt über alle Visiten	216	5,86 (14,612)	-0,51 (0,593)	211	5,53 (13,253)	0,63 (0,642)	-1,14 [-2,858; 0,576]	0,1922
Hedges' g SMD							-0,13 [-0,316; 0,064]	0,1925

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error except for endpoint of Hemoptysis where a Toeplitz without heterogeneity matrix was used. SMD = standardised mean difference. * p<0.05.
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Anhang 4-G7.4: EORTC QLQ-LC13 - deskriptive Analyse und Verlaufsgrafik

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Baseline [a]	217	17,97	16,342	0,0	11,11	66,7
		Woche 1	208	17,79	17,541	0,0	11,11	77,8
		Woche 2	203	19,54	17,041	0,0	22,22	66,7
		Woche 3	205	20,60	19,582	0,0	22,22	100,0
		Woche 4	235	21,51	19,706	0,0	22,22	88,9
		Woche 5	213	22,27	19,230	0,0	22,22	88,9
		Woche 6	209	23,18	20,879	0,0	22,22	100,0
		Woche 7	209	24,30	22,192	0,0	22,22	100,0
		Woche 8	220	25,05	21,549	0,0	22,22	100,0
		Woche 12	204	23,26	20,798	0,0	22,22	100,0
		Woche 16	189	23,69	19,376	0,0	22,22	88,9
		Woche 20	179	24,08	21,379	0,0	22,22	100,0
		Woche 24	169	22,55	19,337	0,0	22,22	88,9
		Woche 28	166	25,17	21,405	0,0	22,22	100,0
		Woche 32	159	23,83	20,987	0,0	22,22	100,0
		Woche 36	153	23,75	19,290	0,0	22,22	88,9
		Woche 40	137	21,65	19,071	0,0	22,22	88,9
		Woche 44	131	22,39	20,487	0,0	22,22	100,0
		Woche 48	124	23,30	19,705	0,0	22,22	88,9
		Woche 52	124	22,31	19,140	0,0	22,22	88,9
		Woche 56	122	23,50	19,176	0,0	22,22	88,9
		Woche 60	118	21,85	22,596	0,0	22,22	100,0
		Woche 64	113	24,19	22,382	0,0	22,22	100,0
		Woche 68	103	23,52	21,854	0,0	22,22	100,0
		Woche 72	101	23,76	21,604	0,0	22,22	88,9
		Woche 76	98	22,45	21,165	0,0	22,22	88,9
		Woche 80	97	24,05	21,196	0,0	22,22	88,9
		Woche 84	97	21,88	19,802	0,0	22,22	88,9
		Woche 88	92	24,28	21,910	0,0	22,22	88,9
		Woche 92	92	24,15	21,198	0,0	22,22	88,9
		Woche 96	87	24,90	21,895	0,0	22,22	88,9

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Woche 100	95	22,11	19,683	0,0	22,22	88,9
		Woche 104	80	24,72	22,291	0,0	22,22	100,0
		Woche 108	77	24,39	19,993	0,0	22,22	88,9
		Woche 112	73	26,64	21,969	0,0	22,22	100,0
		Woche 116	68	25,49	24,438	0,0	22,22	100,0
		Woche 120	63	27,16	24,341	0,0	22,22	100,0
		Woche 124	59	23,35	21,011	0,0	22,22	88,9
		Woche 128	59	22,22	20,216	0,0	22,22	66,7
		Woche 132	54	21,40	20,460	0,0	22,22	77,8
		Woche 136	52	20,51	19,104	0,0	22,22	66,7
		Woche 140	48	20,14	22,881	0,0	11,11	88,9
		Woche 144	39	22,51	22,293	0,0	22,22	88,9
		Woche 148	43	22,74	21,950	0,0	22,22	88,9
		Woche 152	41	22,22	21,802	0,0	22,22	88,9
		Woche 156	38	25,44	25,034	0,0	22,22	88,9
		Woche 160	33	22,22	20,787	0,0	22,22	66,7
		Woche 164	33	22,22	22,906	0,0	22,22	66,7
		Woche 168	29	23,75	21,357	0,0	22,22	66,7
		Woche 172	32	24,31	23,347	0,0	22,22	77,8
		Woche 176	23	31,40	23,126	0,0	22,22	77,8
		Woche 180	21	24,87	26,505	0,0	22,22	77,8
		Woche 184	19	24,56	24,450	0,0	22,22	77,8
		Woche 188	17	31,37	29,196	0,0	33,33	77,8
		Woche 192	17	27,45	26,678	0,0	22,22	88,9
		Woche 196	14	19,05	20,640	0,0	16,67	66,7
		Woche 200	11	25,25	21,135	0,0	22,22	55,6
		Woche 204	7	14,29	16,623	0,0	11,11	44,4
		Woche 208	8	11,11	11,878	0,0	11,11	33,3
		Woche 212	7	12,70	11,878	0,0	11,11	33,3
		Woche 216	9	18,52	16,667	0,0	22,22	44,4
		Woche 220	7	15,87	22,090	0,0	0,00	55,6

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Durvalumab (N=264)	Woche 224	6	9,26	10,924	0,0	5,56	22,2
		Woche 228	6	11,11	12,172	0,0	11,11	22,2
		Woche 232	6	9,26	8,364	0,0	11,11	22,2
		Woche 236	4	8,33	5,556	0,0	11,11	11,1
		Woche 240	3	7,41	6,415	0,0	11,11	11,1
		Woche 244	2	5,56	7,857	0,0	5,56	11,1
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	5,56	7,857	0,0	5,56	11,1
	Placebo (N=266)	Baseline [a]	215	21,24	17,802	0,0	22,22	100,0
		Woche 1	209	20,41	18,174	0,0	22,22	100,0
		Woche 2	212	21,96	19,783	0,0	22,22	77,8
		Woche 3	204	21,62	18,395	0,0	22,22	100,0
		Woche 4	231	23,18	20,518	0,0	22,22	100,0
		Woche 5	216	25,15	20,304	0,0	22,22	100,0
		Woche 6	207	24,53	19,859	0,0	22,22	100,0
		Woche 7	203	25,23	20,656	0,0	22,22	100,0
		Woche 8	211	26,22	20,062	0,0	22,22	88,9
		Woche 12	202	24,59	18,904	0,0	22,22	88,9
		Woche 16	198	25,14	20,001	0,0	22,22	88,9
		Woche 20	180	23,83	21,014	0,0	22,22	100,0
		Woche 24	172	23,58	20,400	0,0	22,22	100,0
		Woche 28	158	23,77	18,872	0,0	22,22	100,0
		Woche 32	150	22,89	20,525	0,0	22,22	100,0
		Woche 36	141	23,33	19,259	0,0	22,22	77,8
		Woche 40	122	24,95	21,299	0,0	22,22	88,9
		Woche 44	125	21,87	18,012	0,0	22,22	77,8
		Woche 48	121	24,24	20,935	0,0	22,22	100,0
		Woche 52	118	22,98	21,337	0,0	22,22	100,0
		Woche 56	106	27,25	22,123	0,0	22,22	88,9
		Woche 60	98	23,24	19,284	0,0	22,22	100,0
		Woche 64	95	23,39	19,881	0,0	22,22	88,9

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Placebo (N=266)	Woche 68	92	22,71	21,598	0,0	22,22	100,0
		Woche 72	87	22,86	19,640	0,0	22,22	66,7
		Woche 76	77	22,94	19,855	0,0	22,22	100,0
		Woche 80	75	23,26	19,086	0,0	22,22	77,8
		Woche 84	75	25,33	18,678	0,0	22,22	77,8
		Woche 88	70	24,92	17,890	0,0	22,22	66,7
		Woche 92	69	21,42	16,427	0,0	22,22	77,8
		Woche 96	64	24,65	17,648	0,0	22,22	77,8
		Woche 100	67	21,39	18,684	0,0	22,22	66,7
		Woche 104	63	23,10	18,858	0,0	22,22	77,8
		Woche 108	59	22,03	22,742	0,0	22,22	100,0
		Woche 112	54	24,07	18,536	0,0	22,22	66,7
		Woche 116	56	23,21	18,137	0,0	22,22	77,8
		Woche 120	51	23,97	19,547	0,0	22,22	66,7
		Woche 124	51	24,40	17,072	0,0	22,22	66,7
		Woche 128	45	23,46	18,076	0,0	22,22	66,7
		Woche 132	44	27,78	19,833	0,0	22,22	77,8
		Woche 136	39	25,07	19,533	0,0	22,22	66,7
		Woche 140	39	26,78	19,366	0,0	33,33	66,7
		Woche 144	35	23,17	18,548	0,0	22,22	55,6
		Woche 148	32	25,35	17,902	0,0	22,22	66,7
		Woche 152	33	23,57	16,377	0,0	22,22	55,6
		Woche 156	32	25,35	19,396	0,0	22,22	66,7
		Woche 160	31	26,16	18,932	0,0	33,33	55,6
		Woche 164	24	30,09	20,587	0,0	33,33	55,6
		Woche 168	28	23,41	19,443	0,0	22,22	55,6
		Woche 172	23	26,57	22,903	0,0	22,22	66,7
		Woche 176	21	26,46	20,631	0,0	33,33	55,6
		Woche 180	19	30,41	19,543	0,0	33,33	66,7
		Woche 184	20	26,67	22,046	0,0	22,22	66,7
		Woche 188	18	24,69	20,365	0,0	27,78	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dyspnoe	Placebo (N=266)	Woche 192	16	28,47	18,130	0,0	33,33	55,6
		Woche 196	18	24,07	20,256	0,0	22,22	66,7
		Woche 200	19	26,32	20,357	0,0	22,22	55,6
		Woche 204	13	31,62	20,208	0,0	33,33	66,7
		Woche 208	12	27,78	18,653	0,0	22,22	55,6
		Woche 212	15	24,44	21,082	0,0	22,22	55,6
		Woche 216	12	27,78	19,820	0,0	27,78	55,6
		Woche 220	9	24,69	19,859	0,0	33,33	55,6
		Woche 224	11	22,22	17,916	0,0	22,22	55,6
		Woche 228	9	28,40	17,666	0,0	22,22	55,6
		Woche 232	5	24,44	18,257	0,0	33,33	44,4
		Woche 236	5	31,11	21,373	0,0	33,33	55,6
		Woche 240	5	26,67	21,660	0,0	33,33	55,6
		Woche 244	4	22,22	15,713	0,0	27,78	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Alopezie	Durvalumab (N=264)	Baseline [a]	217	19,05	30,861	0,0	0,00	100,0
		Woche 1	208	17,79	28,163	0,0	0,00	100,0
		Woche 2	203	13,14	26,166	0,0	0,00	100,0
		Woche 3	205	13,17	26,300	0,0	0,00	100,0
		Woche 4	235	10,50	23,741	0,0	0,00	100,0
		Woche 5	213	11,89	25,584	0,0	0,00	100,0
		Woche 6	209	10,37	24,327	0,0	0,00	100,0
		Woche 7	209	10,21	24,936	0,0	0,00	100,0
		Woche 8	220	8,64	22,775	0,0	0,00	100,0
		Woche 12	204	5,88	16,813	0,0	0,00	100,0
		Woche 16	189	5,11	16,587	0,0	0,00	100,0
		Woche 20	179	3,54	15,599	0,0	0,00	100,0
		Woche 24	169	5,92	19,699	0,0	0,00	100,0
		Woche 28	166	5,62	19,293	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Alopezie	Durvalumab (N=264)	Woche 32	159	6,29	18,052	0,0	0,00	100,0
		Woche 36	153	3,05	9,642	0,0	0,00	33,3
		Woche 40	137	6,08	17,721	0,0	0,00	100,0
		Woche 44	131	6,36	17,597	0,0	0,00	100,0
		Woche 48	124	6,72	18,518	0,0	0,00	100,0
		Woche 52	124	5,11	16,486	0,0	0,00	100,0
		Woche 56	122	5,46	14,445	0,0	0,00	100,0
		Woche 60	118	4,52	14,399	0,0	0,00	100,0
		Woche 64	113	6,78	14,198	0,0	0,00	66,7
		Woche 68	103	6,80	16,409	0,0	0,00	100,0
		Woche 72	101	7,92	18,348	0,0	0,00	100,0
		Woche 76	98	7,48	18,245	0,0	0,00	100,0
		Woche 80	97	7,90	17,195	0,0	0,00	66,7
		Woche 84	97	7,90	19,108	0,0	0,00	100,0
		Woche 88	92	7,61	17,192	0,0	0,00	66,7
		Woche 92	92	7,97	17,380	0,0	0,00	66,7
		Woche 96	87	7,28	17,182	0,0	0,00	66,7
		Woche 100	95	5,26	14,840	0,0	0,00	66,7
		Woche 104	80	5,42	13,463	0,0	0,00	66,7
		Woche 108	77	5,63	14,712	0,0	0,00	66,7
		Woche 112	73	7,31	15,954	0,0	0,00	66,7
		Woche 116	68	7,84	16,409	0,0	0,00	66,7
		Woche 120	63	7,94	17,673	0,0	0,00	100,0
		Woche 124	59	9,60	19,624	0,0	0,00	100,0
		Woche 128	59	9,04	17,321	0,0	0,00	66,7
		Woche 132	54	5,56	15,527	0,0	0,00	66,7
		Woche 136	52	5,13	15,317	0,0	0,00	66,7
		Woche 140	48	7,64	15,740	0,0	0,00	66,7
		Woche 144	39	7,69	17,871	0,0	0,00	66,7
		Woche 148	43	8,53	14,716	0,0	0,00	33,3
		Woche 152	41	11,38	21,871	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Alopezie	Durvalumab (N=264)	Woche 156	38	11,40	22,295	0,0	0,00	100,0
		Woche 160	33	11,11	23,074	0,0	0,00	100,0
		Woche 164	33	8,08	16,730	0,0	0,00	66,7
		Woche 168	29	3,45	10,331	0,0	0,00	33,3
		Woche 172	32	5,21	14,930	0,0	0,00	66,7
		Woche 176	23	2,90	9,603	0,0	0,00	33,3
		Woche 180	21	1,59	7,274	0,0	0,00	33,3
		Woche 184	19	7,02	13,962	0,0	0,00	33,3
		Woche 188	17	3,92	11,070	0,0	0,00	33,3
		Woche 192	17	5,88	13,098	0,0	0,00	33,3
		Woche 196	14	4,76	12,105	0,0	0,00	33,3
		Woche 200	11	0,00	0,000	0,0	0,00	0,0
		Woche 204	7	4,76	12,599	0,0	0,00	33,3
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	0,00	0,000	0,0	0,00	0,0
		Woche 216	9	0,00	0,000	0,0	0,00	0,0
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	23,72	33,343	0,0	0,00	100,0
		Woche 1	209	20,57	30,608	0,0	0,00	100,0
		Woche 2	212	16,04	27,434	0,0	0,00	100,0
		Woche 3	204	13,89	27,242	0,0	0,00	100,0
		Woche 4	231	13,42	26,518	0,0	0,00	100,0
		Woche 5	216	11,88	25,269	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Alopezie	Placebo (N=266)	Woche 6	207	9,34	22,487	0,0	0,00	100,0
		Woche 7	203	7,72	20,993	0,0	0,00	100,0
		Woche 8	211	9,32	22,829	0,0	0,00	100,0
		Woche 12	202	2,64	10,176	0,0	0,00	66,7
		Woche 16	198	2,86	12,002	0,0	0,00	100,0
		Woche 20	180	3,33	12,256	0,0	0,00	100,0
		Woche 24	172	4,46	14,403	0,0	0,00	100,0
		Woche 28	158	5,49	16,766	0,0	0,00	100,0
		Woche 32	150	6,00	18,549	0,0	0,00	100,0
		Woche 36	141	6,38	20,282	0,0	0,00	100,0
		Woche 40	122	5,46	18,363	0,0	0,00	100,0
		Woche 44	125	6,13	16,604	0,0	0,00	100,0
		Woche 48	121	6,61	18,064	0,0	0,00	100,0
		Woche 52	118	5,65	18,646	0,0	0,00	100,0
		Woche 56	106	6,60	16,213	0,0	0,00	100,0
		Woche 60	98	6,46	16,343	0,0	0,00	100,0
		Woche 64	95	6,32	15,600	0,0	0,00	66,7
		Woche 68	92	7,97	19,994	0,0	0,00	100,0
		Woche 72	87	8,05	19,665	0,0	0,00	100,0
		Woche 76	77	9,09	19,968	0,0	0,00	100,0
		Woche 80	75	5,33	15,538	0,0	0,00	100,0
		Woche 84	75	8,00	17,190	0,0	0,00	66,7
		Woche 88	70	5,24	14,619	0,0	0,00	66,7
		Woche 92	69	3,38	11,639	0,0	0,00	66,7
		Woche 96	64	5,73	13,998	0,0	0,00	66,7
		Woche 100	67	6,47	14,493	0,0	0,00	66,7
		Woche 104	63	5,29	12,279	0,0	0,00	33,3
		Woche 108	59	3,39	10,161	0,0	0,00	33,3
		Woche 112	54	4,32	13,025	0,0	0,00	66,7
		Woche 116	56	5,36	13,892	0,0	0,00	66,7
		Woche 120	51	3,27	10,011	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Alopezie	Placebo (N=266)	Woche 124	51	3,27	10,011	0,0	0,00	33,3
		Woche 128	45	5,93	12,888	0,0	0,00	33,3
		Woche 132	44	6,06	14,860	0,0	0,00	66,7
		Woche 136	39	5,98	12,959	0,0	0,00	33,3
		Woche 140	39	5,98	15,047	0,0	0,00	66,7
		Woche 144	35	6,67	15,760	0,0	0,00	66,7
		Woche 148	32	7,29	16,361	0,0	0,00	66,7
		Woche 152	33	6,06	15,489	0,0	0,00	66,7
		Woche 156	32	8,33	18,932	0,0	0,00	66,7
		Woche 160	31	4,30	11,359	0,0	0,00	33,3
		Woche 164	24	2,78	9,411	0,0	0,00	33,3
		Woche 168	28	3,57	13,876	0,0	0,00	66,7
		Woche 172	23	7,25	19,991	0,0	0,00	66,7
		Woche 176	21	4,76	15,936	0,0	0,00	66,7
		Woche 180	19	3,51	10,510	0,0	0,00	33,3
		Woche 184	20	3,33	10,260	0,0	0,00	33,3
		Woche 188	18	0,00	0,000	0,0	0,00	0,0
		Woche 192	16	2,08	8,333	0,0	0,00	33,3
		Woche 196	18	0,00	0,000	0,0	0,00	0,0
		Woche 200	19	5,26	12,488	0,0	0,00	33,3
		Woche 204	13	5,13	12,518	0,0	0,00	33,3
		Woche 208	12	5,56	12,975	0,0	0,00	33,3
		Woche 212	15	6,67	13,801	0,0	0,00	33,3
		Woche 216	12	2,78	9,623	0,0	0,00	33,3
		Woche 220	9	7,41	14,699	0,0	0,00	33,3
		Woche 224	11	6,06	13,484	0,0	0,00	33,3
		Woche 228	9	3,70	11,111	0,0	0,00	33,3
		Woche 232	5	6,67	14,907	0,0	0,00	33,3
		Woche 236	5	6,67	14,907	0,0	0,00	33,3
		Woche 240	5	6,67	14,907	0,0	0,00	33,3
		Woche 244	4	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Alopezie	Placebo (N=266)	Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Dysphagie	Durvalumab (N=264)	Baseline [a]	217	7,83	17,125	0,0	0,00	100,0
		Woche 1	208	6,89	16,070	0,0	0,00	100,0
		Woche 2	203	6,24	13,853	0,0	0,00	66,7
		Woche 3	205	6,50	14,796	0,0	0,00	66,7
		Woche 4	235	6,38	14,517	0,0	0,00	66,7
		Woche 5	213	6,42	15,031	0,0	0,00	66,7
		Woche 6	209	5,10	14,078	0,0	0,00	66,7
		Woche 7	209	7,34	15,654	0,0	0,00	66,7
		Woche 8	220	7,58	16,951	0,0	0,00	100,0
		Woche 12	204	6,21	13,424	0,0	0,00	66,7
		Woche 16	189	8,29	17,072	0,0	0,00	66,7
		Woche 20	179	7,26	15,095	0,0	0,00	66,7
		Woche 24	169	7,89	15,113	0,0	0,00	66,7
		Woche 28	166	6,63	15,229	0,0	0,00	100,0
		Woche 32	159	5,66	13,103	0,0	0,00	66,7
		Woche 36	153	6,75	14,489	0,0	0,00	66,7
		Woche 40	137	3,89	10,745	0,0	0,00	33,3
		Woche 44	131	4,58	11,520	0,0	0,00	33,3
		Woche 48	124	5,91	14,128	0,0	0,00	66,7
		Woche 52	124	3,23	10,769	0,0	0,00	66,7
		Woche 56	122	5,19	13,566	0,0	0,00	66,7
		Woche 60	118	3,67	11,351	0,0	0,00	66,7
		Woche 64	113	4,42	12,202	0,0	0,00	66,7
		Woche 68	103	3,56	11,350	0,0	0,00	66,7
		Woche 72	101	4,29	11,218	0,0	0,00	33,3
		Woche 76	98	5,78	13,560	0,0	0,00	66,7
		Woche 80	97	4,81	11,775	0,0	0,00	33,3
		Woche 84	97	4,81	12,720	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dysphagie	Durvalumab (N=264)	Woche 88	92	3,62	10,432	0,0	0,00	33,3
		Woche 92	92	4,71	11,675	0,0	0,00	33,3
		Woche 96	87	4,60	12,629	0,0	0,00	66,7
		Woche 100	95	3,86	10,722	0,0	0,00	33,3
		Woche 104	80	3,75	11,852	0,0	0,00	66,7
		Woche 108	77	4,76	14,012	0,0	0,00	66,7
		Woche 112	73	4,57	13,961	0,0	0,00	66,7
		Woche 116	68	3,92	10,820	0,0	0,00	33,3
		Woche 120	63	3,70	13,535	0,0	0,00	66,7
		Woche 124	59	2,82	9,363	0,0	0,00	33,3
		Woche 128	59	3,95	10,871	0,0	0,00	33,3
		Woche 132	54	1,85	7,707	0,0	0,00	33,3
		Woche 136	52	4,49	14,803	0,0	0,00	66,7
		Woche 140	48	3,47	10,290	0,0	0,00	33,3
		Woche 144	39	1,71	7,449	0,0	0,00	33,3
		Woche 148	43	3,10	12,202	0,0	0,00	66,7
		Woche 152	41	5,69	12,698	0,0	0,00	33,3
		Woche 156	38	7,89	16,319	0,0	0,00	66,7
		Woche 160	33	4,04	11,048	0,0	0,00	33,3
		Woche 164	33	5,05	12,137	0,0	0,00	33,3
		Woche 168	29	3,45	10,331	0,0	0,00	33,3
		Woche 172	32	4,17	11,200	0,0	0,00	33,3
		Woche 176	23	4,35	11,478	0,0	0,00	33,3
		Woche 180	21	4,76	11,952	0,0	0,00	33,3
		Woche 184	19	3,51	10,510	0,0	0,00	33,3
		Woche 188	17	1,96	8,085	0,0	0,00	33,3
		Woche 192	17	3,92	11,070	0,0	0,00	33,3
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	0,00	0,000	0,0	0,00	0,0
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dysphagie	Durvalumab (N=264)	Woche 212	7	0,00	0,000	0,0	0,00	0,0
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	9,30	18,407	0,0	0,00	100,0
		Woche 1	209	8,93	16,505	0,0	0,00	66,7
		Woche 2	212	8,49	16,901	0,0	0,00	100,0
		Woche 3	204	8,99	16,898	0,0	0,00	66,7
		Woche 4	231	9,67	18,852	0,0	0,00	100,0
		Woche 5	216	8,95	17,077	0,0	0,00	66,7
		Woche 6	207	9,18	17,271	0,0	0,00	66,7
		Woche 7	203	10,67	19,081	0,0	0,00	66,7
		Woche 8	211	9,79	18,938	0,0	0,00	100,0
		Woche 12	202	10,07	18,300	0,0	0,00	66,7
		Woche 16	198	9,43	17,152	0,0	0,00	100,0
		Woche 20	180	7,22	15,865	0,0	0,00	100,0
		Woche 24	172	7,75	16,656	0,0	0,00	100,0
		Woche 28	158	7,38	17,085	0,0	0,00	100,0
		Woche 32	150	7,33	17,215	0,0	0,00	100,0
		Woche 36	141	6,38	14,318	0,0	0,00	66,7
		Woche 40	122	5,46	13,112	0,0	0,00	66,7
		Woche 44	125	5,33	14,293	0,0	0,00	66,7
		Woche 48	121	6,89	14,219	0,0	0,00	66,7
		Woche 52	118	6,78	16,048	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dysphagie	Placebo (N=266)	Woche 56	106	6,92	15,060	0,0	0,00	66,7
		Woche 60	98	5,10	12,063	0,0	0,00	33,3
		Woche 64	95	4,91	12,835	0,0	0,00	66,7
		Woche 68	92	5,43	12,381	0,0	0,00	33,3
		Woche 72	87	6,51	13,294	0,0	0,00	33,3
		Woche 76	77	6,06	12,941	0,0	0,00	33,3
		Woche 80	75	7,11	14,799	0,0	0,00	66,7
		Woche 84	75	5,33	12,302	0,0	0,00	33,3
		Woche 88	70	5,24	13,472	0,0	0,00	66,7
		Woche 92	69	3,86	12,176	0,0	0,00	66,7
		Woche 96	64	8,85	15,983	0,0	0,00	66,7
		Woche 100	67	4,98	11,968	0,0	0,00	33,3
		Woche 104	63	5,82	14,091	0,0	0,00	66,7
		Woche 108	59	7,34	16,456	0,0	0,00	66,7
		Woche 112	54	6,79	15,019	0,0	0,00	66,7
		Woche 116	56	4,76	13,377	0,0	0,00	66,7
		Woche 120	51	3,27	10,011	0,0	0,00	33,3
		Woche 124	51	6,54	14,936	0,0	0,00	66,7
		Woche 128	45	5,19	12,218	0,0	0,00	33,3
		Woche 132	44	4,55	11,571	0,0	0,00	33,3
		Woche 136	39	7,69	16,153	0,0	0,00	66,7
		Woche 140	39	9,40	18,651	0,0	0,00	66,7
		Woche 144	35	5,71	12,746	0,0	0,00	33,3
		Woche 148	32	6,25	13,219	0,0	0,00	33,3
		Woche 152	33	5,05	14,722	0,0	0,00	66,7
		Woche 156	32	7,29	14,000	0,0	0,00	33,3
		Woche 160	31	6,45	13,387	0,0	0,00	33,3
		Woche 164	24	5,56	12,690	0,0	0,00	33,3
		Woche 168	28	4,76	11,878	0,0	0,00	33,3
		Woche 172	23	4,35	11,478	0,0	0,00	33,3
		Woche 176	21	4,76	11,952	0,0	0,00	33,3

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Dysphagie	Placebo (N=266)	Woche 180	19	5,26	12,488	0,0	0,00	33,3
		Woche 184	20	5,00	12,212	0,0	0,00	33,3
		Woche 188	18	1,85	7,857	0,0	0,00	33,3
		Woche 192	16	4,17	11,386	0,0	0,00	33,3
		Woche 196	18	3,70	10,779	0,0	0,00	33,3
		Woche 200	19	5,26	12,488	0,0	0,00	33,3
		Woche 204	13	10,26	21,014	0,0	0,00	66,7
		Woche 208	12	11,11	16,412	0,0	0,00	33,3
		Woche 212	15	6,67	13,801	0,0	0,00	33,3
		Woche 216	12	11,11	16,412	0,0	0,00	33,3
		Woche 220	9	7,41	14,699	0,0	0,00	33,3
		Woche 224	11	6,06	13,484	0,0	0,00	33,3
		Woche 228	9	7,41	14,699	0,0	0,00	33,3
		Woche 232	5	20,00	29,814	0,0	0,00	66,7
		Woche 236	5	13,33	18,257	0,0	0,00	33,3
		Woche 240	5	13,33	18,257	0,0	0,00	33,3
		Woche 244	4	8,33	16,667	0,0	0,00	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Hämoptoe	Durvalumab (N=264)	Baseline [a]	217	2,15	8,812	0,0	0,00	66,7
		Woche 1	208	1,76	7,478	0,0	0,00	33,3
		Woche 2	203	1,15	7,693	0,0	0,00	66,7
		Woche 3	205	0,98	6,528	0,0	0,00	66,7
		Woche 4	235	0,71	4,820	0,0	0,00	33,3
		Woche 5	213	0,94	6,406	0,0	0,00	66,7
		Woche 6	209	0,80	6,063	0,0	0,00	66,7
		Woche 7	209	1,28	7,904	0,0	0,00	66,7
		Woche 8	220	1,52	10,455	0,0	0,00	100,0
		Woche 12	204	1,63	9,790	0,0	0,00	66,7
		Woche 16	189	0,71	5,913	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Hämoptoe	Durvalumab (N=264)	Woche 20	179	0,37	3,514	0,0	0,00	33,3
		Woche 24	169	1,38	6,662	0,0	0,00	33,3
		Woche 28	166	0,80	5,127	0,0	0,00	33,3
		Woche 32	159	0,42	3,727	0,0	0,00	33,3
		Woche 36	153	0,87	5,336	0,0	0,00	33,3
		Woche 40	137	1,70	8,403	0,0	0,00	66,7
		Woche 44	131	1,02	9,188	0,0	0,00	100,0
		Woche 48	124	1,08	5,913	0,0	0,00	33,3
		Woche 52	124	1,08	7,283	0,0	0,00	66,7
		Woche 56	122	0,27	3,018	0,0	0,00	33,3
		Woche 60	118	0,56	4,321	0,0	0,00	33,3
		Woche 64	113	0,29	3,136	0,0	0,00	33,3
		Woche 68	103	0,65	4,622	0,0	0,00	33,3
		Woche 72	101	0,99	5,687	0,0	0,00	33,3
		Woche 76	98	0,34	3,367	0,0	0,00	33,3
		Woche 80	97	0,34	3,384	0,0	0,00	33,3
		Woche 84	97	1,03	5,801	0,0	0,00	33,3
		Woche 88	92	0,72	4,888	0,0	0,00	33,3
		Woche 92	92	1,09	5,953	0,0	0,00	33,3
		Woche 96	87	0,38	3,574	0,0	0,00	33,3
		Woche 100	95	0,70	4,811	0,0	0,00	33,3
		Woche 104	80	0,42	3,727	0,0	0,00	33,3
		Woche 108	77	0,43	3,799	0,0	0,00	33,3
		Woche 112	73	1,37	6,663	0,0	0,00	33,3
		Woche 116	68	0,98	5,674	0,0	0,00	33,3
		Woche 120	63	2,65	13,785	0,0	0,00	100,0
		Woche 124	59	0,00	0,000	0,0	0,00	0,0
		Woche 128	59	1,69	7,386	0,0	0,00	33,3
		Woche 132	54	0,00	0,000	0,0	0,00	0,0
		Woche 136	52	0,00	0,000	0,0	0,00	0,0
		Woche 140	48	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Hämoptoe	Durvalumab (N=264)	Woche 144	39	0,00	0,000	0,0	0,00	0,0
		Woche 148	43	0,78	5,083	0,0	0,00	33,3
		Woche 152	41	2,44	11,524	0,0	0,00	66,7
		Woche 156	38	0,88	5,407	0,0	0,00	33,3
		Woche 160	33	0,00	0,000	0,0	0,00	0,0
		Woche 164	33	0,00	0,000	0,0	0,00	0,0
		Woche 168	29	0,00	0,000	0,0	0,00	0,0
		Woche 172	32	0,00	0,000	0,0	0,00	0,0
		Woche 176	23	0,00	0,000	0,0	0,00	0,0
		Woche 180	21	0,00	0,000	0,0	0,00	0,0
		Woche 184	19	0,00	0,000	0,0	0,00	0,0
		Woche 188	17	1,96	8,085	0,0	0,00	33,3
		Woche 192	17	1,96	8,085	0,0	0,00	33,3
		Woche 196	14	0,00	0,000	0,0	0,00	0,0
		Woche 200	11	0,00	0,000	0,0	0,00	0,0
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	0,00	0,000	0,0	0,00	0,0
		Woche 216	9	0,00	0,000	0,0	0,00	0,0
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Hämoptoe	Placebo (N=266)	Baseline [a]	215	1,86	8,319	0,0	0,00	66,7
		Woche 1	209	1,75	9,366	0,0	0,00	100,0
		Woche 2	212	1,73	8,090	0,0	0,00	66,7
		Woche 3	204	1,80	8,880	0,0	0,00	66,7
		Woche 4	231	1,01	6,516	0,0	0,00	66,7
		Woche 5	216	0,46	3,910	0,0	0,00	33,3
		Woche 6	207	1,29	7,230	0,0	0,00	66,7
		Woche 7	203	2,13	9,430	0,0	0,00	66,7
		Woche 8	211	1,26	6,381	0,0	0,00	33,3
		Woche 12	202	1,16	6,112	0,0	0,00	33,3
		Woche 16	198	1,01	5,728	0,0	0,00	33,3
		Woche 20	180	1,30	7,360	0,0	0,00	66,7
		Woche 24	172	0,58	4,376	0,0	0,00	33,3
		Woche 28	158	0,21	2,652	0,0	0,00	33,3
		Woche 32	150	0,67	4,682	0,0	0,00	33,3
		Woche 36	141	1,42	7,840	0,0	0,00	66,7
		Woche 40	122	1,09	9,520	0,0	0,00	100,0
		Woche 44	125	1,33	6,558	0,0	0,00	33,3
		Woche 48	121	1,65	7,266	0,0	0,00	33,3
		Woche 52	118	0,28	3,069	0,0	0,00	33,3
		Woche 56	106	1,26	7,867	0,0	0,00	66,7
		Woche 60	98	0,00	0,000	0,0	0,00	0,0
		Woche 64	95	0,70	4,811	0,0	0,00	33,3
		Woche 68	92	0,72	4,888	0,0	0,00	33,3
		Woche 72	87	0,77	5,025	0,0	0,00	33,3
		Woche 76	77	1,73	9,202	0,0	0,00	66,7
		Woche 80	75	0,44	3,849	0,0	0,00	33,3
		Woche 84	75	0,44	3,849	0,0	0,00	33,3
		Woche 88	70	0,48	3,984	0,0	0,00	33,3
		Woche 92	69	0,00	0,000	0,0	0,00	0,0
		Woche 96	64	0,00	0,000	0,0	0,00	0,0

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Hämoptoe	Placebo (N=266)	Woche 100	67	1,00	5,715	0,0	0,00	33,3
		Woche 104	63	0,53	4,200	0,0	0,00	33,3
		Woche 108	59	0,00	0,000	0,0	0,00	0,0
		Woche 112	54	1,23	6,354	0,0	0,00	33,3
		Woche 116	56	1,19	6,242	0,0	0,00	33,3
		Woche 120	51	0,65	4,668	0,0	0,00	33,3
		Woche 124	51	1,96	7,921	0,0	0,00	33,3
		Woche 128	45	2,96	9,593	0,0	0,00	33,3
		Woche 132	44	1,52	7,024	0,0	0,00	33,3
		Woche 136	39	1,71	7,449	0,0	0,00	33,3
		Woche 140	39	0,85	5,338	0,0	0,00	33,3
		Woche 144	35	0,00	0,000	0,0	0,00	0,0
		Woche 148	32	1,04	5,893	0,0	0,00	33,3
		Woche 152	33	0,00	0,000	0,0	0,00	0,0
		Woche 156	32	1,04	5,893	0,0	0,00	33,3
		Woche 160	31	1,08	5,987	0,0	0,00	33,3
		Woche 164	24	1,39	6,804	0,0	0,00	33,3
		Woche 168	28	0,00	0,000	0,0	0,00	0,0
		Woche 172	23	1,45	6,950	0,0	0,00	33,3
		Woche 176	21	0,00	0,000	0,0	0,00	0,0
		Woche 180	19	0,00	0,000	0,0	0,00	0,0
		Woche 184	20	0,00	0,000	0,0	0,00	0,0
		Woche 188	18	0,00	0,000	0,0	0,00	0,0
		Woche 192	16	0,00	0,000	0,0	0,00	0,0
		Woche 196	18	0,00	0,000	0,0	0,00	0,0
		Woche 200	19	0,00	0,000	0,0	0,00	0,0
		Woche 204	13	0,00	0,000	0,0	0,00	0,0
		Woche 208	12	0,00	0,000	0,0	0,00	0,0
		Woche 212	15	2,22	8,607	0,0	0,00	33,3
		Woche 216	12	0,00	0,000	0,0	0,00	0,0
		Woche 220	9	0,00	0,000	0,0	0,00	0,0

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SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Hämoptoe	Placebo (N=266)	Woche 224	11	3,03	10,050	0,0	0,00	33,3
		Woche 228	9	0,00	0,000	0,0	0,00	0,0
		Woche 232	5	0,00	0,000	0,0	0,00	0,0
		Woche 236	5	0,00	0,000	0,0	0,00	0,0
		Woche 240	5	0,00	0,000	0,0	0,00	0,0
		Woche 244	4	0,00	0,000	0,0	0,00	0,0
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Husten	Durvalumab (N=264)	Baseline [a]	217	23,04	21,791	0,0	33,33	100,0
		Woche 1	208	24,20	22,388	0,0	33,33	100,0
		Woche 2	203	24,79	21,835	0,0	33,33	100,0
		Woche 3	205	26,18	22,453	0,0	33,33	100,0
		Woche 4	235	27,66	22,770	0,0	33,33	100,0
		Woche 5	213	30,05	24,966	0,0	33,33	100,0
		Woche 6	209	28,39	24,504	0,0	33,33	100,0
		Woche 7	209	29,98	25,622	0,0	33,33	100,0
		Woche 8	220	30,91	24,347	0,0	33,33	100,0
		Woche 12	204	28,76	23,877	0,0	33,33	100,0
		Woche 16	189	27,51	23,221	0,0	33,33	100,0
		Woche 20	179	26,26	23,693	0,0	33,33	100,0
		Woche 24	169	27,22	22,020	0,0	33,33	100,0
		Woche 28	166	25,70	22,815	0,0	33,33	100,0
		Woche 32	159	26,42	21,892	0,0	33,33	66,7
		Woche 36	153	25,27	21,298	0,0	33,33	66,7
		Woche 40	137	24,82	20,223	0,0	33,33	66,7
		Woche 44	131	24,43	22,197	0,0	33,33	100,0
		Woche 48	124	26,08	23,497	0,0	33,33	100,0
		Woche 52	124	22,58	22,309	0,0	33,33	100,0
		Woche 56	122	27,60	23,742	0,0	33,33	100,0
		Woche 60	118	21,75	22,383	0,0	33,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Husten	Durvalumab (N=264)	Woche 64	113	27,14	24,620	0,0	33,33	100,0
		Woche 68	103	22,98	23,352	0,0	33,33	100,0
		Woche 72	101	22,77	21,567	0,0	33,33	66,7
		Woche 76	98	22,45	22,842	0,0	33,33	66,7
		Woche 80	97	22,68	21,809	0,0	33,33	66,7
		Woche 84	97	20,96	21,688	0,0	33,33	66,7
		Woche 88	92	22,83	23,663	0,0	33,33	100,0
		Woche 92	92	19,93	22,133	0,0	16,67	66,7
		Woche 96	87	22,61	20,645	0,0	33,33	100,0
		Woche 100	95	22,46	21,439	0,0	33,33	100,0
		Woche 104	80	24,17	25,422	0,0	33,33	100,0
		Woche 108	77	24,24	23,344	0,0	33,33	100,0
		Woche 112	73	23,29	23,363	0,0	33,33	100,0
		Woche 116	68	23,53	21,594	0,0	33,33	66,7
		Woche 120	63	26,98	26,678	0,0	33,33	100,0
		Woche 124	59	20,90	23,076	0,0	33,33	66,7
		Woche 128	59	20,90	20,434	0,0	33,33	66,7
		Woche 132	54	16,05	21,221	0,0	0,00	66,7
		Woche 136	52	17,31	20,335	0,0	0,00	66,7
		Woche 140	48	16,67	19,449	0,0	0,00	66,7
		Woche 144	39	17,09	20,046	0,0	0,00	66,7
		Woche 148	43	16,28	18,362	0,0	0,00	66,7
		Woche 152	41	17,89	22,482	0,0	0,00	66,7
		Woche 156	38	15,79	20,115	0,0	0,00	66,7
		Woche 160	33	25,25	23,615	0,0	33,33	66,7
		Woche 164	33	15,15	18,803	0,0	0,00	66,7
		Woche 168	29	19,54	18,934	0,0	33,33	66,7
		Woche 172	32	15,62	18,902	0,0	0,00	66,7
		Woche 176	23	23,19	18,627	0,0	33,33	66,7
		Woche 180	21	15,87	20,053	0,0	0,00	66,7
		Woche 184	19	15,79	20,393	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Husten	Durvalumab (N=264)	Woche 188	17	21,57	28,726	0,0	0,00	100,0
		Woche 192	17	21,57	20,211	0,0	33,33	66,7
		Woche 196	14	19,05	21,540	0,0	16,67	66,7
		Woche 200	11	9,09	15,570	0,0	0,00	33,3
		Woche 204	7	14,29	17,817	0,0	0,00	33,3
		Woche 208	8	12,50	24,801	0,0	0,00	66,7
		Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	18,52	17,568	0,0	33,33	33,3
		Woche 220	7	4,76	12,599	0,0	0,00	33,3
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	11,11	17,213	0,0	0,00	33,3
		Woche 232	6	5,56	13,608	0,0	0,00	33,3
		Woche 236	4	8,33	16,667	0,0	0,00	33,3
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	26,20	23,916	0,0	33,33	100,0
		Woche 1	209	26,16	24,165	0,0	33,33	100,0
		Woche 2	212	27,52	23,463	0,0	33,33	100,0
		Woche 3	204	25,98	23,752	0,0	33,33	100,0
		Woche 4	231	30,30	24,583	0,0	33,33	100,0
		Woche 5	216	28,55	25,166	0,0	33,33	100,0
		Woche 6	207	27,70	23,580	0,0	33,33	100,0
		Woche 7	203	29,06	24,895	0,0	33,33	100,0
		Woche 8	211	29,86	23,425	0,0	33,33	100,0
		Woche 12	202	26,73	23,285	0,0	33,33	100,0
		Woche 16	198	30,47	23,931	0,0	33,33	100,0
		Woche 20	180	28,70	23,041	0,0	33,33	100,0
		Woche 24	172	27,13	22,519	0,0	33,33	100,0
		Woche 28	158	28,90	25,267	0,0	33,33	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Husten	Placebo (N=266)	Woche 32	150	30,67	24,583	0,0	33,33	100,0
		Woche 36	141	25,53	24,442	0,0	33,33	100,0
		Woche 40	122	28,96	24,600	0,0	33,33	100,0
		Woche 44	125	27,47	26,795	0,0	33,33	100,0
		Woche 48	121	28,93	24,699	0,0	33,33	100,0
		Woche 52	118	26,27	24,207	0,0	33,33	100,0
		Woche 56	106	27,99	21,645	0,0	33,33	100,0
		Woche 60	98	22,45	21,285	0,0	33,33	100,0
		Woche 64	95	25,26	22,658	0,0	33,33	100,0
		Woche 68	92	26,09	24,121	0,0	33,33	100,0
		Woche 72	87	25,29	22,714	0,0	33,33	66,7
		Woche 76	77	28,14	24,222	0,0	33,33	100,0
		Woche 80	75	25,78	21,626	0,0	33,33	66,7
		Woche 84	75	28,89	24,095	0,0	33,33	100,0
		Woche 88	70	27,62	24,058	0,0	33,33	100,0
		Woche 92	69	23,19	23,083	0,0	33,33	66,7
		Woche 96	64	24,48	24,662	0,0	33,33	100,0
		Woche 100	67	21,89	20,558	0,0	33,33	66,7
		Woche 104	63	25,40	22,171	0,0	33,33	66,7
		Woche 108	59	26,55	28,216	0,0	33,33	100,0
		Woche 112	54	28,40	25,417	0,0	33,33	100,0
		Woche 116	56	26,19	26,753	0,0	33,33	100,0
		Woche 120	51	25,49	22,694	0,0	33,33	66,7
		Woche 124	51	27,45	26,420	0,0	33,33	100,0
		Woche 128	45	25,19	23,736	0,0	33,33	100,0
		Woche 132	44	24,24	23,143	0,0	33,33	100,0
		Woche 136	39	21,37	22,278	0,0	33,33	66,7
		Woche 140	39	24,79	23,839	0,0	33,33	100,0
		Woche 144	35	24,76	20,361	0,0	33,33	66,7
		Woche 148	32	25,00	20,739	0,0	33,33	66,7
		Woche 152	33	24,24	20,871	0,0	33,33	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Husten	Placebo (N=266)	Woche 156	32	25,00	22,401	0,0	33,33	66,7
		Woche 160	31	27,96	25,958	0,0	33,33	100,0
		Woche 164	24	27,78	18,822	0,0	33,33	66,7
		Woche 168	28	22,62	20,394	0,0	33,33	66,7
		Woche 172	23	26,09	22,375	0,0	33,33	100,0
		Woche 176	21	25,40	17,965	0,0	33,33	66,7
		Woche 180	19	24,56	18,732	0,0	33,33	66,7
		Woche 184	20	26,67	25,592	0,0	33,33	66,7
		Woche 188	18	22,22	16,169	0,0	33,33	33,3
		Woche 192	16	29,17	23,960	0,0	33,33	66,7
		Woche 196	18	24,07	27,548	0,0	33,33	100,0
		Woche 200	19	22,81	29,508	0,0	0,00	100,0
		Woche 204	13	30,77	25,318	0,0	33,33	66,7
		Woche 208	12	25,00	20,719	0,0	33,33	66,7
		Woche 212	15	17,78	21,331	0,0	0,00	66,7
		Woche 216	12	27,78	23,925	0,0	33,33	66,7
		Woche 220	9	29,63	20,031	0,0	33,33	66,7
		Woche 224	11	24,24	21,556	0,0	33,33	66,7
		Woche 228	9	25,93	22,222	0,0	33,33	66,7
		Woche 232	5	26,67	14,907	0,0	33,33	33,3
		Woche 236	5	46,67	18,257	33,3	33,33	66,7
		Woche 240	5	40,00	14,907	33,3	33,33	66,7
		Woche 244	4	41,67	16,667	33,3	33,33	66,7
		Woche 248	2	16,67	23,570	0,0	16,67	33,3
		Woche 252	1	33,33	NC	33,3	33,33	33,3
		Woche 256	1	33,33	NC	33,3	33,33	33,3
Periphere Neuropathie	Durvalumab (N=264)	Baseline [a]	217	7,53	16,657	0,0	0,00	100,0
		Woche 1	208	9,29	19,081	0,0	0,00	100,0
		Woche 2	203	9,85	19,660	0,0	0,00	100,0
		Woche 3	205	10,57	18,434	0,0	0,00	66,7
		Woche 4	235	10,07	19,435	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Periphere Neuropathie	Durvalumab (N=264)	Woche 5	213	12,21	20,912	0,0	0,00	100,0
		Woche 6	209	11,48	21,333	0,0	0,00	100,0
		Woche 7	209	12,76	22,094	0,0	0,00	100,0
		Woche 8	220	13,33	21,931	0,0	0,00	100,0
		Woche 12	204	12,91	19,908	0,0	0,00	66,7
		Woche 16	189	12,70	22,880	0,0	0,00	100,0
		Woche 20	179	13,97	21,137	0,0	0,00	100,0
		Woche 24	169	14,00	21,999	0,0	0,00	100,0
		Woche 28	166	13,65	21,105	0,0	0,00	100,0
		Woche 32	159	12,16	19,277	0,0	0,00	100,0
		Woche 36	153	13,07	20,317	0,0	0,00	66,7
		Woche 40	137	12,90	19,490	0,0	0,00	66,7
		Woche 44	131	12,21	19,039	0,0	0,00	66,7
		Woche 48	124	12,10	20,088	0,0	0,00	66,7
		Woche 52	124	11,83	20,024	0,0	0,00	66,7
		Woche 56	122	12,30	17,774	0,0	0,00	66,7
		Woche 60	118	12,71	18,956	0,0	0,00	66,7
		Woche 64	113	13,86	20,279	0,0	0,00	66,7
		Woche 68	103	12,30	18,072	0,0	0,00	66,7
		Woche 72	101	13,20	18,903	0,0	0,00	66,7
		Woche 76	98	13,95	20,821	0,0	0,00	100,0
		Woche 80	97	15,81	21,023	0,0	0,00	66,7
		Woche 84	97	13,06	19,577	0,0	0,00	66,7
		Woche 88	92	13,04	22,622	0,0	0,00	100,0
		Woche 92	92	12,32	18,958	0,0	0,00	66,7
		Woche 96	87	13,41	21,240	0,0	0,00	66,7
		Woche 100	95	14,39	21,555	0,0	0,00	66,7
		Woche 104	80	13,75	20,330	0,0	0,00	66,7
		Woche 108	77	10,82	17,473	0,0	0,00	66,7
		Woche 112	73	10,96	18,472	0,0	0,00	66,7
		Woche 116	68	12,75	19,126	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Periphere Neuropathie	Durvalumab (N=264)	Woche 120	63	14,81	21,401	0,0	0,00	66,7
		Woche 124	59	12,99	19,591	0,0	0,00	66,7
		Woche 128	59	11,30	19,189	0,0	0,00	66,7
		Woche 132	54	8,64	17,357	0,0	0,00	66,7
		Woche 136	52	10,90	19,494	0,0	0,00	66,7
		Woche 140	48	11,81	17,517	0,0	0,00	66,7
		Woche 144	39	8,55	18,286	0,0	0,00	66,7
		Woche 148	43	11,63	21,680	0,0	0,00	100,0
		Woche 152	41	12,20	19,374	0,0	0,00	66,7
		Woche 156	38	14,04	21,409	0,0	0,00	66,7
		Woche 160	33	14,14	23,615	0,0	0,00	100,0
		Woche 164	33	16,16	22,238	0,0	0,00	66,7
		Woche 168	29	13,79	20,925	0,0	0,00	66,7
		Woche 172	32	14,58	22,300	0,0	0,00	66,7
		Woche 176	23	15,94	22,178	0,0	0,00	66,7
		Woche 180	21	17,46	24,987	0,0	0,00	66,7
		Woche 184	19	17,54	28,040	0,0	0,00	100,0
		Woche 188	17	21,57	23,396	0,0	33,33	66,7
		Woche 192	17	17,65	20,809	0,0	0,00	66,7
		Woche 196	14	16,67	25,318	0,0	0,00	66,7
		Woche 200	11	15,15	22,918	0,0	0,00	66,7
		Woche 204	7	9,52	16,265	0,0	0,00	33,3
		Woche 208	8	8,33	15,430	0,0	0,00	33,3
		Woche 212	7	14,29	17,817	0,0	0,00	33,3
		Woche 216	9	7,41	14,699	0,0	0,00	33,3
		Woche 220	7	4,76	12,599	0,0	0,00	33,3
		Woche 224	6	11,11	17,213	0,0	0,00	33,3
		Woche 228	6	5,56	13,608	0,0	0,00	33,3
		Woche 232	6	11,11	17,213	0,0	0,00	33,3
		Woche 236	4	16,67	19,245	0,0	16,67	33,3
		Woche 240	3	22,22	19,245	0,0	33,33	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Periphere Neuropathie	Durvalumab (N=264)	Woche 244	2	33,33	0,000	33,3	33,33	33,3
		Woche 248	1	33,33	NC	33,3	33,33	33,3
		Woche 252	2	33,33	0,000	33,3	33,33	33,3
	Placebo (N=266)	Baseline [a]	215	8,53	16,888	0,0	0,00	100,0
		Woche 1	209	9,89	18,721	0,0	0,00	100,0
		Woche 2	212	10,22	17,933	0,0	0,00	66,7
		Woche 3	204	12,75	20,686	0,0	0,00	100,0
		Woche 4	231	13,71	22,834	0,0	0,00	100,0
		Woche 5	216	14,35	21,199	0,0	0,00	100,0
		Woche 6	207	15,14	21,701	0,0	0,00	100,0
		Woche 7	203	16,42	24,231	0,0	0,00	100,0
		Woche 8	211	16,75	23,766	0,0	0,00	100,0
		Woche 12	202	15,02	23,746	0,0	0,00	100,0
		Woche 16	198	15,15	23,401	0,0	0,00	100,0
		Woche 20	180	13,70	22,225	0,0	0,00	100,0
		Woche 24	172	14,73	20,774	0,0	0,00	100,0
		Woche 28	158	13,29	22,238	0,0	0,00	100,0
		Woche 32	150	13,33	21,152	0,0	0,00	100,0
		Woche 36	141	12,53	19,736	0,0	0,00	66,7
		Woche 40	122	12,84	19,846	0,0	0,00	100,0
		Woche 44	125	13,33	20,302	0,0	0,00	100,0
		Woche 48	121	11,57	18,614	0,0	0,00	66,7
		Woche 52	118	12,15	17,249	0,0	0,00	66,7
		Woche 56	106	15,72	21,680	0,0	0,00	66,7
		Woche 60	98	13,27	19,583	0,0	0,00	66,7
		Woche 64	95	13,68	18,511	0,0	0,00	66,7
		Woche 68	92	12,32	18,302	0,0	0,00	66,7
		Woche 72	87	13,03	19,920	0,0	0,00	66,7
		Woche 76	77	12,99	21,735	0,0	0,00	100,0
		Woche 80	75	13,78	20,572	0,0	0,00	66,7
		Woche 84	75	15,56	23,464	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Periphere Neuropathie	Placebo (N=266)	Woche 88	70	14,29	22,394	0,0	0,00	100,0
		Woche 92	69	13,04	23,021	0,0	0,00	100,0
		Woche 96	64	13,54	20,331	0,0	0,00	66,7
		Woche 100	67	10,95	19,582	0,0	0,00	66,7
		Woche 104	63	14,81	21,401	0,0	0,00	66,7
		Woche 108	59	15,25	21,728	0,0	0,00	100,0
		Woche 112	54	15,43	23,978	0,0	0,00	100,0
		Woche 116	56	11,31	17,147	0,0	0,00	66,7
		Woche 120	51	10,46	15,621	0,0	0,00	33,3
		Woche 124	51	10,46	18,245	0,0	0,00	66,7
		Woche 128	45	9,63	16,851	0,0	0,00	66,7
		Woche 132	44	10,61	17,272	0,0	0,00	66,7
		Woche 136	39	12,82	19,669	0,0	0,00	66,7
		Woche 140	39	11,11	19,245	0,0	0,00	66,7
		Woche 144	35	12,38	19,944	0,0	0,00	66,7
		Woche 148	32	13,54	22,175	0,0	0,00	66,7
		Woche 152	33	10,10	19,516	0,0	0,00	66,7
		Woche 156	32	12,50	20,302	0,0	0,00	66,7
		Woche 160	31	9,68	17,625	0,0	0,00	66,7
		Woche 164	24	11,11	18,822	0,0	0,00	66,7
		Woche 168	28	11,90	22,616	0,0	0,00	66,7
		Woche 172	23	17,39	17,025	0,0	33,33	33,3
		Woche 176	21	15,87	22,655	0,0	0,00	66,7
		Woche 180	19	19,30	23,083	0,0	0,00	66,7
		Woche 184	20	18,33	22,878	0,0	0,00	66,7
		Woche 188	18	18,52	20,523	0,0	16,67	66,7
		Woche 192	16	20,83	23,960	0,0	16,67	66,7
		Woche 196	18	14,81	20,523	0,0	0,00	66,7
		Woche 200	19	17,54	23,223	0,0	0,00	66,7
		Woche 204	13	25,64	24,167	0,0	33,33	66,7
		Woche 208	12	16,67	26,591	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Periphere Neuropathie	Placebo (N=266)	Woche 212	15	15,56	21,331	0,0	0,00	66,7
		Woche 216	12	16,67	22,473	0,0	0,00	66,7
		Woche 220	9	22,22	23,570	0,0	33,33	66,7
		Woche 224	11	18,18	27,340	0,0	0,00	66,7
		Woche 228	9	25,93	22,222	0,0	33,33	66,7
		Woche 232	5	26,67	14,907	0,0	33,33	33,3
		Woche 236	5	33,33	23,570	0,0	33,33	66,7
		Woche 240	5	26,67	27,889	0,0	33,33	66,7
		Woche 244	4	33,33	27,217	0,0	33,33	66,7
		Woche 248	2	16,67	23,570	0,0	16,67	33,3
		Woche 252	1	33,33	NC	33,3	33,33	33,3
		Woche 256	1	33,33	NC	33,3	33,33	33,3
Schmerzen an anderen Stellen des Körpers	Durvalumab (N=264)	Baseline [a]	217	12,44	18,808	0,0	0,00	66,7
		Woche 1	208	13,62	19,966	0,0	0,00	66,7
		Woche 2	203	12,64	19,593	0,0	0,00	66,7
		Woche 3	205	13,33	18,553	0,0	0,00	66,7
		Woche 4	235	13,33	20,019	0,0	0,00	100,0
		Woche 5	213	15,18	21,332	0,0	0,00	100,0
		Woche 6	209	15,63	20,935	0,0	0,00	66,7
		Woche 7	209	15,31	21,171	0,0	0,00	100,0
		Woche 8	220	16,36	21,952	0,0	0,00	100,0
		Woche 12	204	14,05	22,409	0,0	0,00	100,0
		Woche 16	189	16,05	22,438	0,0	0,00	100,0
		Woche 20	179	15,64	19,446	0,0	0,00	66,7
		Woche 24	169	17,75	21,833	0,0	0,00	100,0
		Woche 28	166	15,26	21,897	0,0	0,00	100,0
		Woche 32	159	16,56	21,503	0,0	0,00	100,0
		Woche 36	153	15,47	19,878	0,0	0,00	66,7
		Woche 40	137	14,11	20,099	0,0	0,00	100,0
		Woche 44	131	17,05	22,783	0,0	0,00	100,0
		Woche 48	124	15,59	22,666	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen an anderen Stellen des Körpers	Durvalumab (N=264)	Woche 52	124	16,40	24,230	0,0	0,00	100,0
		Woche 56	122	15,03	21,039	0,0	0,00	100,0
		Woche 60	118	14,41	19,235	0,0	0,00	66,7
		Woche 64	113	16,81	24,039	0,0	0,00	100,0
		Woche 68	103	14,89	20,200	0,0	0,00	66,7
		Woche 72	101	13,86	20,148	0,0	0,00	100,0
		Woche 76	98	12,24	19,959	0,0	0,00	66,7
		Woche 80	97	15,46	20,447	0,0	0,00	66,7
		Woche 84	97	12,03	18,121	0,0	0,00	66,7
		Woche 88	92	12,32	21,379	0,0	0,00	100,0
		Woche 92	92	14,13	20,515	0,0	0,00	66,7
		Woche 96	87	18,01	25,822	0,0	0,00	100,0
		Woche 100	95	12,28	18,227	0,0	0,00	66,7
		Woche 104	80	13,75	21,670	0,0	0,00	66,7
		Woche 108	77	16,02	22,692	0,0	0,00	100,0
		Woche 112	73	16,44	23,651	0,0	0,00	100,0
		Woche 116	68	13,73	21,729	0,0	0,00	100,0
		Woche 120	63	17,46	24,580	0,0	0,00	100,0
		Woche 124	59	14,69	21,683	0,0	0,00	100,0
		Woche 128	59	12,43	20,434	0,0	0,00	100,0
		Woche 132	54	12,35	18,651	0,0	0,00	66,7
		Woche 136	52	10,90	18,342	0,0	0,00	66,7
		Woche 140	48	13,19	21,459	0,0	0,00	100,0
		Woche 144	39	10,26	15,586	0,0	0,00	33,3
		Woche 148	43	13,18	20,752	0,0	0,00	66,7
		Woche 152	41	14,63	22,421	0,0	0,00	100,0
		Woche 156	38	18,42	22,855	0,0	0,00	66,7
		Woche 160	33	12,12	20,101	0,0	0,00	66,7
		Woche 164	33	11,11	19,837	0,0	0,00	66,7
		Woche 168	29	8,05	17,032	0,0	0,00	66,7
		Woche 172	32	11,46	23,355	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen an anderen Stellen des Körpers	Durvalumab (N=264)	Woche 176	23	11,59	21,576	0,0	0,00	66,7
		Woche 180	21	9,52	18,687	0,0	0,00	66,7
		Woche 184	19	7,02	17,843	0,0	0,00	66,7
		Woche 188	17	9,80	19,596	0,0	0,00	66,7
		Woche 192	17	7,84	18,743	0,0	0,00	66,7
		Woche 196	14	7,14	14,194	0,0	0,00	33,3
		Woche 200	11	9,09	15,570	0,0	0,00	33,3
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	9,52	16,265	0,0	0,00	33,3
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	5,56	13,608	0,0	0,00	33,3
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	8,33	16,667	0,0	0,00	33,3
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	16,67	23,570	0,0	16,67	33,3
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	15,35	21,786	0,0	0,00	100,0
		Woche 1	209	16,75	20,705	0,0	0,00	100,0
		Woche 2	212	18,55	22,522	0,0	0,00	100,0
		Woche 3	204	18,46	23,443	0,0	0,00	100,0
		Woche 4	231	19,62	24,860	0,0	0,00	100,0
		Woche 5	216	18,06	22,230	0,0	0,00	100,0
		Woche 6	207	20,93	23,951	0,0	33,33	100,0
		Woche 7	203	18,56	22,991	0,0	0,00	100,0
		Woche 8	211	20,06	24,834	0,0	0,00	100,0
		Woche 12	202	18,65	24,859	0,0	0,00	100,0
		Woche 16	198	18,86	23,105	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen an anderen Stellen des Körpers	Placebo (N=266)	Woche 20	180	20,56	25,958	0,0	0,00	100,0
		Woche 24	172	18,41	23,712	0,0	0,00	100,0
		Woche 28	158	20,68	25,408	0,0	0,00	100,0
		Woche 32	150	19,78	24,454	0,0	0,00	100,0
		Woche 36	141	19,39	23,956	0,0	0,00	100,0
		Woche 40	122	23,22	26,029	0,0	33,33	100,0
		Woche 44	125	20,53	25,324	0,0	0,00	100,0
		Woche 48	121	19,28	21,838	0,0	0,00	100,0
		Woche 52	118	20,34	25,048	0,0	0,00	100,0
		Woche 56	106	20,13	23,313	0,0	16,67	100,0
		Woche 60	98	17,69	22,554	0,0	0,00	100,0
		Woche 64	95	19,65	24,064	0,0	0,00	100,0
		Woche 68	92	19,57	24,286	0,0	0,00	100,0
		Woche 72	87	21,07	22,798	0,0	33,33	66,7
		Woche 76	77	21,65	25,228	0,0	33,33	100,0
		Woche 80	75	22,67	22,701	0,0	33,33	66,7
		Woche 84	75	22,22	22,815	0,0	33,33	66,7
		Woche 88	70	22,86	25,088	0,0	33,33	100,0
		Woche 92	69	17,87	20,276	0,0	0,00	66,7
		Woche 96	64	19,27	22,852	0,0	0,00	66,7
		Woche 100	67	19,40	25,392	0,0	0,00	100,0
		Woche 104	63	20,11	22,828	0,0	33,33	100,0
		Woche 108	59	21,47	24,575	0,0	33,33	100,0
		Woche 112	54	19,14	24,743	0,0	0,00	100,0
		Woche 116	56	18,45	22,847	0,0	0,00	66,7
		Woche 120	51	17,65	22,463	0,0	0,00	100,0
		Woche 124	51	20,26	23,169	0,0	33,33	100,0
		Woche 128	45	23,70	25,248	0,0	33,33	66,7
		Woche 132	44	18,18	20,903	0,0	0,00	66,7
		Woche 136	39	23,08	24,368	0,0	33,33	66,7
		Woche 140	39	17,09	22,778	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen an anderen Stellen des Körpers	Placebo (N=266)	Woche 144	35	20,00	24,522	0,0	0,00	100,0
		Woche 148	32	18,75	23,854	0,0	0,00	66,7
		Woche 152	33	20,20	26,272	0,0	0,00	66,7
		Woche 156	32	17,71	26,753	0,0	0,00	100,0
		Woche 160	31	19,35	25,494	0,0	0,00	66,7
		Woche 164	24	20,83	23,698	0,0	16,67	66,7
		Woche 168	28	22,62	22,321	0,0	33,33	66,7
		Woche 172	23	20,29	26,091	0,0	0,00	66,7
		Woche 176	21	22,22	24,343	0,0	33,33	66,7
		Woche 180	19	21,05	25,363	0,0	0,00	66,7
		Woche 184	20	16,67	25,363	0,0	0,00	66,7
		Woche 188	18	18,52	20,523	0,0	16,67	66,7
		Woche 192	16	27,08	25,000	0,0	33,33	66,7
		Woche 196	18	20,37	23,260	0,0	16,67	66,7
		Woche 200	19	24,56	26,856	0,0	33,33	66,7
		Woche 204	13	23,08	31,578	0,0	0,00	100,0
		Woche 208	12	13,89	22,285	0,0	0,00	66,7
		Woche 212	15	13,33	21,082	0,0	0,00	66,7
		Woche 216	12	27,78	23,925	0,0	33,33	66,7
		Woche 220	9	11,11	16,667	0,0	0,00	33,3
		Woche 224	11	15,15	17,408	0,0	0,00	33,3
		Woche 228	9	18,52	24,216	0,0	0,00	66,7
		Woche 232	5	33,33	23,570	0,0	33,33	66,7
		Woche 236	5	33,33	23,570	0,0	33,33	66,7
		Woche 240	5	26,67	27,889	0,0	33,33	66,7
		Woche 244	4	25,00	16,667	0,0	33,33	33,3
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	33,33	NC	33,3	33,33	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen im Arm oder in der Schulter	Durvalumab (N=264)	Baseline [a]	217	8,60	17,793	0,0	0,00	66,7
		Woche 1	208	8,33	16,545	0,0	0,00	66,7
		Woche 2	203	9,85	18,802	0,0	0,00	100,0
		Woche 3	205	10,73	19,067	0,0	0,00	100,0
		Woche 4	235	9,93	18,890	0,0	0,00	100,0
		Woche 5	213	8,92	17,696	0,0	0,00	66,7
		Woche 6	209	11,64	20,347	0,0	0,00	100,0
		Woche 7	209	13,40	22,198	0,0	0,00	100,0
		Woche 8	220	12,88	21,388	0,0	0,00	100,0
		Woche 12	204	11,27	20,881	0,0	0,00	100,0
		Woche 16	189	13,05	19,604	0,0	0,00	100,0
		Woche 20	179	12,29	19,619	0,0	0,00	100,0
		Woche 24	169	13,81	22,568	0,0	0,00	100,0
		Woche 28	166	13,86	21,761	0,0	0,00	100,0
		Woche 32	159	15,09	22,407	0,0	0,00	100,0
		Woche 36	153	16,78	23,609	0,0	0,00	100,0
		Woche 40	137	14,60	22,456	0,0	0,00	100,0
		Woche 44	131	16,54	23,525	0,0	0,00	100,0
		Woche 48	124	19,09	25,915	0,0	0,00	100,0
		Woche 52	124	14,52	23,375	0,0	0,00	100,0
		Woche 56	122	16,12	23,171	0,0	0,00	100,0
		Woche 60	118	13,56	20,551	0,0	0,00	66,7
		Woche 64	113	15,63	22,303	0,0	0,00	100,0
		Woche 68	103	14,89	19,653	0,0	0,00	66,7
		Woche 72	101	14,85	21,846	0,0	0,00	100,0
		Woche 76	98	14,63	21,441	0,0	0,00	100,0
		Woche 80	97	16,15	22,107	0,0	0,00	100,0
		Woche 84	97	15,46	22,598	0,0	0,00	100,0
		Woche 88	92	15,22	22,327	0,0	0,00	100,0
		Woche 92	92	14,49	21,712	0,0	0,00	100,0
		Woche 96	87	16,09	24,305	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen im Arm oder in der Schulter	Durvalumab (N=264)	Woche 100	95	13,33	21,416	0,0	0,00	100,0
		Woche 104	80	13,33	20,948	0,0	0,00	100,0
		Woche 108	77	15,15	21,320	0,0	0,00	100,0
		Woche 112	73	17,81	22,961	0,0	0,00	100,0
		Woche 116	68	14,71	23,310	0,0	0,00	100,0
		Woche 120	63	14,81	23,780	0,0	0,00	100,0
		Woche 124	59	11,86	20,307	0,0	0,00	100,0
		Woche 128	59	12,99	21,457	0,0	0,00	100,0
		Woche 132	54	11,11	20,477	0,0	0,00	100,0
		Woche 136	52	14,74	24,176	0,0	0,00	100,0
		Woche 140	48	14,58	21,642	0,0	0,00	100,0
		Woche 144	39	16,24	20,046	0,0	0,00	66,7
		Woche 148	43	10,08	18,595	0,0	0,00	66,7
		Woche 152	41	18,70	23,628	0,0	0,00	100,0
		Woche 156	38	16,67	22,924	0,0	0,00	66,7
		Woche 160	33	16,16	23,748	0,0	0,00	66,7
		Woche 164	33	11,11	19,837	0,0	0,00	66,7
		Woche 168	29	11,49	18,422	0,0	0,00	66,7
		Woche 172	32	12,50	20,302	0,0	0,00	66,7
		Woche 176	23	10,14	18,627	0,0	0,00	66,7
		Woche 180	21	12,70	19,653	0,0	0,00	66,7
		Woche 184	19	15,79	30,161	0,0	0,00	100,0
		Woche 188	17	11,76	20,211	0,0	0,00	66,7
		Woche 192	17	5,88	13,098	0,0	0,00	33,3
		Woche 196	14	7,14	19,298	0,0	0,00	66,7
		Woche 200	11	3,03	10,050	0,0	0,00	33,3
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	7,41	14,699	0,0	0,00	33,3
		Woche 220	7	9,52	16,265	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen im Arm oder in der Schulter	Durvalumab (N=264)	Woche 224	6	11,11	17,213	0,0	0,00	33,3
		Woche 228	6	5,56	13,608	0,0	0,00	33,3
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	33,33	0,000	33,3	33,33	33,3
		Woche 248	1	33,33	NC	33,3	33,33	33,3
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	8,06	15,692	0,0	0,00	66,7
		Woche 1	209	10,53	18,368	0,0	0,00	100,0
		Woche 2	212	13,05	19,540	0,0	0,00	66,7
		Woche 3	204	13,07	20,480	0,0	0,00	100,0
		Woche 4	231	14,14	22,026	0,0	0,00	100,0
		Woche 5	216	13,12	21,513	0,0	0,00	100,0
		Woche 6	207	13,85	20,808	0,0	0,00	100,0
		Woche 7	203	15,60	23,044	0,0	0,00	100,0
		Woche 8	211	15,32	21,628	0,0	0,00	100,0
		Woche 12	202	12,71	20,449	0,0	0,00	100,0
		Woche 16	198	17,00	23,924	0,0	0,00	100,0
		Woche 20	180	15,74	24,266	0,0	0,00	100,0
		Woche 24	172	19,19	25,746	0,0	0,00	100,0
		Woche 28	158	15,40	22,459	0,0	0,00	100,0
		Woche 32	150	18,89	24,552	0,0	0,00	100,0
		Woche 36	141	18,44	23,713	0,0	0,00	100,0
		Woche 40	122	18,31	24,281	0,0	0,00	100,0
		Woche 44	125	16,80	23,806	0,0	0,00	100,0
		Woche 48	121	18,46	25,802	0,0	0,00	100,0
		Woche 52	118	16,10	20,779	0,0	0,00	100,0
		Woche 56	106	16,35	23,115	0,0	0,00	100,0
		Woche 60	98	17,69	22,554	0,0	0,00	100,0
		Woche 64	95	16,84	21,675	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen im Arm oder in der Schulter	Placebo (N=266)	Woche 68	92	16,67	21,255	0,0	0,00	66,7
		Woche 72	87	19,16	24,183	0,0	0,00	100,0
		Woche 76	77	17,32	22,038	0,0	0,00	100,0
		Woche 80	75	19,56	21,290	0,0	33,33	66,7
		Woche 84	75	21,78	22,920	0,0	33,33	100,0
		Woche 88	70	18,57	21,711	0,0	0,00	66,7
		Woche 92	69	18,84	20,194	0,0	33,33	66,7
		Woche 96	64	18,23	21,356	0,0	0,00	66,7
		Woche 100	67	16,42	19,569	0,0	0,00	66,7
		Woche 104	63	17,46	18,796	0,0	0,00	66,7
		Woche 108	59	14,69	19,838	0,0	0,00	66,7
		Woche 112	54	17,28	21,221	0,0	0,00	66,7
		Woche 116	56	16,07	20,092	0,0	0,00	66,7
		Woche 120	51	18,30	21,410	0,0	0,00	66,7
		Woche 124	51	18,30	21,410	0,0	0,00	66,7
		Woche 128	45	18,52	21,968	0,0	0,00	66,7
		Woche 132	44	15,91	19,673	0,0	0,00	66,7
		Woche 136	39	19,66	22,579	0,0	0,00	66,7
		Woche 140	39	15,38	18,490	0,0	0,00	66,7
		Woche 144	35	17,14	20,407	0,0	0,00	66,7
		Woche 148	32	14,58	18,813	0,0	0,00	66,7
		Woche 152	33	15,15	20,566	0,0	0,00	66,7
		Woche 156	32	13,54	18,664	0,0	0,00	66,7
		Woche 160	31	17,20	18,995	0,0	0,00	66,7
		Woche 164	24	15,28	16,966	0,0	0,00	33,3
		Woche 168	28	17,86	19,207	0,0	16,67	66,7
		Woche 172	23	17,39	19,770	0,0	0,00	66,7
		Woche 176	21	19,05	19,920	0,0	33,33	66,7
		Woche 180	19	21,05	19,909	0,0	33,33	66,7
		Woche 184	20	23,33	21,898	0,0	33,33	66,7
		Woche 188	18	12,96	16,721	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen im Arm oder in der Schulter	Placebo (N=266)	Woche 192	16	18,75	20,972	0,0	16,67	66,7
		Woche 196	18	11,11	16,169	0,0	0,00	33,3
		Woche 200	19	15,79	23,223	0,0	0,00	66,7
		Woche 204	13	17,95	22,008	0,0	0,00	66,7
		Woche 208	12	19,44	22,285	0,0	16,67	66,7
		Woche 212	15	13,33	21,082	0,0	0,00	66,7
		Woche 216	12	16,67	22,473	0,0	0,00	66,7
		Woche 220	9	18,52	17,568	0,0	33,33	33,3
		Woche 224	11	12,12	22,473	0,0	0,00	66,7
		Woche 228	9	18,52	24,216	0,0	0,00	66,7
		Woche 232	5	40,00	27,889	0,0	33,33	66,7
		Woche 236	5	33,33	23,570	0,0	33,33	66,7
		Woche 240	5	33,33	23,570	0,0	33,33	66,7
		Woche 244	4	25,00	16,667	0,0	33,33	33,3
		Woche 248	2	16,67	23,570	0,0	16,67	33,3
		Woche 252	1	33,33	NC	33,3	33,33	33,3
		Woche 256	1	33,33	NC	33,3	33,33	33,3
Schmerzen in der Brust	Durvalumab (N=264)	Baseline [a]	217	8,45	15,559	0,0	0,00	66,7
		Woche 1	208	8,17	15,103	0,0	0,00	66,7
		Woche 2	203	10,02	16,362	0,0	0,00	66,7
		Woche 3	205	10,89	18,243	0,0	0,00	100,0
		Woche 4	235	10,78	17,892	0,0	0,00	66,7
		Woche 5	213	10,49	17,120	0,0	0,00	66,7
		Woche 6	209	12,28	19,697	0,0	0,00	100,0
		Woche 7	209	14,67	20,866	0,0	0,00	100,0
		Woche 8	220	13,79	19,811	0,0	0,00	100,0
		Woche 12	204	12,25	19,211	0,0	0,00	100,0
		Woche 16	189	12,70	17,627	0,0	0,00	66,7
		Woche 20	179	13,04	18,801	0,0	0,00	100,0
		Woche 24	169	13,61	20,058	0,0	0,00	100,0
		Woche 28	166	13,05	18,989	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen in der Brust	Durvalumab (N=264)	Woche 32	159	10,90	18,179	0,0	0,00	100,0
		Woche 36	153	8,71	16,119	0,0	0,00	66,7
		Woche 40	137	10,22	18,330	0,0	0,00	100,0
		Woche 44	131	8,40	17,218	0,0	0,00	100,0
		Woche 48	124	11,02	19,349	0,0	0,00	100,0
		Woche 52	124	7,80	15,389	0,0	0,00	66,7
		Woche 56	122	10,38	16,643	0,0	0,00	66,7
		Woche 60	118	7,34	14,543	0,0	0,00	66,7
		Woche 64	113	8,55	17,694	0,0	0,00	100,0
		Woche 68	103	7,44	15,433	0,0	0,00	66,7
		Woche 72	101	8,58	16,769	0,0	0,00	66,7
		Woche 76	98	7,14	14,557	0,0	0,00	66,7
		Woche 80	97	8,93	15,602	0,0	0,00	66,7
		Woche 84	97	7,90	15,792	0,0	0,00	66,7
		Woche 88	92	9,42	18,039	0,0	0,00	66,7
		Woche 92	92	7,61	15,707	0,0	0,00	66,7
		Woche 96	87	8,43	17,026	0,0	0,00	66,7
		Woche 100	95	8,07	15,916	0,0	0,00	66,7
		Woche 104	80	7,92	14,275	0,0	0,00	33,3
		Woche 108	77	6,49	13,288	0,0	0,00	33,3
		Woche 112	73	8,68	15,740	0,0	0,00	66,7
		Woche 116	68	7,35	13,924	0,0	0,00	33,3
		Woche 120	63	6,88	14,857	0,0	0,00	66,7
		Woche 124	59	6,21	14,483	0,0	0,00	66,7
		Woche 128	59	6,78	16,117	0,0	0,00	66,7
		Woche 132	54	7,41	15,414	0,0	0,00	66,7
		Woche 136	52	7,05	16,616	0,0	0,00	66,7
		Woche 140	48	4,86	11,889	0,0	0,00	33,3
		Woche 144	39	6,84	13,636	0,0	0,00	33,3
		Woche 148	43	6,20	13,125	0,0	0,00	33,3
		Woche 152	41	8,13	14,492	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen in der Brust	Durvalumab (N=264)	Woche 156	38	7,89	14,362	0,0	0,00	33,3
		Woche 160	33	10,10	15,556	0,0	0,00	33,3
		Woche 164	33	7,07	16,154	0,0	0,00	66,7
		Woche 168	29	5,75	15,607	0,0	0,00	66,7
		Woche 172	32	6,25	13,219	0,0	0,00	33,3
		Woche 176	23	10,14	15,682	0,0	0,00	33,3
		Woche 180	21	4,76	11,952	0,0	0,00	33,3
		Woche 184	19	7,02	13,962	0,0	0,00	33,3
		Woche 188	17	9,80	19,596	0,0	0,00	66,7
		Woche 192	17	9,80	15,656	0,0	0,00	33,3
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	3,03	10,050	0,0	0,00	33,3
		Woche 204	7	0,00	0,000	0,0	0,00	0,0
		Woche 208	8	0,00	0,000	0,0	0,00	0,0
		Woche 212	7	0,00	0,000	0,0	0,00	0,0
		Woche 216	9	14,81	24,216	0,0	0,00	66,7
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	5,56	13,608	0,0	0,00	33,3
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	16,67	23,570	0,0	16,67	33,3
	Placebo (N=266)	Baseline [a]	215	11,01	16,361	0,0	0,00	66,7
		Woche 1	209	11,32	16,807	0,0	0,00	66,7
		Woche 2	212	14,47	20,015	0,0	0,00	66,7
		Woche 3	204	13,24	18,838	0,0	0,00	66,7
		Woche 4	231	16,16	22,165	0,0	0,00	100,0
		Woche 5	216	14,35	21,441	0,0	0,00	100,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen in der Brust	Placebo (N=266)	Woche 6	207	15,94	20,465	0,0	0,00	100,0
		Woche 7	203	16,42	21,590	0,0	0,00	100,0
		Woche 8	211	18,17	21,617	0,0	0,00	100,0
		Woche 12	202	15,51	21,582	0,0	0,00	100,0
		Woche 16	198	15,32	20,316	0,0	0,00	100,0
		Woche 20	180	13,89	22,249	0,0	0,00	100,0
		Woche 24	172	12,79	18,848	0,0	0,00	66,7
		Woche 28	158	13,08	20,203	0,0	0,00	100,0
		Woche 32	150	12,44	18,740	0,0	0,00	100,0
		Woche 36	141	10,17	16,876	0,0	0,00	66,7
		Woche 40	122	12,30	18,779	0,0	0,00	66,7
		Woche 44	125	12,27	18,226	0,0	0,00	66,7
		Woche 48	121	11,85	18,688	0,0	0,00	100,0
		Woche 52	118	9,89	17,052	0,0	0,00	66,7
		Woche 56	106	10,38	16,817	0,0	0,00	66,7
		Woche 60	98	9,86	15,293	0,0	0,00	33,3
		Woche 64	95	7,02	14,501	0,0	0,00	66,7
		Woche 68	92	9,06	15,707	0,0	0,00	66,7
		Woche 72	87	9,96	16,167	0,0	0,00	66,7
		Woche 76	77	10,39	16,455	0,0	0,00	66,7
		Woche 80	75	10,22	16,416	0,0	0,00	66,7
		Woche 84	75	11,56	16,884	0,0	0,00	66,7
		Woche 88	70	13,81	20,846	0,0	0,00	100,0
		Woche 92	69	11,59	16,983	0,0	0,00	66,7
		Woche 96	64	10,42	16,667	0,0	0,00	66,7
		Woche 100	67	8,96	15,978	0,0	0,00	66,7
		Woche 104	63	10,58	17,785	0,0	0,00	66,7
		Woche 108	59	10,73	16,884	0,0	0,00	66,7
		Woche 112	54	12,35	18,651	0,0	0,00	66,7
		Woche 116	56	8,93	16,195	0,0	0,00	66,7
		Woche 120	51	9,15	15,024	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen in der Brust	Placebo (N=266)	Woche 124	51	10,46	15,621	0,0	0,00	33,3
		Woche 128	45	11,11	15,891	0,0	0,00	33,3
		Woche 132	44	6,82	13,601	0,0	0,00	33,3
		Woche 136	39	11,11	17,660	0,0	0,00	66,7
		Woche 140	39	11,97	16,199	0,0	0,00	33,3
		Woche 144	35	11,43	16,053	0,0	0,00	33,3
		Woche 148	32	10,42	15,698	0,0	0,00	33,3
		Woche 152	33	12,12	18,292	0,0	0,00	66,7
		Woche 156	32	10,42	15,698	0,0	0,00	33,3
		Woche 160	31	11,83	16,212	0,0	0,00	33,3
		Woche 164	24	12,50	16,485	0,0	0,00	33,3
		Woche 168	28	10,71	15,853	0,0	0,00	33,3
		Woche 172	23	8,70	14,966	0,0	0,00	33,3
		Woche 176	21	11,11	16,102	0,0	0,00	33,3
		Woche 180	19	7,02	13,962	0,0	0,00	33,3
		Woche 184	20	11,67	16,312	0,0	0,00	33,3
		Woche 188	18	7,41	14,260	0,0	0,00	33,3
		Woche 192	16	14,58	20,972	0,0	0,00	66,7
		Woche 196	18	9,26	15,363	0,0	0,00	33,3
		Woche 200	19	8,77	18,732	0,0	0,00	66,7
		Woche 204	13	12,82	16,879	0,0	0,00	33,3
		Woche 208	12	11,11	16,412	0,0	0,00	33,3
		Woche 212	15	4,44	11,729	0,0	0,00	33,3
		Woche 216	12	2,78	9,623	0,0	0,00	33,3
		Woche 220	9	3,70	11,111	0,0	0,00	33,3
		Woche 224	11	9,09	15,570	0,0	0,00	33,3
		Woche 228	9	11,11	23,570	0,0	0,00	66,7
		Woche 232	5	13,33	18,257	0,0	0,00	33,3
		Woche 236	5	13,33	18,257	0,0	0,00	33,3
		Woche 240	5	20,00	18,257	0,0	33,33	33,3
		Woche 244	4	16,67	19,245	0,0	16,67	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Schmerzen in der Brust	Placebo (N=266)	Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0
Wunder Mund	Durvalumab (N=264)	Baseline [a]	217	5,84	14,584	0,0	0,00	100,0
		Woche 1	208	4,65	12,891	0,0	0,00	100,0
		Woche 2	203	6,08	15,246	0,0	0,00	100,0
		Woche 3	205	4,72	11,645	0,0	0,00	33,3
		Woche 4	235	3,83	11,089	0,0	0,00	66,7
		Woche 5	213	4,54	11,459	0,0	0,00	33,3
		Woche 6	209	4,63	12,864	0,0	0,00	66,7
		Woche 7	209	4,94	12,744	0,0	0,00	66,7
		Woche 8	220	4,70	12,053	0,0	0,00	66,7
		Woche 12	204	4,90	11,835	0,0	0,00	33,3
		Woche 16	189	5,47	14,158	0,0	0,00	100,0
		Woche 20	179	7,45	16,010	0,0	0,00	100,0
		Woche 24	169	5,33	15,146	0,0	0,00	100,0
		Woche 28	166	5,82	16,804	0,0	0,00	100,0
		Woche 32	159	6,08	13,960	0,0	0,00	66,7
		Woche 36	153	5,45	12,942	0,0	0,00	66,7
		Woche 40	137	4,62	11,563	0,0	0,00	33,3
		Woche 44	131	3,82	10,655	0,0	0,00	33,3
		Woche 48	124	6,72	15,893	0,0	0,00	66,7
		Woche 52	124	3,49	11,099	0,0	0,00	66,7
		Woche 56	122	4,10	12,551	0,0	0,00	66,7
		Woche 60	118	3,95	11,669	0,0	0,00	66,7
		Woche 64	113	4,13	11,031	0,0	0,00	33,3
		Woche 68	103	6,15	14,573	0,0	0,00	66,7
		Woche 72	101	4,29	12,169	0,0	0,00	66,7
		Woche 76	98	4,42	12,332	0,0	0,00	66,7
		Woche 80	97	5,50	13,334	0,0	0,00	66,7
		Woche 84	97	3,44	12,252	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Wunder Mund	Durvalumab (N=264)	Woche 88	92	3,26	11,116	0,0	0,00	66,7
		Woche 92	92	5,07	14,771	0,0	0,00	66,7
		Woche 96	87	4,21	12,247	0,0	0,00	66,7
		Woche 100	95	4,21	13,085	0,0	0,00	66,7
		Woche 104	80	2,50	10,305	0,0	0,00	66,7
		Woche 108	77	3,03	11,058	0,0	0,00	66,7
		Woche 112	73	5,02	14,349	0,0	0,00	66,7
		Woche 116	68	4,90	13,214	0,0	0,00	66,7
		Woche 120	63	4,23	12,689	0,0	0,00	66,7
		Woche 124	59	4,52	13,069	0,0	0,00	66,7
		Woche 128	59	4,52	11,510	0,0	0,00	33,3
		Woche 132	54	3,09	9,753	0,0	0,00	33,3
		Woche 136	52	4,49	14,803	0,0	0,00	66,7
		Woche 140	48	3,47	10,290	0,0	0,00	33,3
		Woche 144	39	1,71	7,449	0,0	0,00	33,3
		Woche 148	43	3,88	13,031	0,0	0,00	66,7
		Woche 152	41	6,50	15,311	0,0	0,00	66,7
		Woche 156	38	5,26	12,318	0,0	0,00	33,3
		Woche 160	33	5,05	14,722	0,0	0,00	66,7
		Woche 164	33	5,05	12,137	0,0	0,00	33,3
		Woche 168	29	1,15	6,190	0,0	0,00	33,3
		Woche 172	32	6,25	13,219	0,0	0,00	33,3
		Woche 176	23	5,80	12,918	0,0	0,00	33,3
		Woche 180	21	6,35	17,059	0,0	0,00	66,7
		Woche 184	19	1,75	7,647	0,0	0,00	33,3
		Woche 188	17	9,80	19,596	0,0	0,00	66,7
		Woche 192	17	3,92	11,070	0,0	0,00	33,3
		Woche 196	14	2,38	8,909	0,0	0,00	33,3
		Woche 200	11	0,00	0,000	0,0	0,00	0,0
		Woche 204	7	4,76	12,599	0,0	0,00	33,3
		Woche 208	8	4,17	11,785	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Wunder Mund	Durvalumab (N=264)	Woche 212	7	4,76	12,599	0,0	0,00	33,3
		Woche 216	9	3,70	11,111	0,0	0,00	33,3
		Woche 220	7	0,00	0,000	0,0	0,00	0,0
		Woche 224	6	0,00	0,000	0,0	0,00	0,0
		Woche 228	6	0,00	0,000	0,0	0,00	0,0
		Woche 232	6	0,00	0,000	0,0	0,00	0,0
		Woche 236	4	0,00	0,000	0,0	0,00	0,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0
		Woche 244	2	0,00	0,000	0,0	0,00	0,0
		Woche 248	1	0,00	NC	0,0	0,00	0,0
		Woche 252	2	0,00	0,000	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	215	5,43	13,149	0,0	0,00	66,7
		Woche 1	209	4,78	12,163	0,0	0,00	66,7
		Woche 2	212	6,45	14,706	0,0	0,00	66,7
		Woche 3	204	5,23	13,022	0,0	0,00	66,7
		Woche 4	231	5,63	13,623	0,0	0,00	66,7
		Woche 5	216	6,33	14,236	0,0	0,00	66,7
		Woche 6	207	5,96	14,389	0,0	0,00	66,7
		Woche 7	203	6,24	14,625	0,0	0,00	66,7
		Woche 8	211	6,00	14,021	0,0	0,00	66,7
		Woche 12	202	6,11	15,278	0,0	0,00	100,0
		Woche 16	198	7,58	15,891	0,0	0,00	66,7
		Woche 20	180	7,04	16,142	0,0	0,00	100,0
		Woche 24	172	7,56	16,939	0,0	0,00	100,0
		Woche 28	158	6,54	16,164	0,0	0,00	100,0
		Woche 32	150	7,33	17,215	0,0	0,00	100,0
		Woche 36	141	6,62	15,024	0,0	0,00	66,7
		Woche 40	122	4,37	12,821	0,0	0,00	66,7
		Woche 44	125	4,00	12,415	0,0	0,00	66,7
		Woche 48	121	4,41	12,128	0,0	0,00	66,7
		Woche 52	118	3,67	12,159	0,0	0,00	66,7

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Wunder Mund	Placebo (N=266)	Woche 56	106	5,97	13,645	0,0	0,00	66,7
		Woche 60	98	3,06	10,795	0,0	0,00	66,7
		Woche 64	95	4,21	13,959	0,0	0,00	100,0
		Woche 68	92	4,35	11,288	0,0	0,00	33,3
		Woche 72	87	5,75	15,424	0,0	0,00	66,7
		Woche 76	77	4,33	11,279	0,0	0,00	33,3
		Woche 80	75	5,78	13,834	0,0	0,00	66,7
		Woche 84	75	5,33	14,540	0,0	0,00	66,7
		Woche 88	70	4,29	11,238	0,0	0,00	33,3
		Woche 92	69	3,86	10,750	0,0	0,00	33,3
		Woche 96	64	6,25	14,396	0,0	0,00	66,7
		Woche 100	67	5,97	14,125	0,0	0,00	66,7
		Woche 104	63	7,41	17,397	0,0	0,00	66,7
		Woche 108	59	3,95	12,510	0,0	0,00	66,7
		Woche 112	54	4,94	13,594	0,0	0,00	66,7
		Woche 116	56	3,57	10,403	0,0	0,00	33,3
		Woche 120	51	4,58	11,585	0,0	0,00	33,3
		Woche 124	51	5,88	12,834	0,0	0,00	33,3
		Woche 128	45	5,93	14,718	0,0	0,00	66,7
		Woche 132	44	6,06	13,005	0,0	0,00	33,3
		Woche 136	39	4,27	11,290	0,0	0,00	33,3
		Woche 140	39	9,40	17,012	0,0	0,00	66,7
		Woche 144	35	6,67	13,528	0,0	0,00	33,3
		Woche 148	32	6,25	13,219	0,0	0,00	33,3
		Woche 152	33	3,03	9,731	0,0	0,00	33,3
		Woche 156	32	4,17	11,200	0,0	0,00	33,3
		Woche 160	31	9,68	19,614	0,0	0,00	66,7
		Woche 164	24	11,11	18,822	0,0	0,00	66,7
		Woche 168	28	2,38	8,742	0,0	0,00	33,3
		Woche 172	23	4,35	11,478	0,0	0,00	33,3
		Woche 176	21	3,17	10,026	0,0	0,00	33,3

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Table 3.3.2 ADRIATIC: Summary of EORTC QLQ-LC13 results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

					Absolute Werte			
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
Wunder Mund	Placebo (N=266)	Woche 180	19	5,26	12,488	0,0	0,00	33,3
		Woche 184	20	3,33	10,260	0,0	0,00	33,3
		Woche 188	18	0,00	0,000	0,0	0,00	0,0
		Woche 192	16	2,08	8,333	0,0	0,00	33,3
		Woche 196	18	1,85	7,857	0,0	0,00	33,3
		Woche 200	19	5,26	12,488	0,0	0,00	33,3
		Woche 204	13	2,56	9,245	0,0	0,00	33,3
		Woche 208	12	8,33	15,076	0,0	0,00	33,3
		Woche 212	15	4,44	11,729	0,0	0,00	33,3
		Woche 216	12	2,78	9,623	0,0	0,00	33,3
		Woche 220	9	3,70	11,111	0,0	0,00	33,3
		Woche 224	11	3,03	10,050	0,0	0,00	33,3
		Woche 228	9	7,41	14,699	0,0	0,00	33,3
		Woche 232	5	0,00	0,000	0,0	0,00	0,0
		Woche 236	5	6,67	14,907	0,0	0,00	33,3
		Woche 240	5	0,00	0,000	0,0	0,00	0,0
		Woche 244	4	0,00	0,000	0,0	0,00	0,0
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 252	1	0,00	NC	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/smeanpr.sas gsmeanprb 10JUN2025:14:15

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Figure 3.4.2.1 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Symptom scale: Dyspnea across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

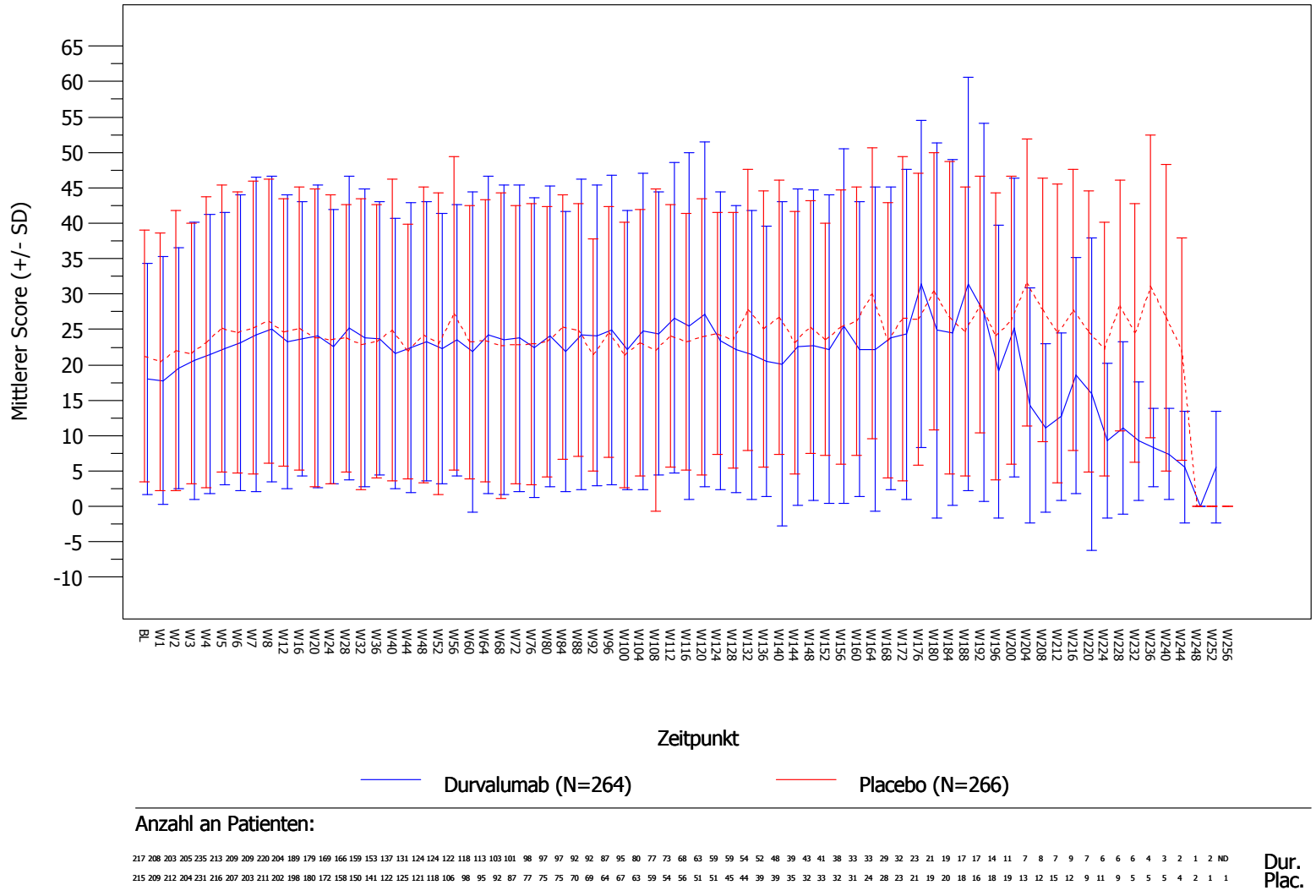

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Figure 3.4.2.2 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Coughing across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

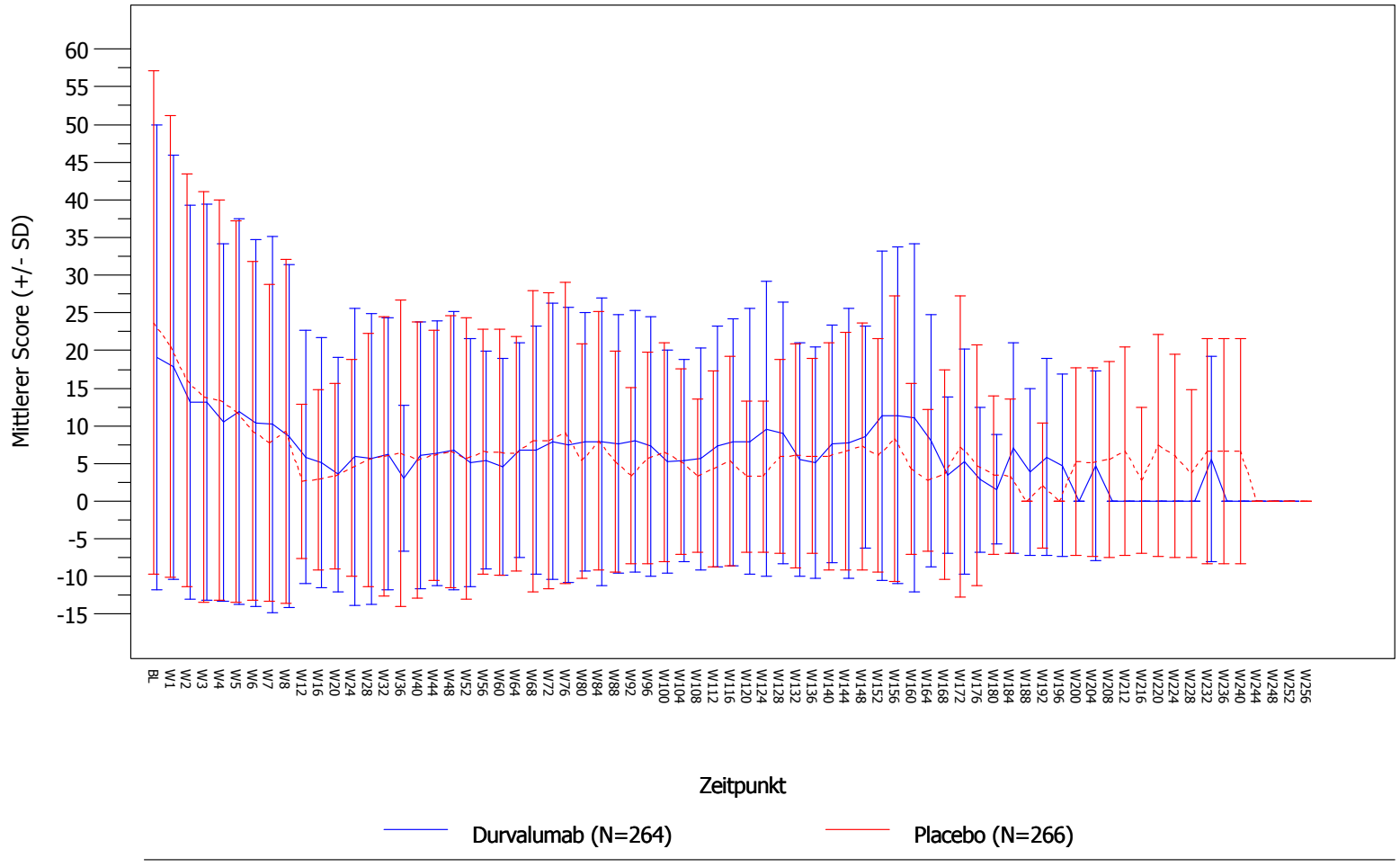

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Figure 3.4.2.3 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Dysphagia across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

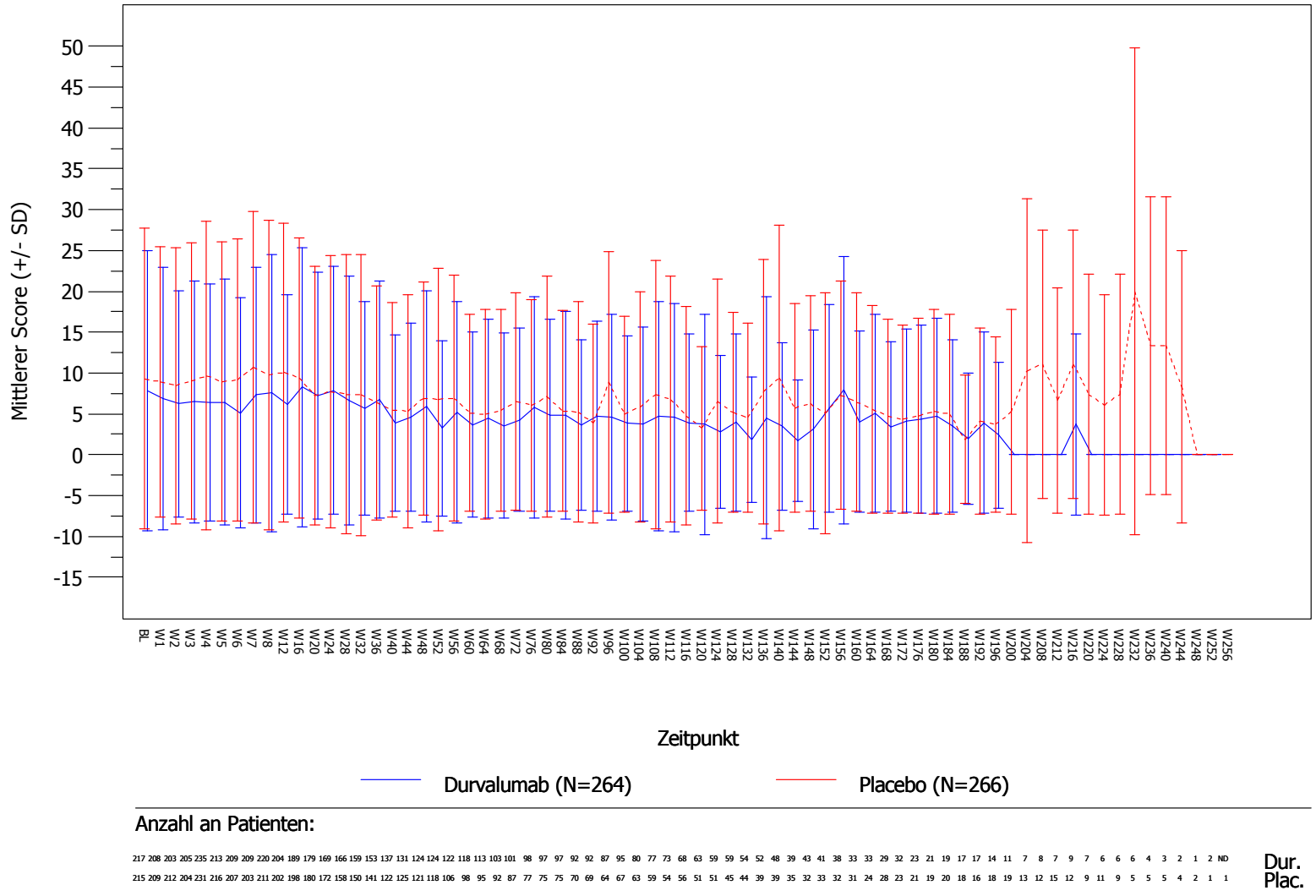

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Figure 3.4.2.4 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Hemoptysis across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

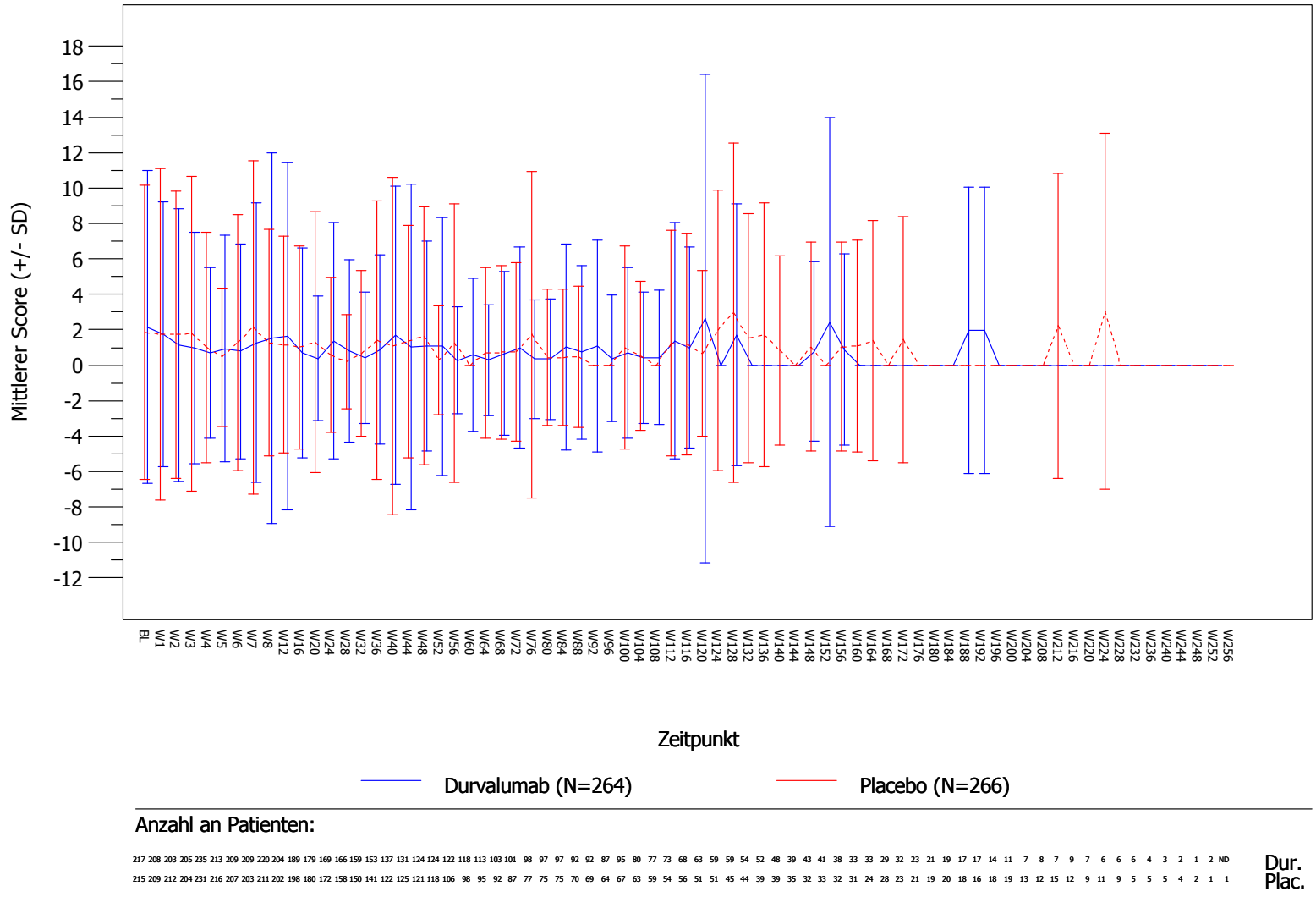

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Figure 3.4.2.5 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Alopecia across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

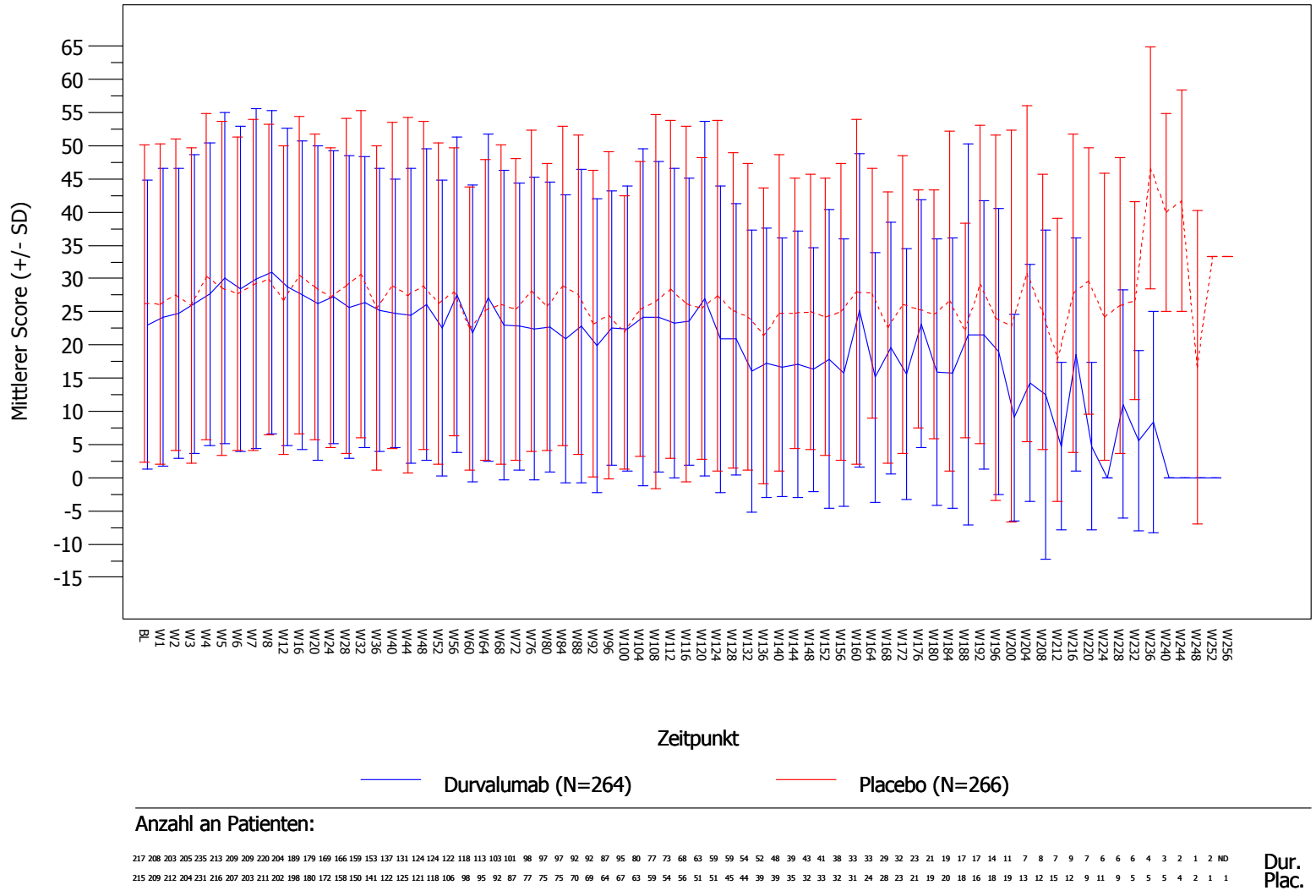

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Figure 3.4.2.6 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Pain in arm or shoulder across timepoints, by treat
Full Analysis Set, DCO 15JAN2024

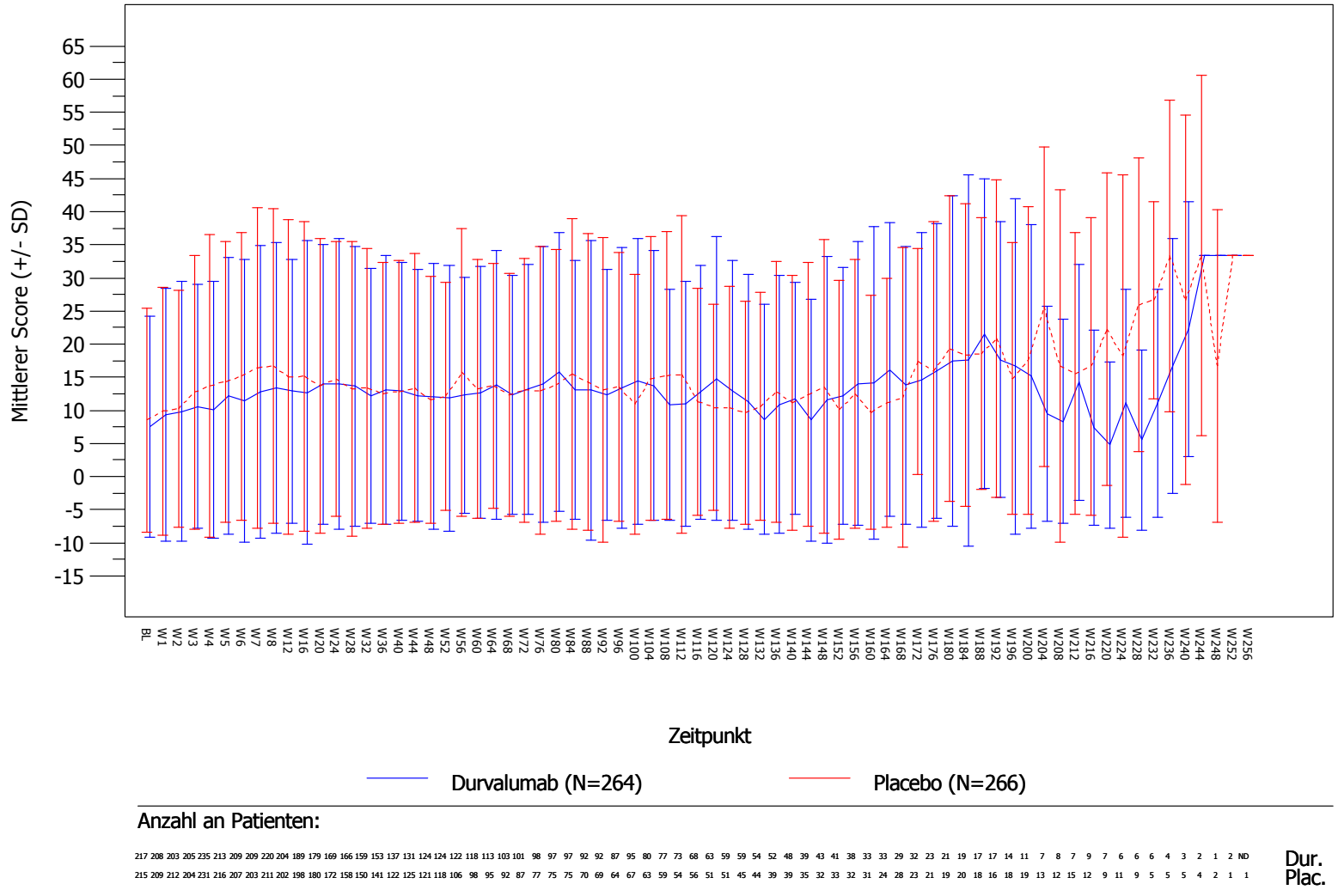

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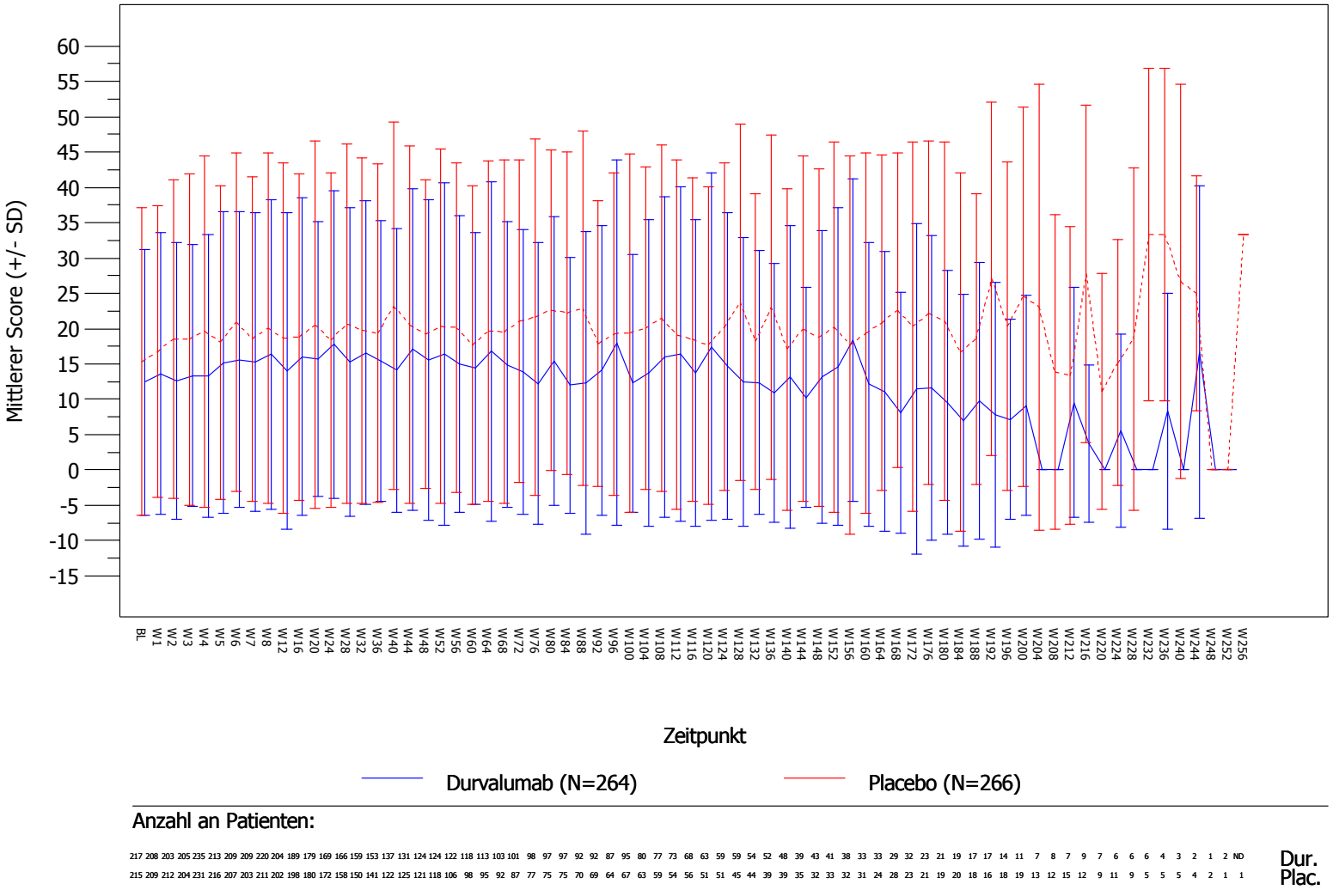
Figure 3.4.2.7 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Pain in chest across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.2.8 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Peripheral neuropathy across timepoints, by treatme
Full Analysis Set, DCO 15JAN2024

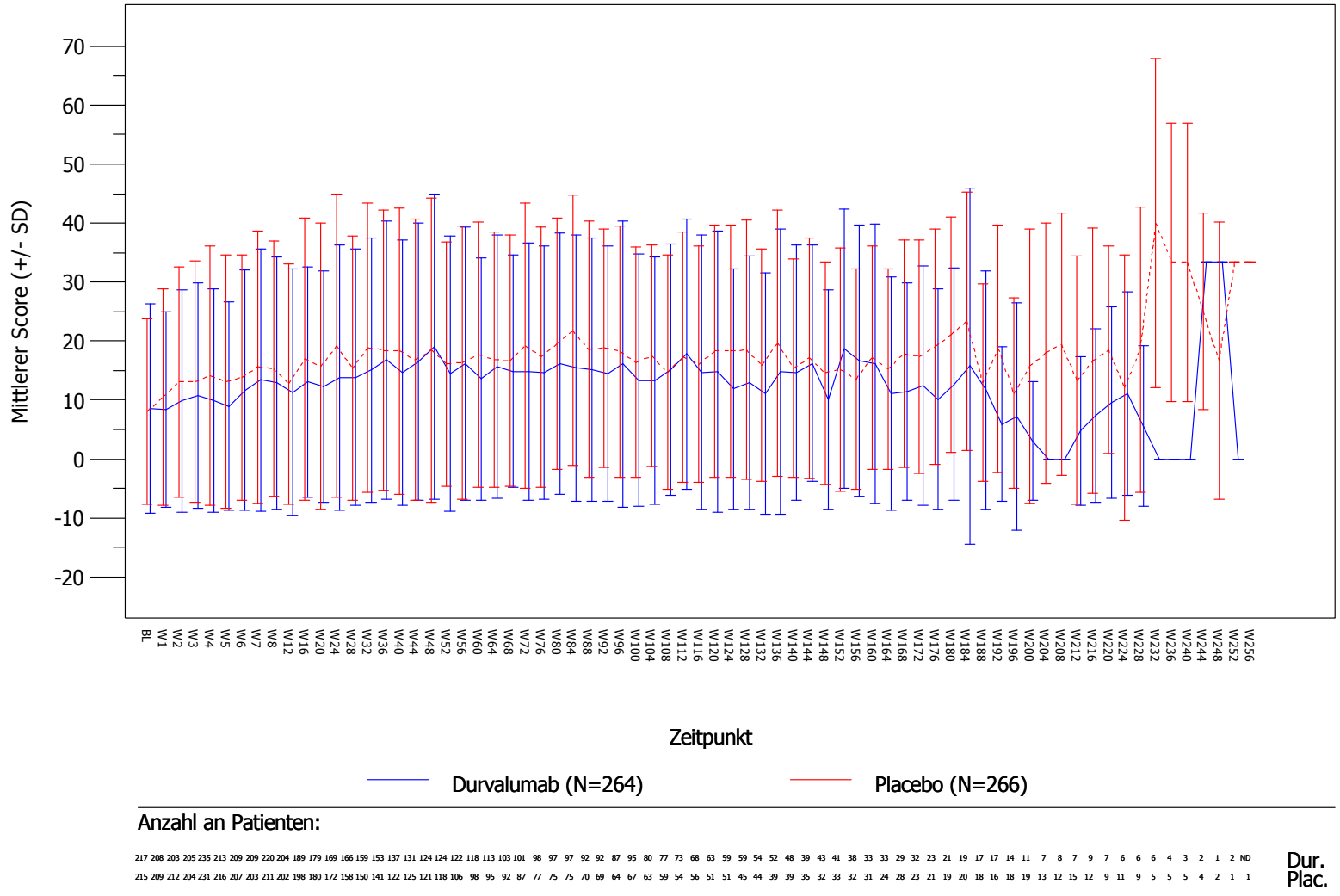

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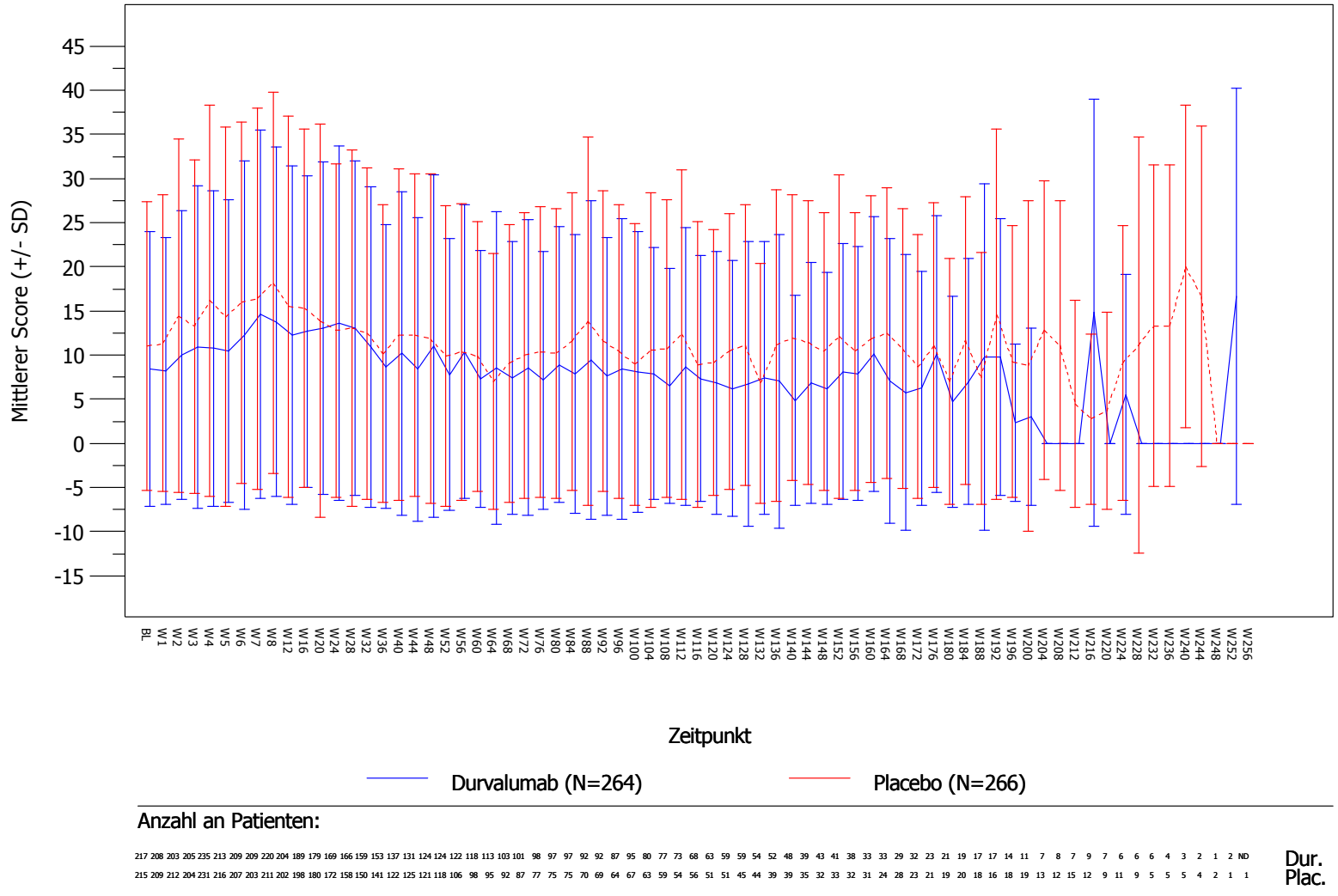
Figure 3.4.2.9 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Pain in other parts across timepoints, by treatment
Full Analysis Set, DCO 15JAN2024



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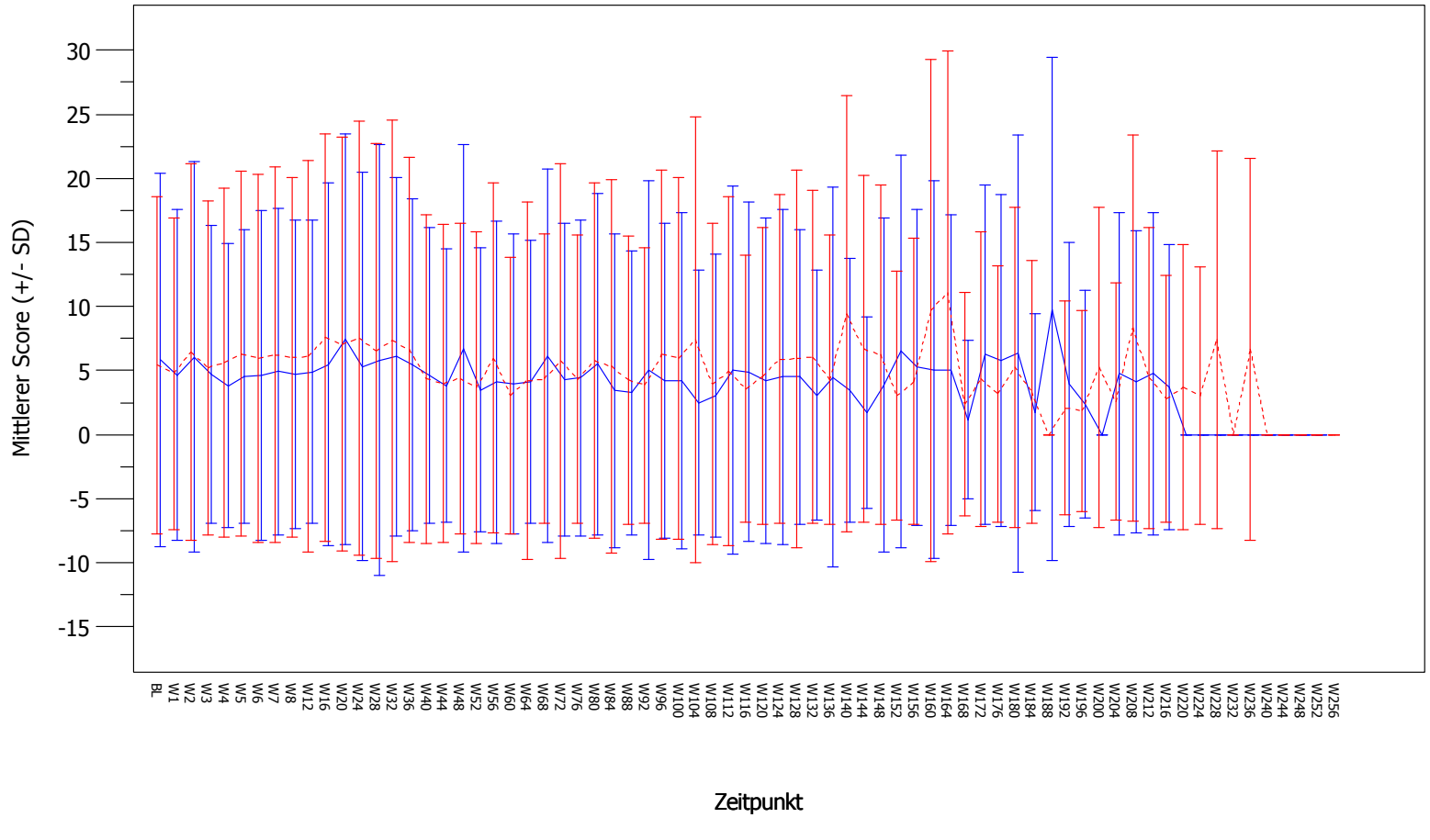
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.4.2.10 ADRIATIC: Mean (+/- SD) EORTC QLQ-LC13 Single item symptom scale: Sore mouth across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



Anzahl an Patienten:

| | | |

Anhang 4-G7.5: EQ-5D VAS - MMRM-Analyse

Nutzenbewertung nach AMNOG

Table 3.8.3.1 ADRIATIC: Summary of analysis of change from baseline over time in EQ-5D VAS (mixed model for repeated measures), Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 8	188	80,34 (14,926)	-7,90 (1,336)	171	77,71 (16,221)	-7,42 (1,395)	-0,48 [-4,287; 3,321]	0,8029
Woche 16	166	79,95 (14,817)	-5,49 (1,318)	162	76,87 (16,161)	-6,36 (1,355)	0,87 [-2,850; 4,594]	0,6452
Woche 24	145	79,94 (14,697)	-4,99 (1,310)	147	77,63 (16,151)	-4,22 (1,334)	-0,77 [-4,449; 2,913]	0,6818
Woche 32	141	79,57 (16,563)	-4,84 (1,382)	127	78,20 (15,026)	-7,11 (1,447)	2,27 [-1,672; 6,207]	0,2583
Woche 40	119	80,76 (12,917)	-5,47 (1,486)	105	78,76 (14,529)	-7,15 (1,567)	1,68 [-2,574; 5,933]	0,4377
Woche 48	109	79,79 (15,210)	-7,19 (1,558)	104	78,89 (14,370)	-5,98 (1,615)	-1,21 [-5,630; 3,210]	0,5904
Woche 56	106	79,98 (15,213)	-5,29 (1,283)	89	78,73 (13,994)	-3,63 (1,375)	-1,65 [-5,357; 2,050]	0,3803
Woche 64	101	80,12 (15,203)	-5,76 (1,335)	82	76,84 (14,004)	-5,53 (1,452)	-0,23 [-4,121; 3,653]	0,9058
Woche 72	90	79,76 (15,610)	-4,86 (1,213)	76	78,17 (13,853)	-5,88 (1,309)	1,02 [-2,501; 4,532]	0,5701
Woche 80	86	79,20 (15,531)	-5,32 (1,310)	64	76,27 (14,696)	-5,23 (1,478)	-0,08 [-3,971; 3,808]	0,9672
Woche 88	83	81,64 (12,370)	-4,50 (1,440)	59	77,17 (14,370)	-7,79 (1,647)	3,29 [-1,035; 7,617]	0,1353
Woche 96	79	80,05 (13,254)	-4,66 (1,345)	54	77,00 (14,521)	-5,52 (1,575)	0,85 [-3,232; 4,941]	0,6808
Woche 104	72	81,04 (12,387)	-5,92 (1,369)	53	77,92 (14,629)	-5,35 (1,576)	-0,57 [-4,691; 3,554]	0,7861
Woche 112	67	78,64 (15,197)	-6,02 (1,467)	46	78,63 (13,828)	-5,74 (1,729)	-0,28 [-4,750; 4,189]	0,9016
Woche 120	57	81,65 (12,101)	-6,82 (1,639)	45	77,49 (14,489)	-6,06 (1,858)	-0,76 [-5,668; 4,146]	0,7600
Woche 128	54	83,07 (11,318)	-6,15 (1,508)	39	77,03 (15,660)	-4,60 (1,746)	-1,55 [-6,142; 3,036]	0,5051
Woche 136	48	83,02 (11,901)	-7,26 (1,702)	33	77,67 (14,645)	-6,07 (2,000)	-1,19 [-6,410; 4,032]	0,6535

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error.
SMD = standardised mean difference. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 3.8.3.1 ADRIATIC: Summary of analysis of change from baseline over time in EQ-5D VAS (mixed model for repeated measures), Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	36	81,31 (13,136)	-6,04 (1,719)	29	77,17 (13,880)	-3,79 (1,953)	-2,25 [-7,419; 2,927]	0,3920
Woche 152	38	82,08 (12,140)	-4,63 (1,938)	27	79,33 (13,471)	-4,17 (2,269)	-0,46 [-6,369; 5,459]	0,8792
Woche 160	31	81,68 (11,516)	-5,97 (2,110)	25	79,44 (13,988)	-6,08 (2,374)	0,11 [-6,191; 6,412]	0,9723
Woche 168	27	84,11 (10,467)	-5,55 (2,218)	23	77,87 (14,467)	-6,50 (2,395)	0,94 [-5,588; 7,473]	0,7754
Woche 176	22	83,59 (10,317)	-7,10 (2,314)	18	79,00 (14,390)	-4,58 (2,521)	-2,52 [-9,356; 4,310]	0,4646
Woche 184	18	82,39 (10,705)	-8,21 (2,778)	17	78,71 (14,777)	-6,06 (2,914)	-2,15 [-10,229; 5,939]	0,5975
Hedges' g SMD							-0,02 [-0,213; 0,182]	0,8757
Mittelwert über alle Visiten	204	79,62 (15,257)	-5,91 (0,955)	190	77,42 (16,083)	-5,69 (1,055)	-0,22 [-3,027; 2,582]	0,8761

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% of non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error.
SMD = standardised mean difference. * p<0.05.
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Anhang 4-G7.6: EQ-5D VAS - deskriptive Analyse und Verlaufsgrafik

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Table 3.3.3 ADRIATIC: Summary of EQ-5D VAS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
EQ-5D VAS	Durvalumab (N=264)	Baseline [a]	215	79,05	15,836	0,0	81,00	100,0
		Woche 8	221	71,45	16,791	21,0	74,00	100,0
		Woche 16	188	73,26	18,338	12,0	79,00	100,0
		Woche 24	166	74,98	16,706	12,0	79,00	100,0
		Woche 32	159	74,91	17,662	19,0	80,00	100,0
		Woche 40	135	75,10	18,197	17,0	80,00	100,0
		Woche 48	122	73,13	19,313	12,0	79,00	100,0
		Woche 56	120	74,49	16,566	21,0	75,00	100,0
		Woche 64	113	74,93	17,385	10,0	80,00	100,0
		Woche 72	99	75,10	16,352	20,0	79,00	100,0
		Woche 80	96	74,21	16,738	24,0	78,50	100,0
		Woche 88	91	75,91	16,857	29,0	80,00	100,0
		Woche 96	87	74,82	16,926	35,0	80,00	100,0
		Woche 104	79	73,99	17,166	26,0	79,00	100,0
		Woche 112	72	72,63	19,033	30,0	78,00	100,0
		Woche 120	63	74,25	18,263	19,0	79,00	100,0
		Woche 128	59	74,90	16,350	34,0	79,00	100,0
		Woche 136	52	75,96	17,324	23,0	79,50	100,0
		Woche 144	39	75,56	18,564	33,0	80,00	100,0
		Woche 152	41	76,61	18,513	34,0	84,00	100,0
		Woche 160	33	74,85	18,507	23,0	80,00	99,0
		Woche 168	29	77,10	15,994	45,0	83,00	94,0
		Woche 176	23	73,96	17,400	35,0	80,00	92,0
		Woche 184	19	71,68	16,895	26,0	74,00	95,0
		Woche 192	17	74,59	20,372	20,0	80,00	100,0
		Woche 200	11	75,91	14,501	40,0	77,00	90,0
		Woche 208	8	79,88	17,117	40,0	84,50	94,0
		Woche 216	9	72,44	23,718	19,0	81,00	90,0
		Woche 224	6	74,33	14,801	46,0	77,50	89,0
		Woche 232	6	74,33	17,489	41,0	78,50	92,0
		Woche 240	3	73,67	29,160	40,0	90,00	91,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.3 ADRIATIC: Summary of EQ-5D VAS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
EQ-5D VAS	Durvalumab (N=264)	Woche 248	1	39,00	NC	39,0	39,00	39,0
	Placebo (N=266)	Baseline [a]	211	77,12	16,400	30,0	80,00	100,0
		Woche 8	204	70,64	19,340	0,0	73,50	100,0
		Woche 16	191	72,11	17,873	11,0	76,00	100,0
		Woche 24	170	74,33	17,359	18,0	79,00	100,0
		Woche 32	149	72,13	18,722	0,0	75,00	100,0
		Woche 40	121	73,36	17,715	21,0	76,00	100,0
		Woche 48	118	75,41	17,252	26,0	79,00	100,0
		Woche 56	102	77,47	16,696	21,0	80,00	100,0
		Woche 64	94	75,01	16,186	33,0	78,50	100,0
		Woche 72	86	74,49	14,823	33,0	75,50	100,0
		Woche 80	74	75,45	17,174	29,0	79,00	100,0
		Woche 88	68	74,43	17,041	30,0	79,00	100,0
		Woche 96	63	75,76	15,632	41,0	78,00	100,0
		Woche 104	60	74,98	15,974	38,0	78,00	100,0
		Woche 112	54	74,91	15,767	43,0	79,50	100,0
		Woche 120	50	75,42	15,570	38,0	78,50	100,0
		Woche 128	45	76,29	14,948	37,0	78,00	100,0
		Woche 136	39	73,97	17,118	38,0	74,00	100,0
		Woche 144	35	74,29	15,738	42,0	76,00	100,0
		Woche 152	33	75,52	15,450	48,0	79,00	100,0
		Woche 160	31	72,35	16,039	37,0	76,00	100,0
		Woche 168	27	73,19	17,247	40,0	77,00	100,0
		Woche 176	21	73,48	17,314	41,0	78,00	97,0
		Woche 184	20	73,85	18,225	40,0	80,50	99,0
		Woche 192	15	72,87	18,601	40,0	81,00	100,0
		Woche 200	19	75,37	16,429	47,0	82,00	100,0
		Woche 208	11	74,73	19,504	46,0	80,00	100,0
		Woche 216	12	75,00	15,661	49,0	80,00	91,0
		Woche 224	10	75,30	16,255	47,0	82,50	91,0
		Woche 232	5	75,00	9,566	60,0	80,00	83,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.3 ADRIATIC: Summary of EQ-5D VAS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
EQ-5D VAS	Placebo (N=266)	Woche 240	5	79,60	7,893	71,0	80,00	92,0
		Woche 248	2	90,00	14,142	80,0	90,00	100,0
		Woche 256	1	80,00	NC	80,0	80,00	80,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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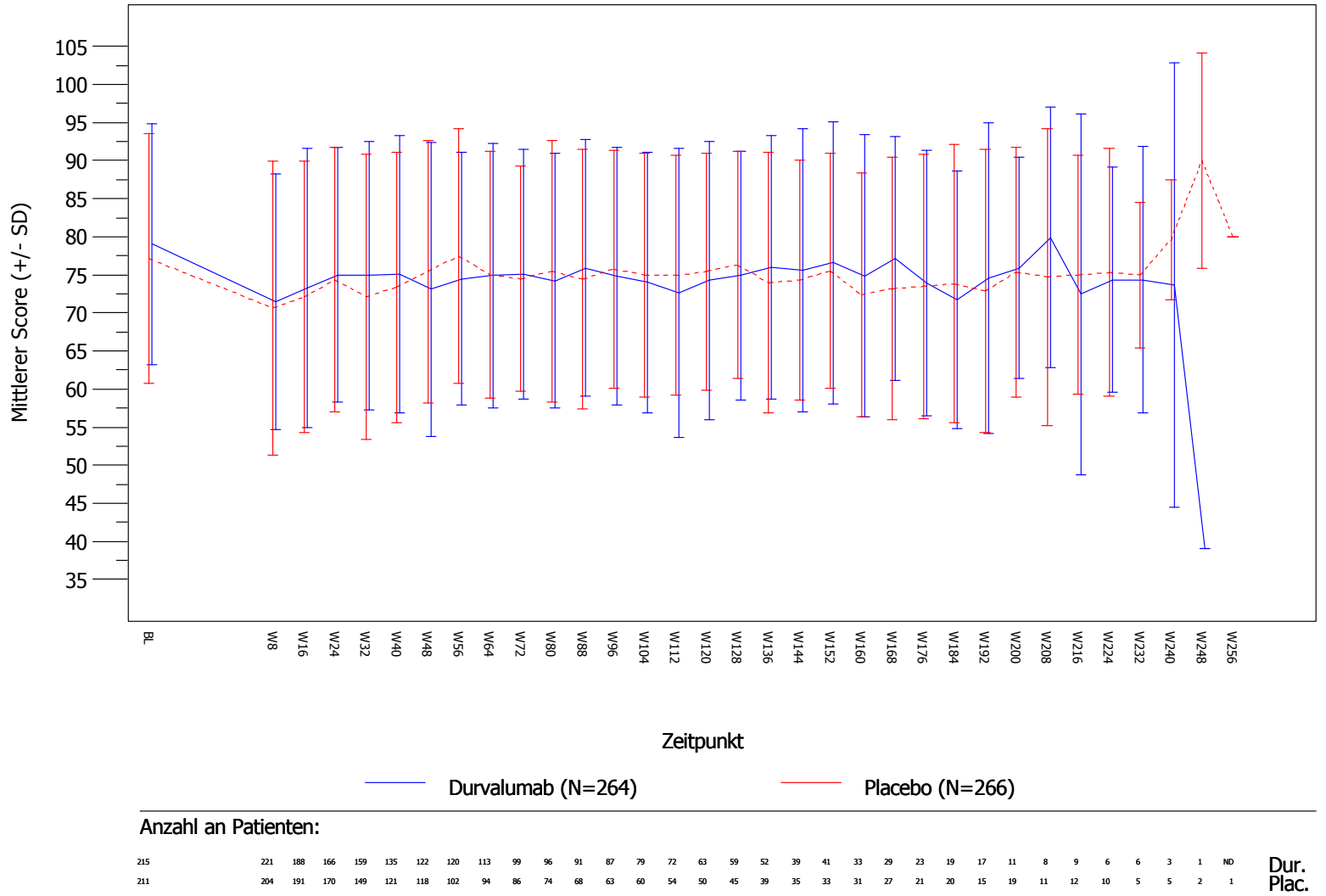
Figure 3.4.3.1 ADRIATIC: Mean (+/- SD) EQ-5D VAS across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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Anhang 4-G7.7: PGIS - MMRM-Analyse

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Table 3.8.4.1 ADRIATIC: Summary of analysis of change from baseline over time in PGIS (mixed model for repeated measures), Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 8	196	1,00 (1,119)	0,59 (0,092)	184	1,20 (1,194)	0,47 (0,094)	0,11 [-0,147; 0,371]	0,3959
Woche 16	169	1,00 (1,150)	0,36 (0,091)	170	1,22 (1,190)	0,40 (0,092)	-0,04 [-0,296; 0,212]	0,7454
Woche 24	149	1,00 (1,151)	0,28 (0,093)	151	1,14 (1,178)	0,31 (0,094)	-0,03 [-0,295; 0,225]	0,7937
Woche 32	142	0,96 (1,154)	0,31 (0,099)	130	1,12 (1,179)	0,32 (0,103)	-0,01 [-0,288; 0,275]	0,9618
Woche 40	122	0,92 (1,147)	0,18 (0,104)	106	1,13 (1,180)	0,31 (0,110)	-0,13 [-0,433; 0,163]	0,3735
Woche 48	108	0,95 (1,203)	0,37 (0,110)	106	1,20 (1,191)	0,42 (0,113)	-0,05 [-0,359; 0,264]	0,7632
Woche 56	107	0,95 (1,200)	0,33 (0,098)	92	1,18 (1,195)	0,31 (0,104)	0,02 [-0,265; 0,299]	0,9046
Woche 64	101	0,94 (1,182)	0,26 (0,100)	83	1,24 (1,226)	0,33 (0,108)	-0,06 [-0,355; 0,226]	0,6619
Woche 72	91	0,93 (1,191)	0,27 (0,103)	78	1,31 (1,188)	0,33 (0,111)	-0,06 [-0,363; 0,234]	0,6717
Woche 80	87	0,91 (1,216)	0,12 (0,102)	64	1,27 (1,185)	0,20 (0,115)	-0,09 [-0,389; 0,219]	0,5816
Woche 88	84	0,85 (1,135)	0,03 (0,098)	60	1,23 (1,212)	0,29 (0,112)	-0,26 [-0,556; 0,033]	0,0811
Woche 96	79	0,92 (1,174)	0,07 (0,097)	54	1,22 (1,239)	-0,01 (0,114)	0,08 [-0,214; 0,377]	0,5858
Woche 104	73	0,78 (1,070)	0,14 (0,098)	55	1,25 (1,265)	0,09 (0,112)	0,05 [-0,241; 0,351]	0,7160
Woche 112	68	0,88 (1,140)	0,00 (0,104)	46	1,17 (1,161)	0,12 (0,122)	-0,13 [-0,443; 0,192]	0,4363
Woche 120	58	0,69 (1,046)	0,16 (0,113)	46	1,09 (1,189)	0,17 (0,126)	-0,01 [-0,345; 0,326]	0,9549
Woche 128	54	0,61 (1,017)	0,15 (0,122)	39	0,95 (1,123)	0,01 (0,138)	0,14 [-0,220; 0,504]	0,4402
Woche 136	48	0,71 (1,110)	-0,04 (0,113)	33	1,06 (1,223)	-0,04 (0,131)	0,00 [-0,342; 0,343]	0,9957

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% o non-missing data in both treatment arms. Patient is used as random effect in the model. A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error. SMD = standardised mean difference. * p<0.05.

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Table 3.8.4.1 ADRIATIC: Summary of analysis of change from baseline over time in PGIS (mixed model for repeated measures), Full Analysis Set, DCO 15JAN2024

	Durvalumab (N=264)			Placebo (N=266)			Behandlungseffekt	
Zeitpunkt	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	n [a]	Ausgangswert MW (SD) [b]	Veränderung MW (SE)	MWD [95%-KI]	p-Wert
Woche 144	37	0,68 (1,002)	-0,05 (0,112)	30	1,17 (1,262)	-0,09 (0,124)	0,04 [-0,298; 0,368]	0,8340
Woche 152	38	0,71 (1,063)	0,05 (0,119)	27	1,33 (1,330)	-0,26 (0,139)	0,31 [-0,052; 0,681]	0,0919
Woche 160	32	0,84 (1,110)	0,11 (0,134)	25	1,40 (1,354)	0,10 (0,154)	0,01 [-0,395; 0,422]	0,9475
Woche 168	28	0,57 (0,836)	0,03 (0,144)	24	1,25 (1,391)	-0,05 (0,155)	0,08 [-0,344; 0,508]	0,7023
Woche 176	22	0,91 (1,109)	0,15 (0,158)	18	1,11 (1,451)	0,10 (0,176)	0,05 [-0,423; 0,521]	0,8368
Woche 184	18	1,00 (1,138)	-0,11 (0,165)	17	1,18 (1,468)	-0,11 (0,176)	0,00 [-0,484; 0,484]	0,9998
Hedges' g SMD							0,00 [-0,194; 0,196]	0,9908
Mittelwert über alle Visiten	207	1,03 (1,121)	0,16 (0,066)	198	1,16 (1,184)	0,16 (0,072)	0,00 [-0,190; 0,193]	0,9908

[a] = Number of patients with change from baseline used for MMRM analysis at each timepoint. [b] = Mean baseline for patients with change from baseline used for MMRM analysis at each timepoint. Treatment difference is calculated from a mixed model for repeated measures (MMRM) analysis of the change from baseline score with treatment, visit, and treatment by visit interaction as fixed effects, baseline score as a covariate and baseline score by visit interaction. The analysis includes all visits with at least 5% o
non-missing data in both treatment arms. Patient is used as random effect in the model.
A Toeplitz with heterogeneity matrix (TOEPH) was used to model within-subject error.
SMD = standardised mean difference. * p<0.05.
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Anhang 4-G7.8: PGIS - deskriptive Analyse und Verlaufsgrafik

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Table 3.3.4 ADRIATIC: Summary of PGIS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
PGIS	Durvalumab (N=264)	Baseline [a]	219	1,03	1,108	0,0	1,00	5,0
		Woche 8	227	1,60	1,245	0,0	2,00	5,0
		Woche 16	190	1,36	1,122	0,0	1,00	4,0
		Woche 24	169	1,28	1,175	0,0	1,00	4,0
		Woche 32	160	1,29	1,174	0,0	1,00	4,0
		Woche 40	138	1,11	1,188	0,0	1,00	5,0
		Woche 48	122	1,30	1,265	0,0	1,00	5,0
		Woche 56	122	1,24	1,260	0,0	1,00	4,0
		Woche 64	113	1,16	1,229	0,0	1,00	4,0
		Woche 72	101	1,15	1,169	0,0	1,00	4,0
		Woche 80	97	1,05	1,294	0,0	0,00	5,0
		Woche 88	92	0,83	1,075	0,0	0,00	4,0
		Woche 96	87	1,00	1,057	0,0	1,00	3,0
		Woche 104	80	0,99	1,217	0,0	0,00	4,0
		Woche 112	73	0,97	1,178	0,0	0,00	4,0
		Woche 120	64	0,91	1,019	0,0	1,00	3,0
		Woche 128	59	0,81	1,137	0,0	0,00	5,0
		Woche 136	52	0,75	1,153	0,0	0,00	4,0
		Woche 144	40	0,68	1,047	0,0	0,00	4,0
		Woche 152	41	0,83	1,243	0,0	0,00	4,0
		Woche 160	34	0,94	1,205	0,0	0,50	4,0
		Woche 168	30	0,77	1,165	0,0	0,00	4,0
		Woche 176	23	0,91	1,276	0,0	0,00	4,0
		Woche 184	19	0,95	1,393	0,0	0,00	4,0
		Woche 192	17	0,88	1,364	0,0	0,00	4,0
		Woche 200	11	0,45	1,036	0,0	0,00	3,0
		Woche 208	8	0,50	0,926	0,0	0,00	2,0
		Woche 216	9	0,89	1,167	0,0	0,00	3,0
		Woche 224	6	0,17	0,408	0,0	0,00	1,0
		Woche 232	6	0,50	0,837	0,0	0,00	2,0
		Woche 240	3	0,00	0,000	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.4 ADRIATIC: Summary of PGIS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
PGIS	Durvalumab (N=264)	Woche 248	1	0,00	NC	0,0	0,00	0,0
	Placebo (N=266)	Baseline [a]	214	1,16	1,180	0,0	1,00	4,0
		Woche 8	216	1,54	1,238	0,0	1,00	4,0
		Woche 16	197	1,42	1,241	0,0	1,00	5,0
		Woche 24	172	1,31	1,196	0,0	1,00	4,0
		Woche 32	150	1,31	1,274	0,0	1,00	5,0
		Woche 40	121	1,25	1,280	0,0	1,00	4,0
		Woche 48	119	1,32	1,255	0,0	1,00	4,0
		Woche 56	105	1,23	1,146	0,0	1,00	4,0
		Woche 64	95	1,26	1,196	0,0	1,00	4,0
		Woche 72	88	1,22	1,208	0,0	1,00	4,0
		Woche 80	74	1,15	1,143	0,0	1,00	4,0
		Woche 88	69	1,25	1,205	0,0	1,00	4,0
		Woche 96	63	0,89	1,049	0,0	1,00	3,0
		Woche 104	62	0,95	1,062	0,0	1,00	3,0
		Woche 112	54	1,02	1,107	0,0	1,00	4,0
		Woche 120	51	1,04	1,166	0,0	1,00	3,0
		Woche 128	45	0,91	1,083	0,0	1,00	3,0
		Woche 136	39	0,95	1,169	0,0	1,00	4,0
		Woche 144	36	1,03	1,055	0,0	1,00	3,0
		Woche 152	33	0,85	1,064	0,0	0,00	3,0
		Woche 160	31	1,19	1,138	0,0	1,00	3,0
		Woche 168	28	0,89	1,031	0,0	1,00	3,0
		Woche 176	21	0,95	1,161	0,0	1,00	3,0
		Woche 184	20	0,80	1,005	0,0	0,50	3,0
		Woche 192	16	0,81	1,167	0,0	0,00	3,0
		Woche 200	19	0,68	1,057	0,0	0,00	3,0
		Woche 208	12	0,75	1,055	0,0	0,00	3,0
		Woche 216	12	0,92	1,084	0,0	1,00	3,0
		Woche 224	11	0,55	1,036	0,0	0,00	3,0
		Woche 232	5	1,20	1,304	0,0	1,00	3,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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Table 3.3.4 ADRIATIC: Summary of PGIS results across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024

				Absolute Werte				
Parameter	Gruppe	Zeitpunkt	n	Mittelwert	SD	Min	Median	Max
PGIS	Placebo (N=266)	Woche 240	5	0,60	0,894	0,0	0,00	2,0
		Woche 248	2	0,00	0,000	0,0	0,00	0,0
		Woche 256	1	0,00	NC	0,0	0,00	0,0

[a] Baseline is defined as last evaluable assessment prior to or on the date of first dose of study drug.
SD = standard deviation; Min = minimum ; Max = maximum; NC = not calculated.
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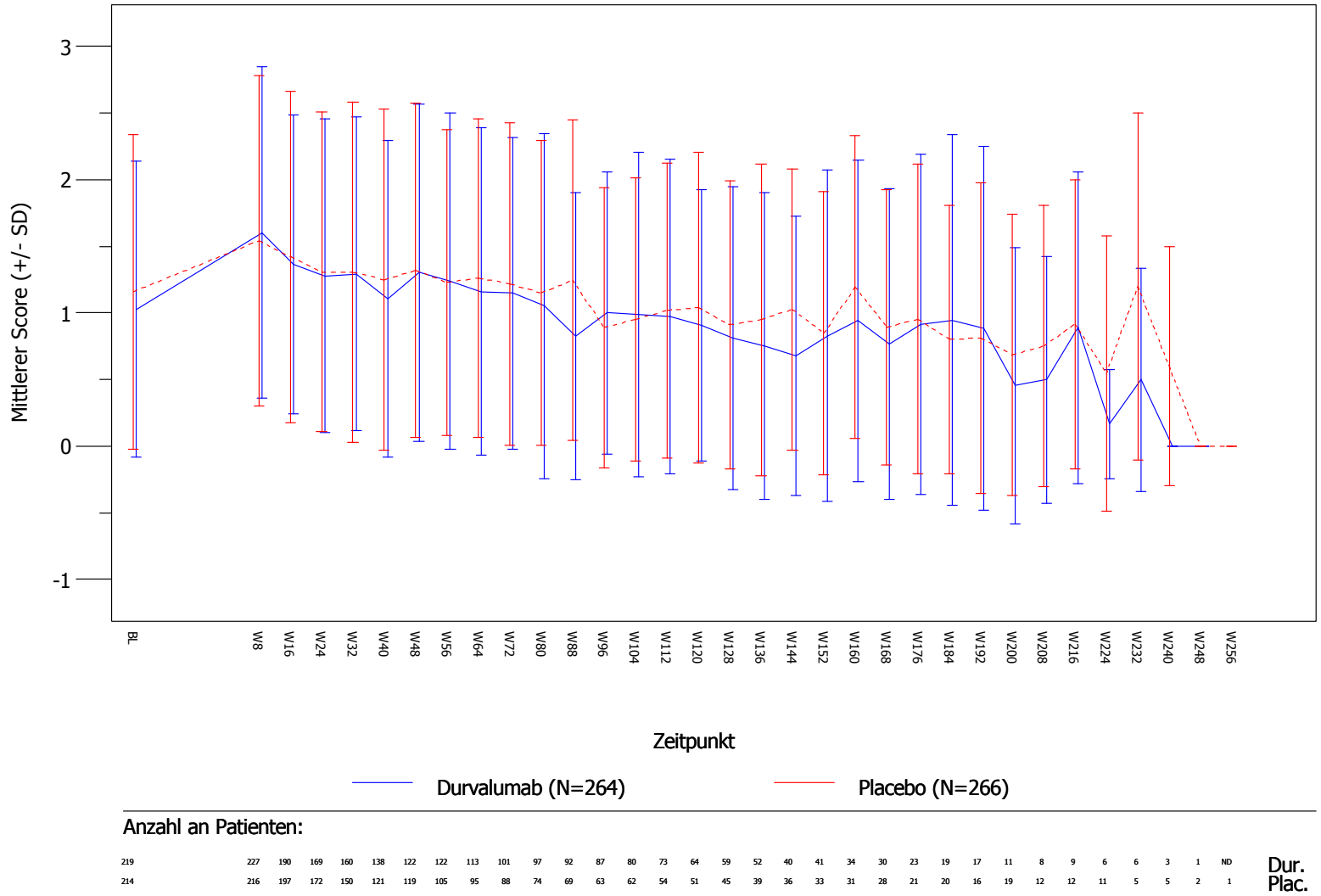
Figure 3.4.4.1 ADRIATIC: Mean (+/- SD) PGIS across timepoints, by treatment group
Full Analysis Set, DCO 15JAN2024



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Anhang 4-G8: Sicherheit: Unerwünschte Ereignisse

Anhang 4-G8.1: UE jeglichen Schweregrades - gesamt und nach SOC/PT

Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UE	262	247 (94,3)	1,0 [0,9; 1,0]	265	234 (88,3)	1,0 [1,0; 1,2]	1,18	[0,99; 1,41]	0,0743
SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	262	89 (34,0)	NE [NE; NE]	265	84 (31,7)	NE [NE; NE]	1,06	[0,78; 1,42]	0,7232
PT: Asthenie	262	26 (9,9)	NE [NE; NE]	265	20 (7,5)	NE [NE; NE]	1,30	[0,73; 2,35]	0,3789
PT: Ermuedung	262	32 (12,2)	NE [NE; NE]	265	34 (12,8)	NE [NE; NE]	0,95	[0,58; 1,53]	0,8229
PT: Fieber	262	11 (4,2)	NE [NE; NE]	265	13 (4,9)	NE [NE; NE]	0,77	[0,34; 1,72]	0,5219
SOC: Augenerkrankungen	262	14 (5,3)	NE [NE; NE]	265	9 (3,4)	NE [NE; NE]	1,51	[0,66; 3,62]	0,3343
SOC: Endokrine Erkrankungen	262	65 (24,8)	NE [NE; NE]	265	15 (5,7)	NE [NE; NE]	4,91	[2,88; 8,94]	<0,0001*
PT: Hyperthyroidismus	262	27 (10,3)	NE [NE; NE]	265	4 (1,5)	NE [NE; NE]	7,07	[2,76; 23,92]	<0,0001*
PT: Hypothyreose	262	42 (16,0)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	4,43	[2,32; 9,34]	<0,0001*
SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums	262	122 (46,6)	12,8 [8,3;24,5]	265	87 (32,8)	NE [NE; NE]	1,45	[1,11; 1,92]	0,0075*

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PT: Dyspnoe	262	25 (9,5)	NE [NE; NE]	265	18 (6,8)	NE [NE; NE]	1,38	[0,76; 2,56]	0,2984
PT: Husten	262	40 (15,3)	NE [NE; NE]	265	32 (12,1)	NE [NE; NE]	1,23	[0,77; 1,97]	0,3809
PT: Husten mit Auswurf	262	12 (4,6)	NE [NE; NE]	265	8 (3,0)	NE [NE; NE]	1,47	[0,61; 3,75]	0,3981
PT: Pneumonitis	262	28 (10,7)	NE [NE; NE]	265	16 (6,0)	NE [NE; NE]	1,75	[0,96; 3,31]	0,0706
SOC: Erkrankungen der Haut und des Unterhautgewebes	262	81 (30,9)	NE [NE; NE]	265	60 (22,6)	NE [NE; NE]	1,38	[0,99; 1,94]	0,0564
PT: Ausschlag	262	28 (10,7)	NE [NE; NE]	265	16 (6,0)	NE [NE; NE]	1,73	[0,95; 3,26]	0,0779
PT: Pruritus	262	34 (13,0)	NE [NE; NE]	265	19 (7,2)	NE [NE; NE]	1,80	[1,04; 3,22]	0,0377*
PT: Trockene Haut	262	8 (3,1)	NE [NE; NE]	265	11 (4,2)	NE [NE; NE]	0,69	[0,27; 1,70]	0,4187
SOC: Erkrankungen der Nieren und Harnwege	262	16 (6,1)	NE [NE; NE]	265	16 (6,0)	NE [NE; NE]	0,98	[0,49; 1,97]	0,9494
SOC: Erkrankungen des Blutes und des Lymphsystems	262	30 (11,5)	NE [NE; NE]	265	24 (9,1)	NE [NE; NE]	1,19	[0,70; 2,06]	0,5172
PT: Anaemie	262	23 (8,8)	NE [NE; NE]	265	16 (6,0)	NE [NE; NE]	1,37	[0,73; 2,64]	0,3304

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
SOC: Erkrankungen des Gastrointestinaltrakts	262	111 (42,4)	18,5 [11,6; NE]	265	101 (38,1)	24,3 [14,0; NE]	1,13	[0,86; 1,48]	0,3898
PT: Diarrhoe	262	29 (11,1)	NE [NE; NE]	265	22 (8,3)	NE [NE; NE]	1,28	[0,74; 2,25]	0,3830
PT: Erbrechen	262	12 (4,6)	NE [NE; NE]	265	18 (6,8)	NE [NE; NE]	0,65	[0,30; 1,33]	0,2427
PT: Obstipation	262	27 (10,3)	NE [NE; NE]	265	26 (9,8)	NE [NE; NE]	0,98	[0,57; 1,69]	0,9441
PT: Uebelkeit	262	33 (12,6)	NE [NE; NE]	265	29 (10,9)	NE [NE; NE]	1,16	[0,70; 1,92]	0,5690
SOC: Erkrankungen des Nervensystems	262	77 (29,4)	NE [NE; NE]	265	76 (28,7)	NE [NE; NE]	0,97	[0,70; 1,33]	0,8284
PT: Kopfschmerzen	262	24 (9,2)	NE [NE; NE]	265	35 (13,2)	NE [NE; NE]	0,64	[0,38; 1,07]	0,0928
PT: Schwindelgefuehl	262	32 (12,2)	NE [NE; NE]	265	20 (7,5)	NE [NE; NE]	1,57	[0,90; 2,78]	0,1118
SOC: Erkrankungen des Ohrs und des Labyrinths	262	14 (5,3)	NE [NE; NE]	265	15 (5,7)	NE [NE; NE]	0,90	[0,43; 1,87]	0,7744
SOC: Gefaesserkrankungen	262	19 (7,3)	NE [NE; NE]	265	17 (6,4)	NE [NE; NE]	1,10	[0,57; 2,13]	0,7838
SOC: Herzerkrankungen	262	32 (12,2)	NE [NE; NE]	265	14 (5,3)	NE [NE; NE]	2,23	[1,22; 4,32]	0,0101*

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
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All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
SOC: Infektionen und parasitaere Erkrankungen	262	99 (37,8)	20,9 [17,9;24,7]	265	87 (32,8)	21,2 [14,8; NE]	1,04	[0,78; 1,40]	0,7653
PT: COVID-19	262	18 (6,9)	NE [NE; NE]	265	17 (6,4)	NE [NE; NE]	0,89	[0,46; 1,74]	0,7275
PT: Harnwegsinfektion	262	10 (3,8)	NE [NE; NE]	265	7 (2,6)	NE [NE; NE]	1,39	[0,53; 3,82]	0,5058
PT: Infektion der oberen Atemwege	262	8 (3,1)	NE [NE; NE]	265	14 (5,3)	NE [NE; NE]	0,55	[0,22; 1,28]	0,1698
PT: Pneumonie	262	29 (11,1)	NE [NE; NE]	265	20 (7,5)	NE [NE; NE]	1,38	[0,79; 2,47]	0,2663
SOC: Leber- und Gallenerkrankungen	262	13 (5,0)	NE [NE; NE]	265	9 (3,4)	NE [NE; NE]	1,34	[0,58; 3,25]	0,4982
SOC: Psychiatrische Erkrankungen	262	31 (11,8)	NE [NE; NE]	265	27 (10,2)	NE [NE; NE]	1,08	[0,65; 1,82]	0,7665
PT: Schlaflosigkeit	262	16 (6,1)	NE [NE; NE]	265	13 (4,9)	NE [NE; NE]	1,19	[0,57; 2,51]	0,6444
SOC: Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	262	73 (27,9)	NE [NE; NE]	265	87 (32,8)	NE [NE; NE]	0,76	[0,56; 1,04]	0,0850
PT: Arthralgie	262	18 (6,9)	NE [NE; NE]	265	29 (10,9)	NE [NE; NE]	0,58	[0,32; 1,04]	0,0686

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
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All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.

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Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PT: Brustschmerzen die Skelettmuskulatur betreffend	262	4 (1,5)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	0,40	[0,11; 1,19]	0,1065
PT: Myalgie	262	11 (4,2)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	1,08	[0,46; 2,60]	0,8584
PT: Rueckenschmerzen	262	17 (6,5)	NE [NE; NE]	265	20 (7,5)	NE [NE; NE]	0,80	[0,42; 1,54]	0,5077
PT: Schmerz in einer Extremitaet	262	12 (4,6)	NE [NE; NE]	265	13 (4,9)	NE [NE; NE]	0,85	[0,38; 1,87]	0,6835
SOC: Stoffwechsel- und Ernaehrungsstoerungen	262	88 (33,6)	NE [NE; NE]	265	66 (24,9)	NE [NE; NE]	1,40	[1,02; 1,93]	0,0379*
PT: Appetit vermindert	262	44 (16,8)	NE [NE; NE]	265	34 (12,8)	NE [NE; NE]	1,33	[0,85; 2,10]	0,2087
PT: Hyperglykaemie	262	11 (4,2)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	1,05	[0,44; 2,53]	0,9046
PT: Hyponatriaemie	262	11 (4,2)	NE [NE; NE]	265	9 (3,4)	NE [NE; NE]	1,20	[0,49; 2,97]	0,6915
SOC: Untersuchungen	262	73 (27,9)	NE [NE; NE]	265	56 (21,1)	NE [NE; NE]	1,34	[0,95; 1,91]	0,0986
PT: Alaninaminotransferase erhoeht	262	15 (5,7)	NE [NE; NE]	265	13 (4,9)	NE [NE; NE]	1,09	[0,52; 2,33]	0,8157

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
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All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Table 2.2.1 ADRIATIC: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

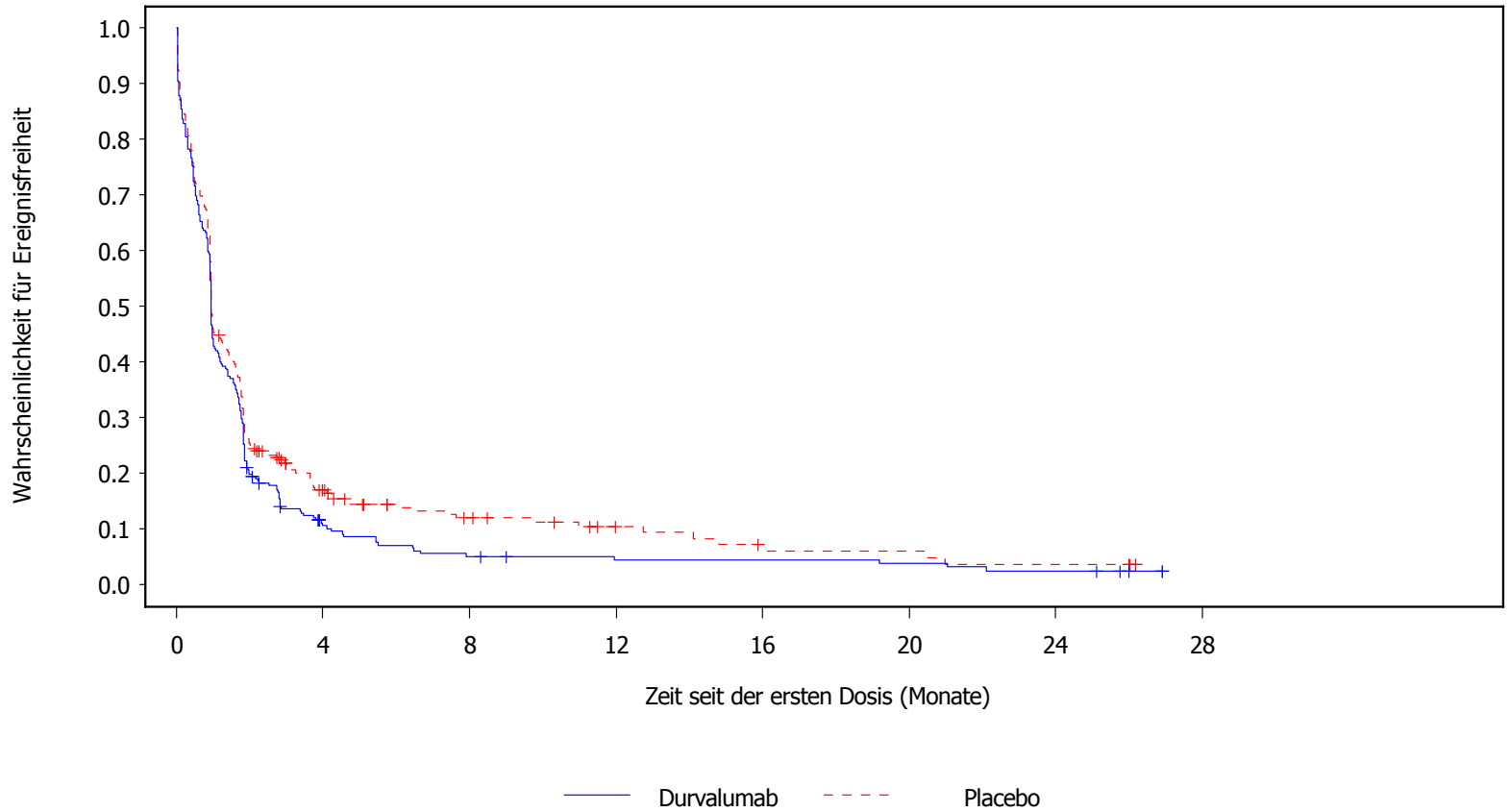
	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
PT: Aspartataminotransferase erhoeht	262	10 (3,8)	NE [NE; NE]	265	8 (3,0)	NE [NE; NE]	1,20	[0,47; 3,15]	0,6984
PT: Bilirubin im Blut erhoeht	262	6 (2,3)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	0,57	[0,19; 1,52]	0,2633
PT: Gewicht erniedrigt	262	19 (7,3)	NE [NE; NE]	265	11 (4,2)	NE [NE; NE]	1,69	[0,82; 3,67]	0,1625
PT: Kreatinin im Blut erhoeht	262	10 (3,8)	NE [NE; NE]	265	5 (1,9)	NE [NE; NE]	1,89	[0,67; 6,07]	0,2380
PT: Leukozytenzahl erniedrigt	262	18 (6,9)	NE [NE; NE]	265	11 (4,2)	NE [NE; NE]	1,61	[0,77; 3,52]	0,2089
PT: Lymphozytenzahl erniedrigt	262	11 (4,2)	NE [NE; NE]	265	6 (2,3)	NE [NE; NE]	1,79	[0,68; 5,20]	0,2443
SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	262	78 (29,8)	NE [NE; NE]	265	80 (30,2)	NE [NE; NE]	0,95	[0,69; 1,29]	0,7207
PT: Strahlenbedingte Pneumonitis	262	60 (22,9)	NE [NE; NE]	265	62 (23,4)	NE [NE; NE]	0,96	[0,67; 1,37]	0,8265

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1aa
05JUN2025:07:1

Anhang 4-G8.1.1: UE jeglichen Schweregrades - gesamt und nach SOC/PT - Kaplan-Meier-Plot

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.1 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UE
Safety Analysis Set, DCO 15JAN2024



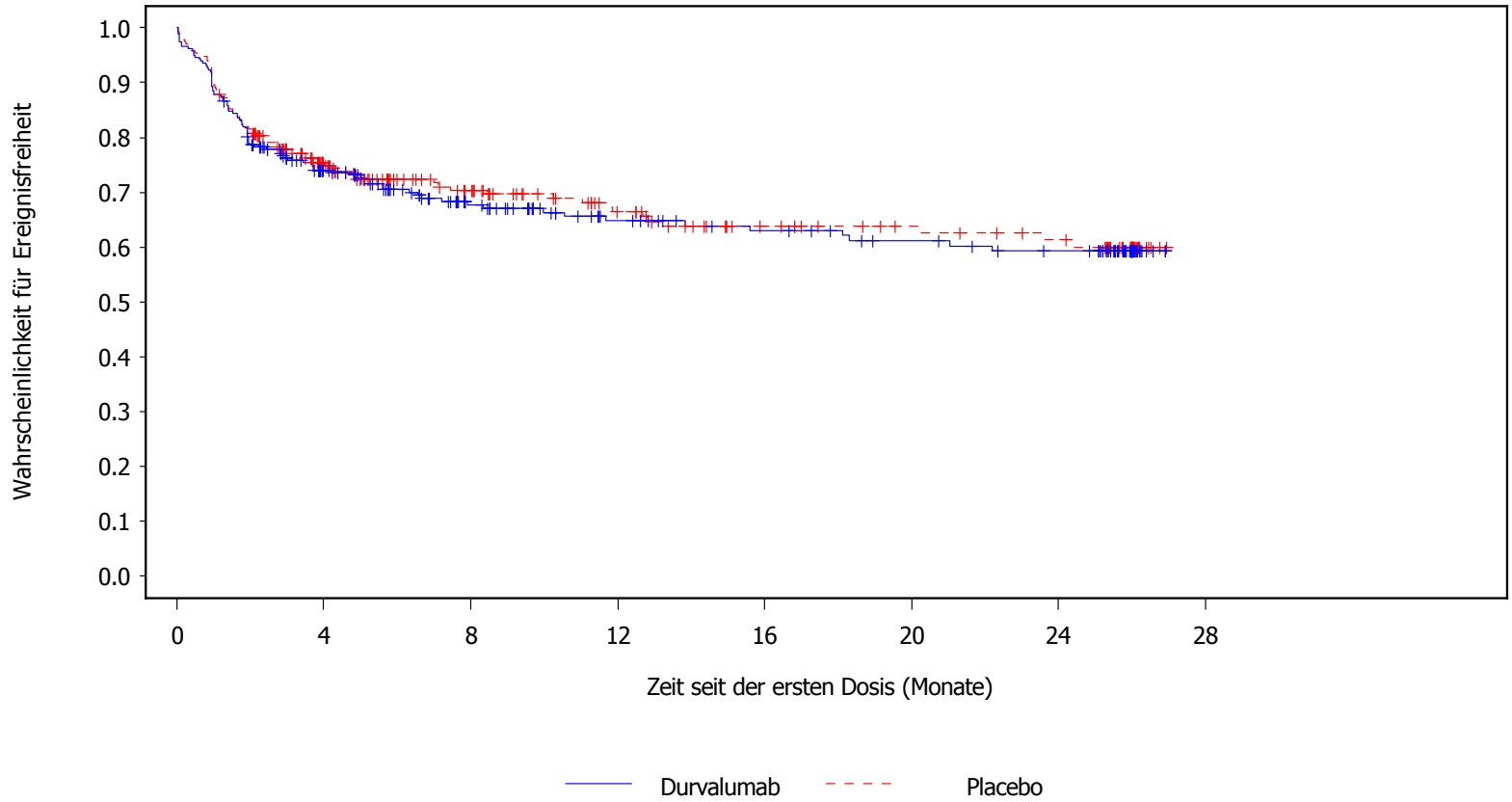
Anzahl an Patienten unter Risiko:

262	21	10	7	7	6	4	0	Durvalumab
265	36	18	10	6	5	3	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baa 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.2 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort
Safety Analysis Set, DCO 15JAN2024



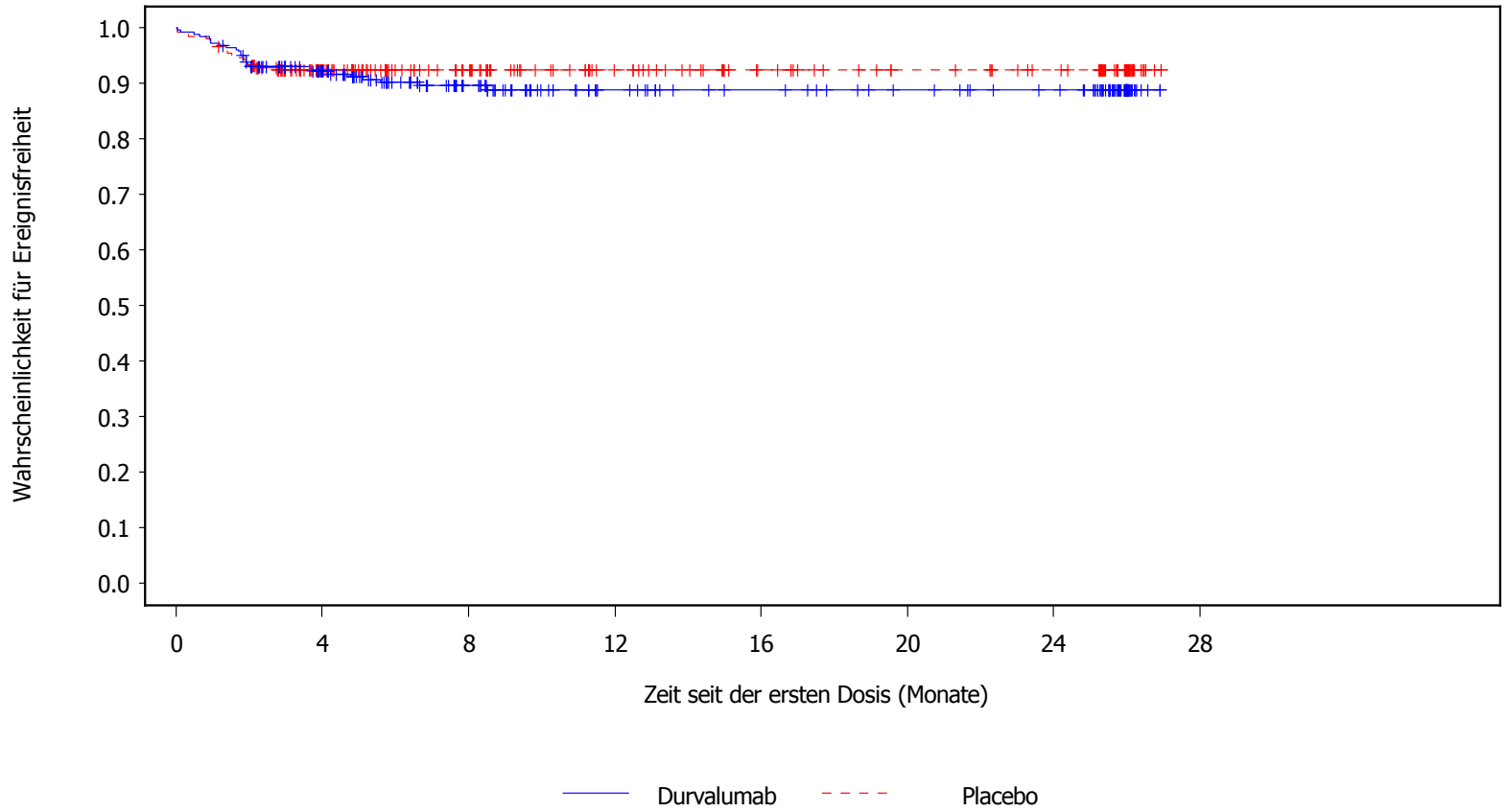
Anzahl an Patienten unter Risiko:

262	156	108	81	72	65	59	0	Durvalumab
265	155	107	79	61	53	48	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bab 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.3 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Asthenie
Safety Analysis Set, DCO 15JAN2024



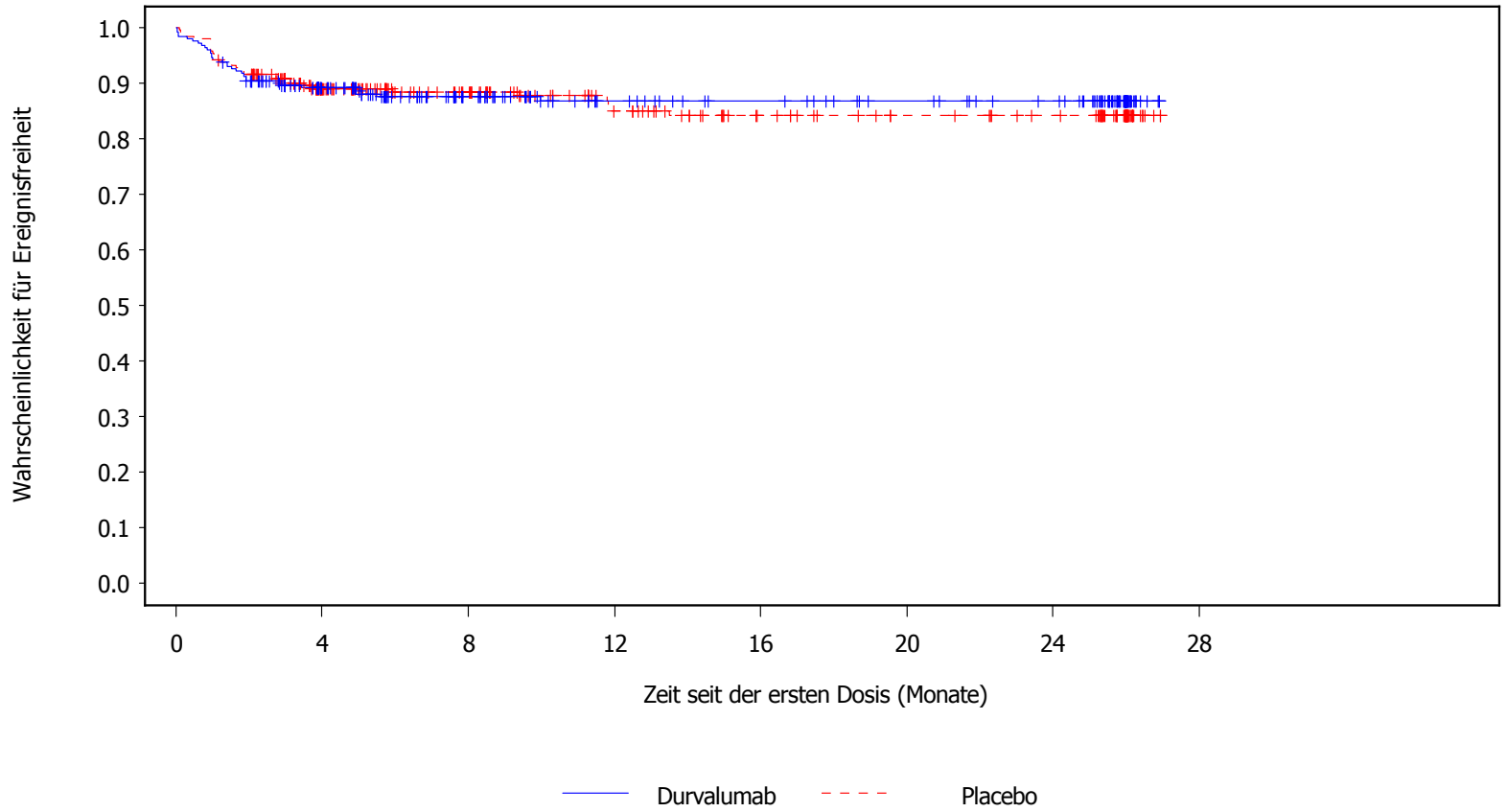
Anzahl an Patienten unter Risiko:

262	193	141	106	96	89	83	0	Durvalumab
265	188	139	107	88	77	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bac 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.4 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Ermuedung
Safety Analysis Set, DCO 15JAN2024



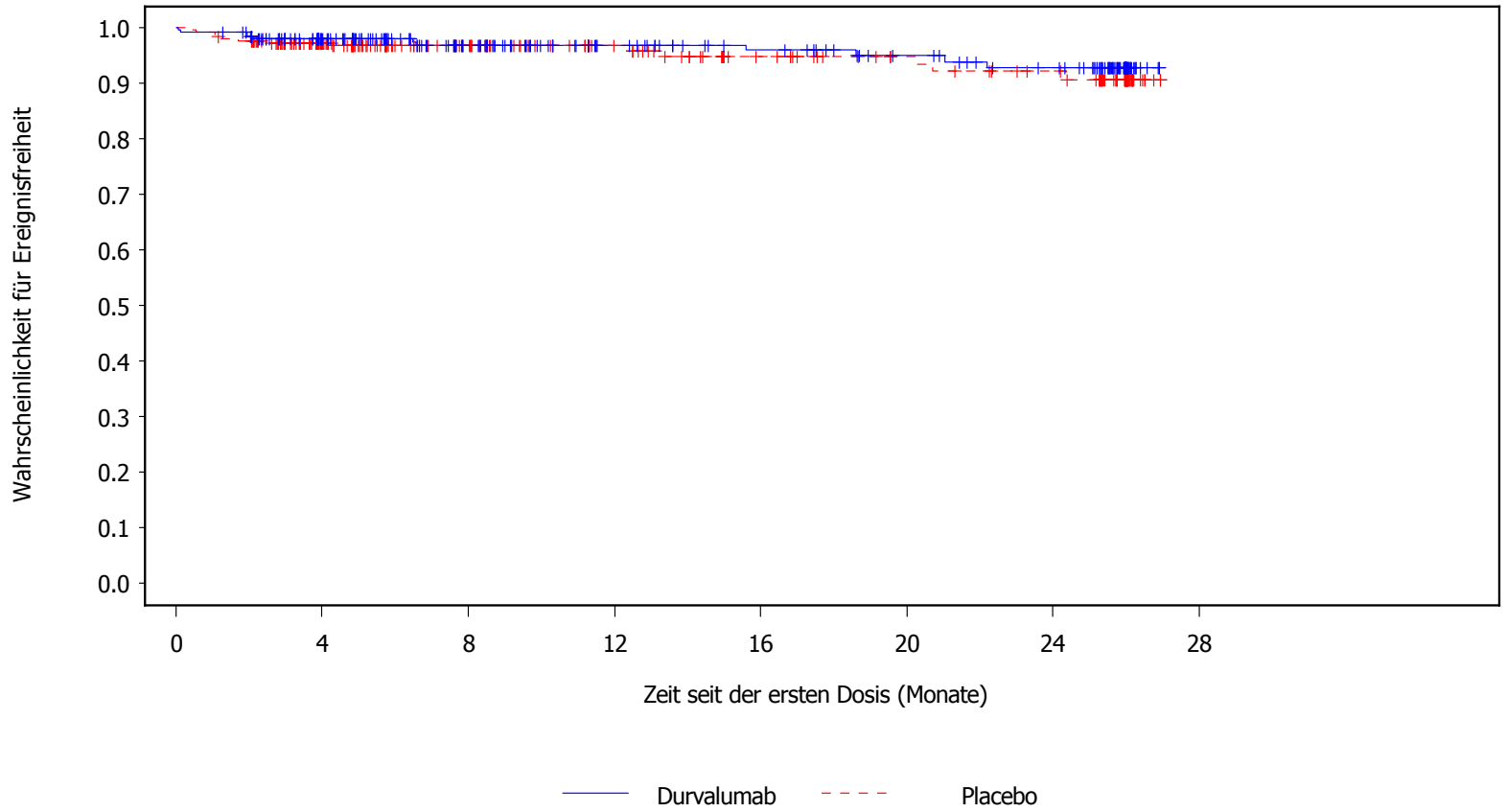
Anzahl an Patienten unter Risiko:

262	187	137	105	96	88	81	0	Durvalumab
265	185	133	96	75	65	59	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bad 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.5 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Fieber
Safety Analysis Set, DCO 15JAN2024



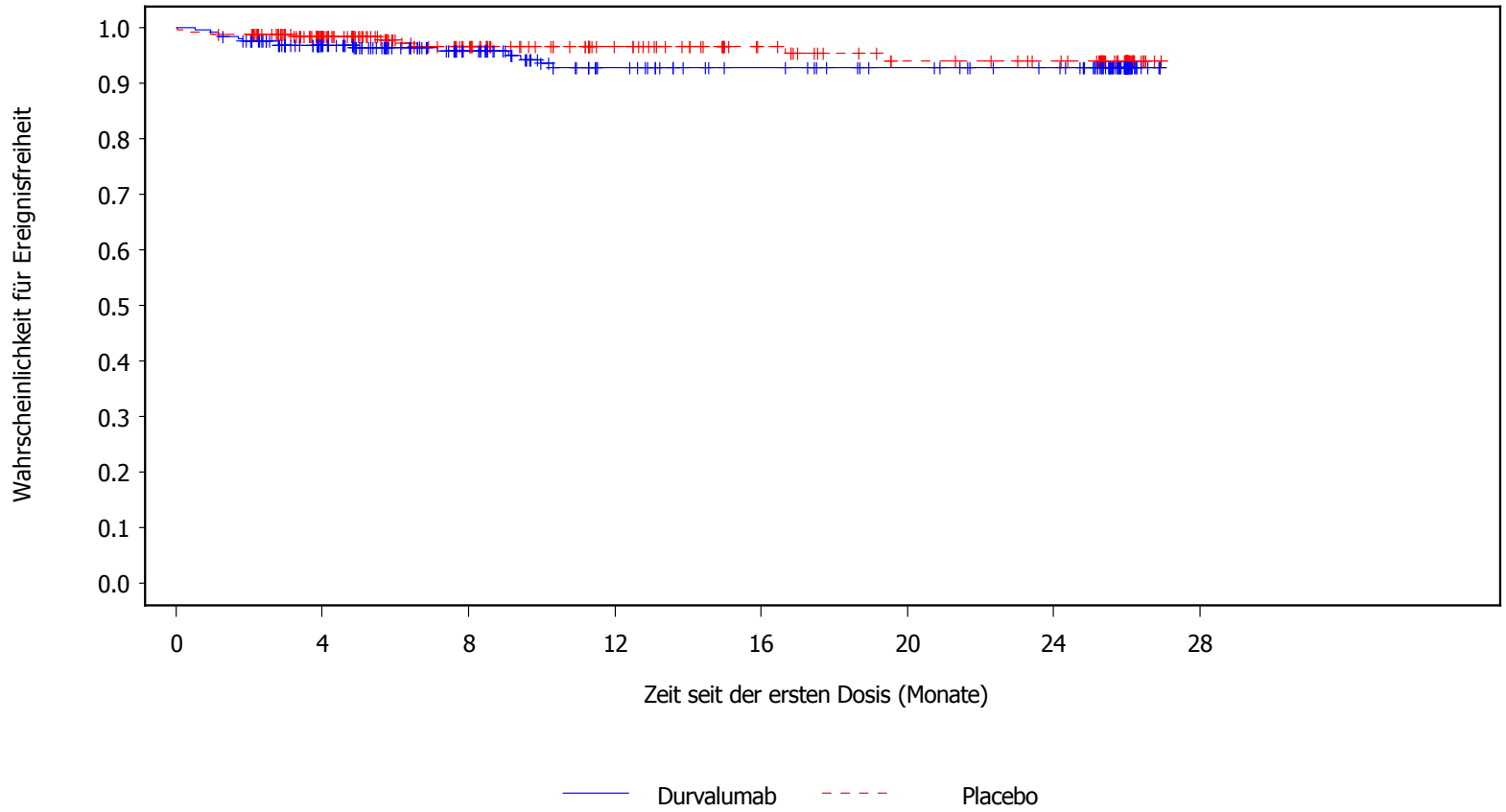
Anzahl an Patienten unter Risiko:

262	205	150	118	104	93	84	0	Durvalumab
265	198	139	105	83	71	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bae 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.6 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Augenerkrankungen
Safety Analysis Set, DCO 15JAN2024



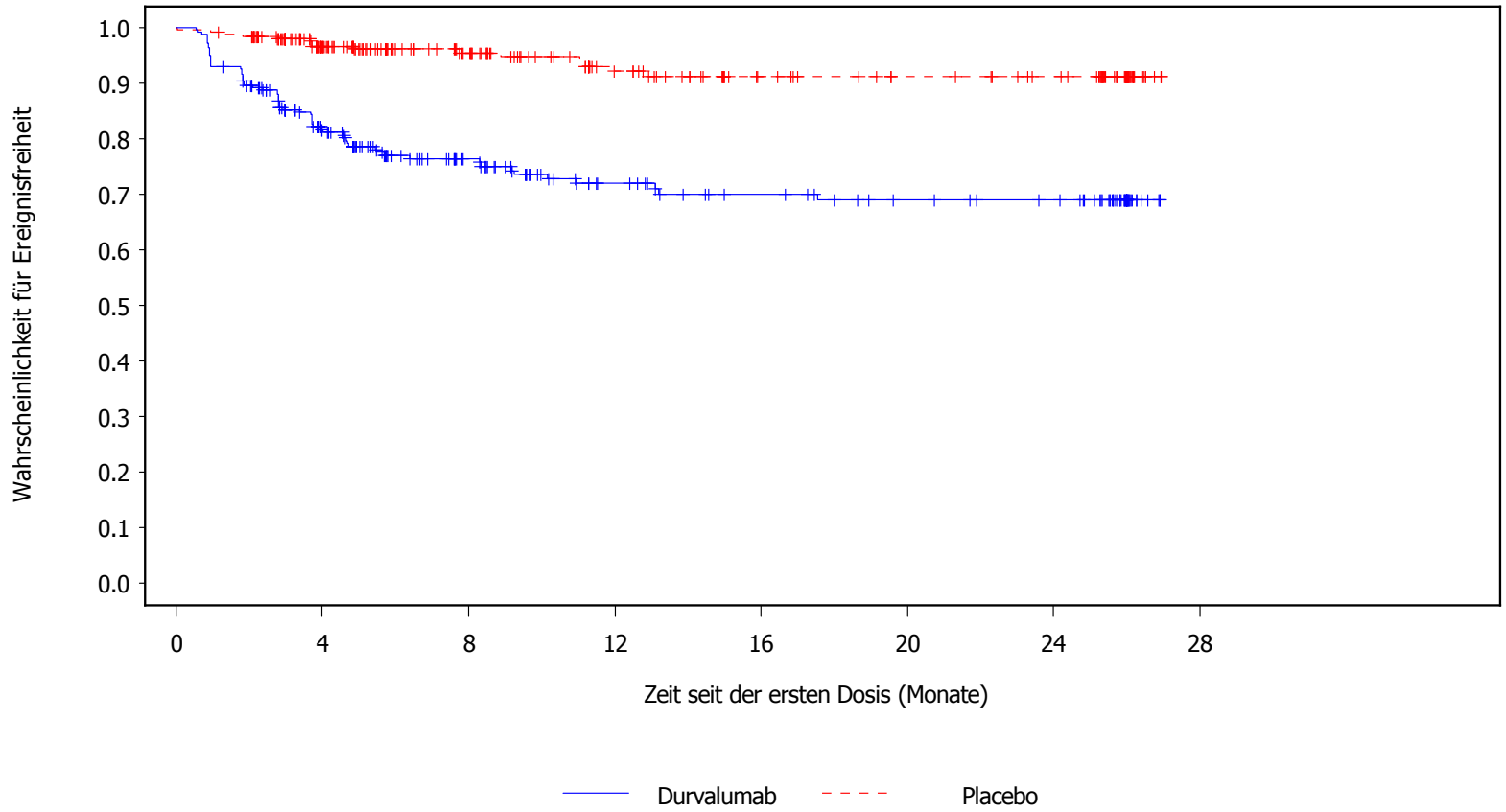
Anzahl an Patienten unter Risiko:

262	203	149	112	99	91	84	0	Durvalumab
265	202	141	108	86	72	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baf 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.7 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Endokrine Erkrankungen
Safety Analysis Set, DCO 15JAN2024



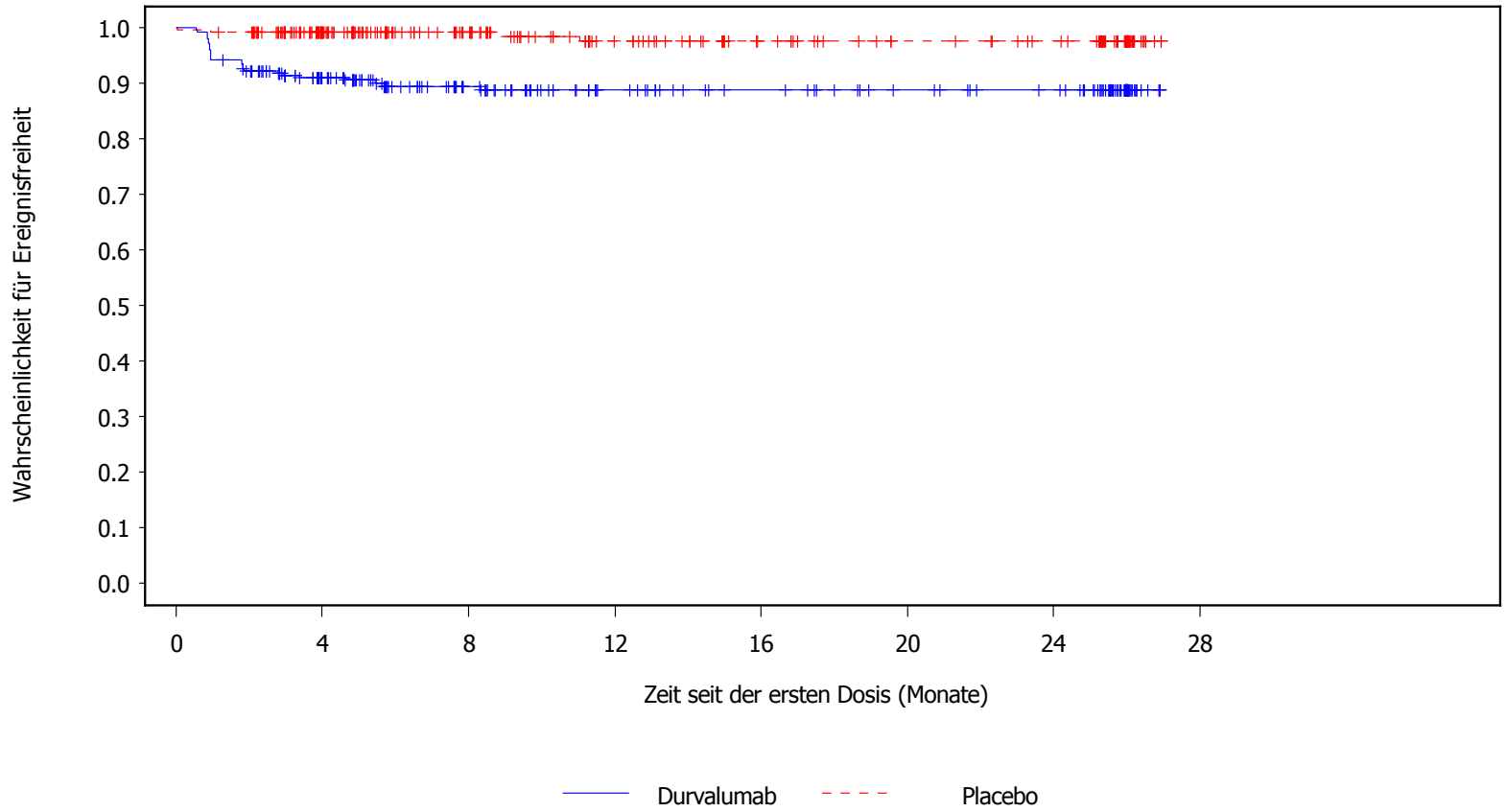
Anzahl an Patienten unter Risiko:

262	167	114	81	69	61	57	0	Durvalumab
265	199	141	102	79	71	65	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bag 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.8 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Hyperthyroidismus
Safety Analysis Set, DCO 15JAN2024



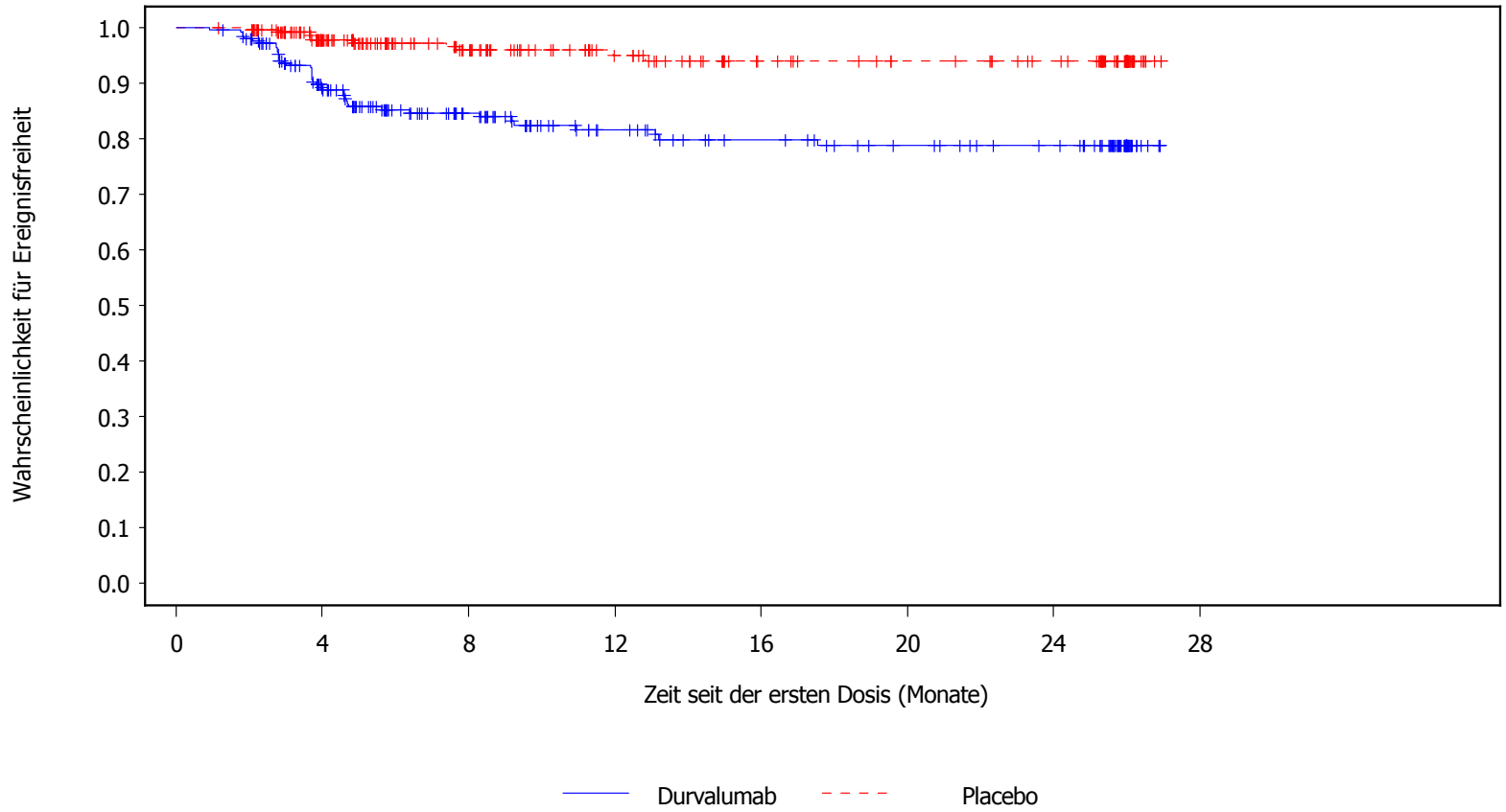
Anzahl an Patienten unter Risiko:

262	189	138	108	96	87	81	0	Durvalumab
265	204	146	109	87	75	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bah 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.9 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Hypothyreose
Safety Analysis Set, DCO 15JAN2024



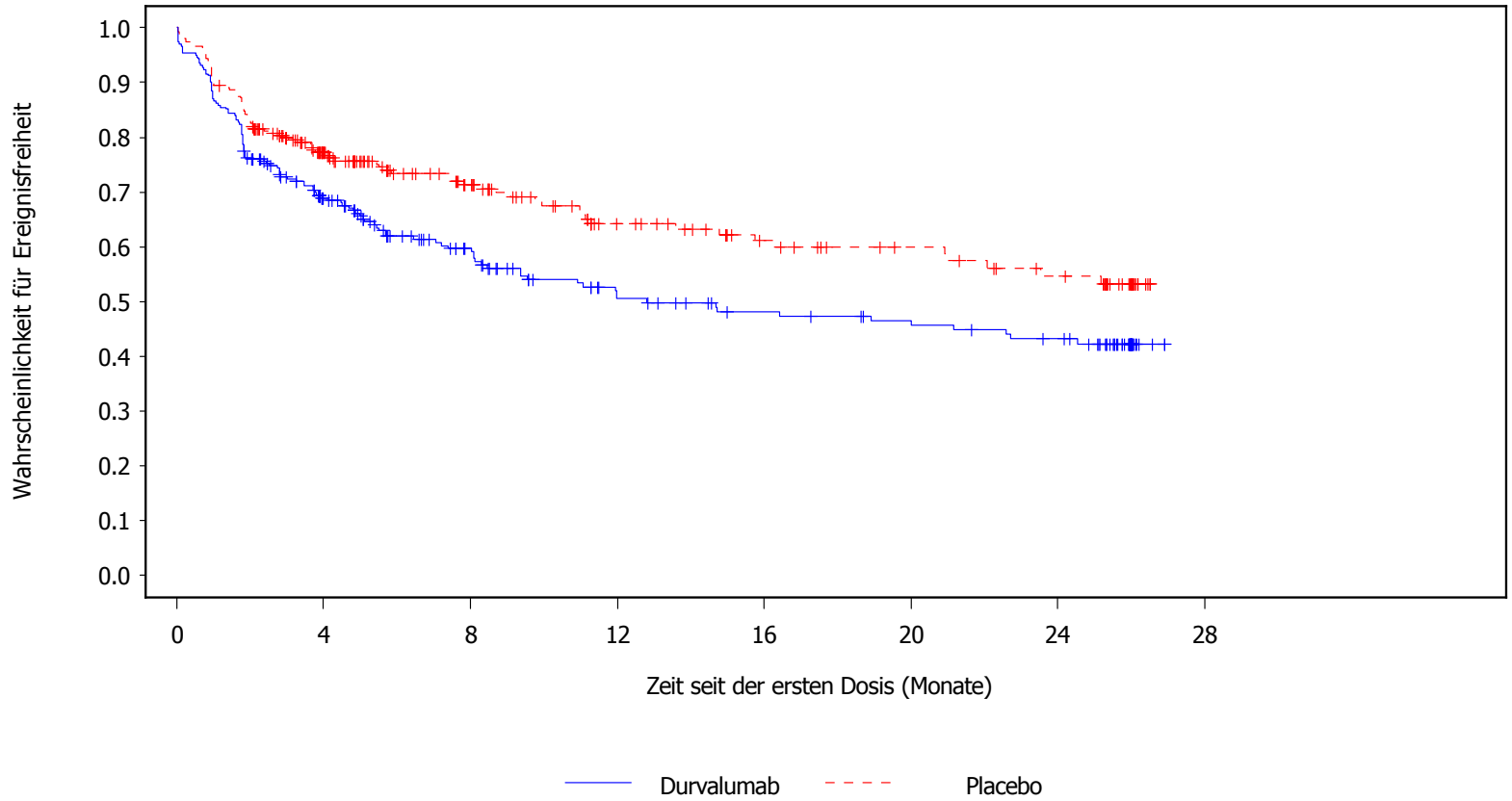
Anzahl an Patienten unter Risiko:

262	184	129	95	82	73	66	0	Durvalumab
265	200	141	105	82	74	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bai 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.10 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024



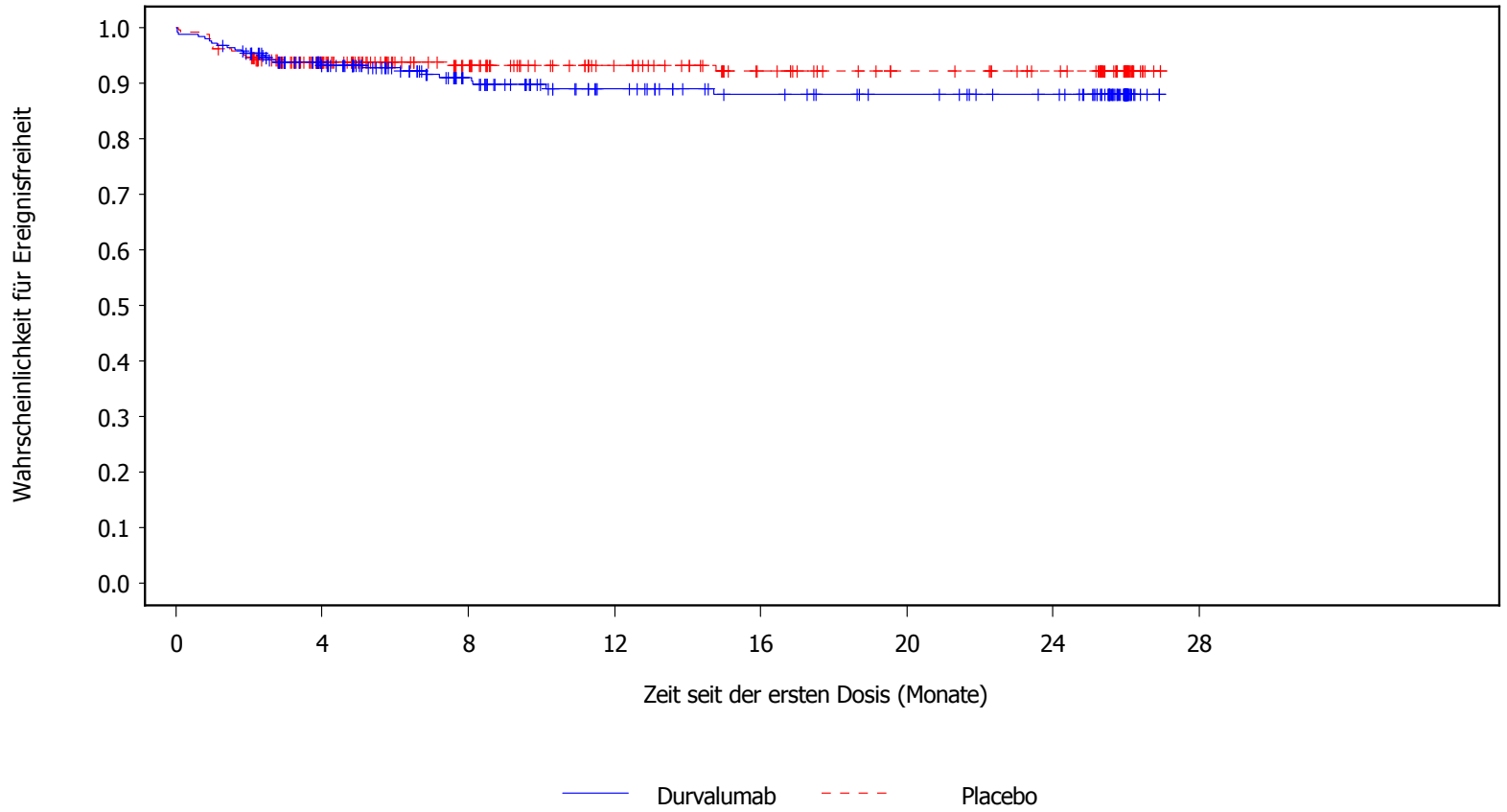
Anzahl an Patienten unter Risiko:

262	148	99	70	60	55	49	0	Durvalumab
265	158	104	70	54	46	38	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baj 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.11 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Dyspnoe
Safety Analysis Set, DCO 15JAN2024



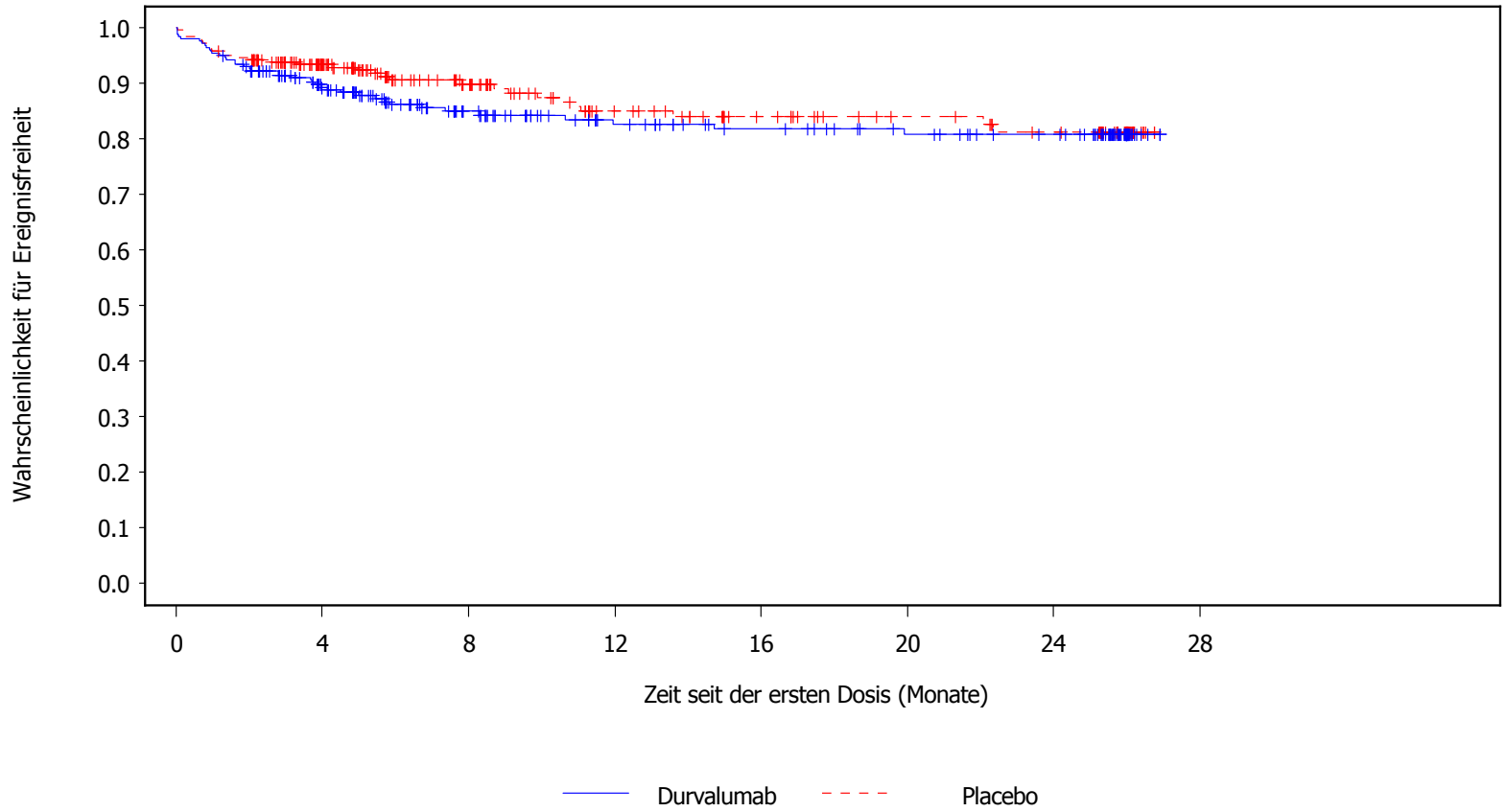
Anzahl an Patienten unter Risiko:

262	193	143	110	96	89	82	0	Durvalumab
265	192	137	104	82	70	63	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bak 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.12 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Husten
Safety Analysis Set, DCO 15JAN2024



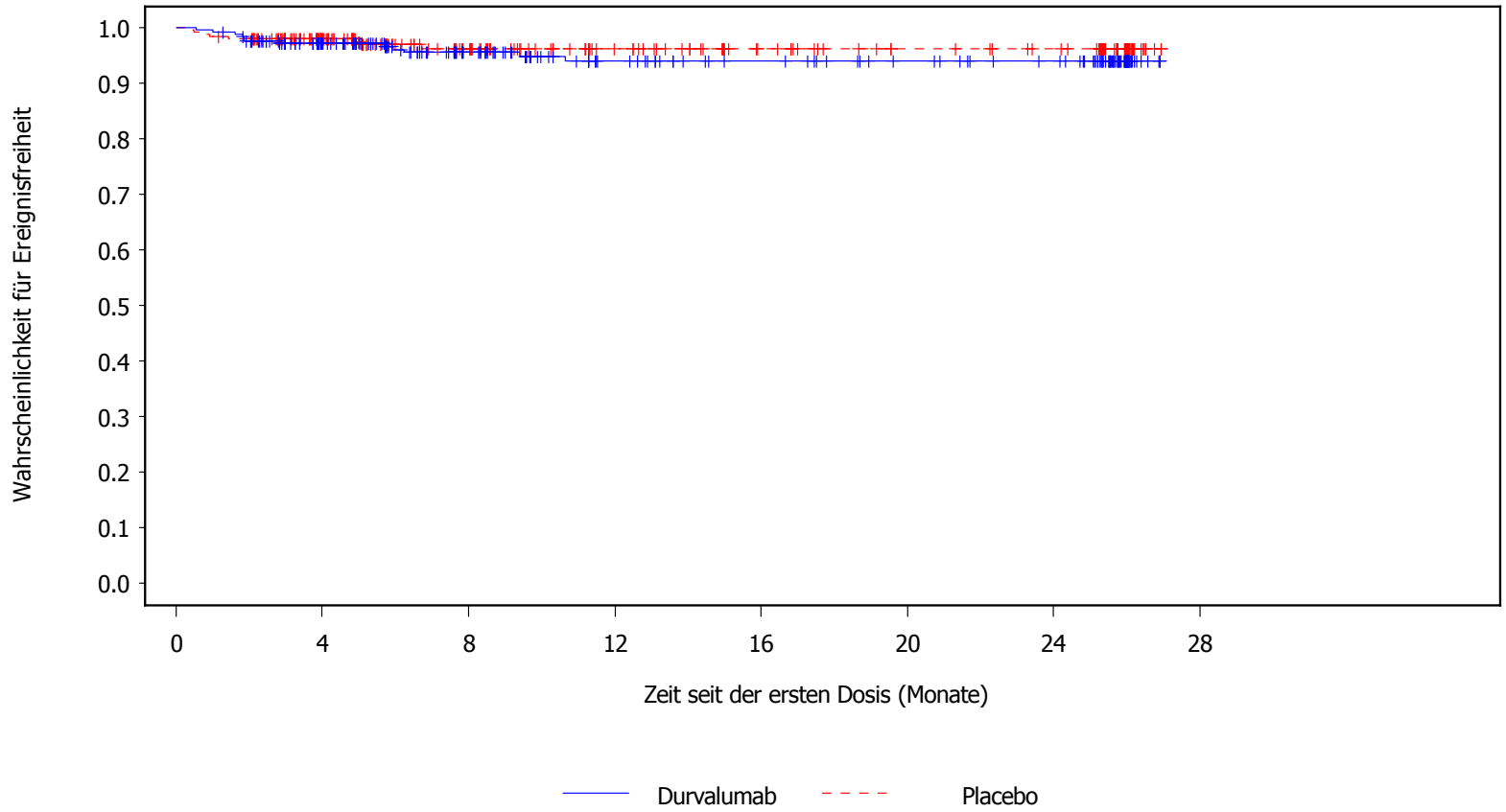
Anzahl an Patienten unter Risiko:

262	186	131	102	90	81	73	0	Durvalumab
265	191	128	90	74	63	56	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bal 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.13 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Husten mit Auswurf
Safety Analysis Set, DCO 15JAN2024



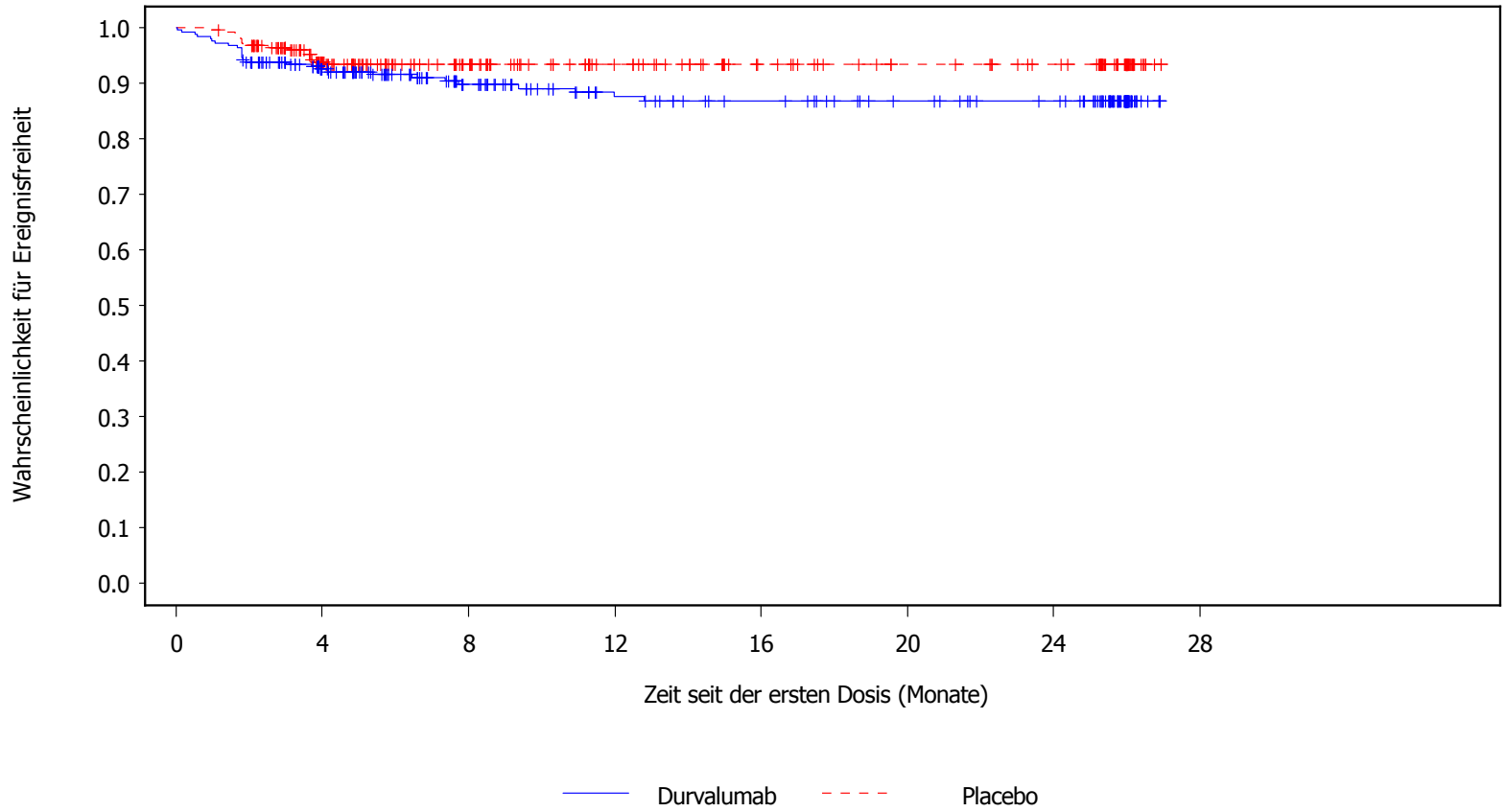
Anzahl an Patienten unter Risiko:

262	202	148	115	102	93	86	0	Durvalumab
265	201	141	106	85	73	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bam 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.14 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024



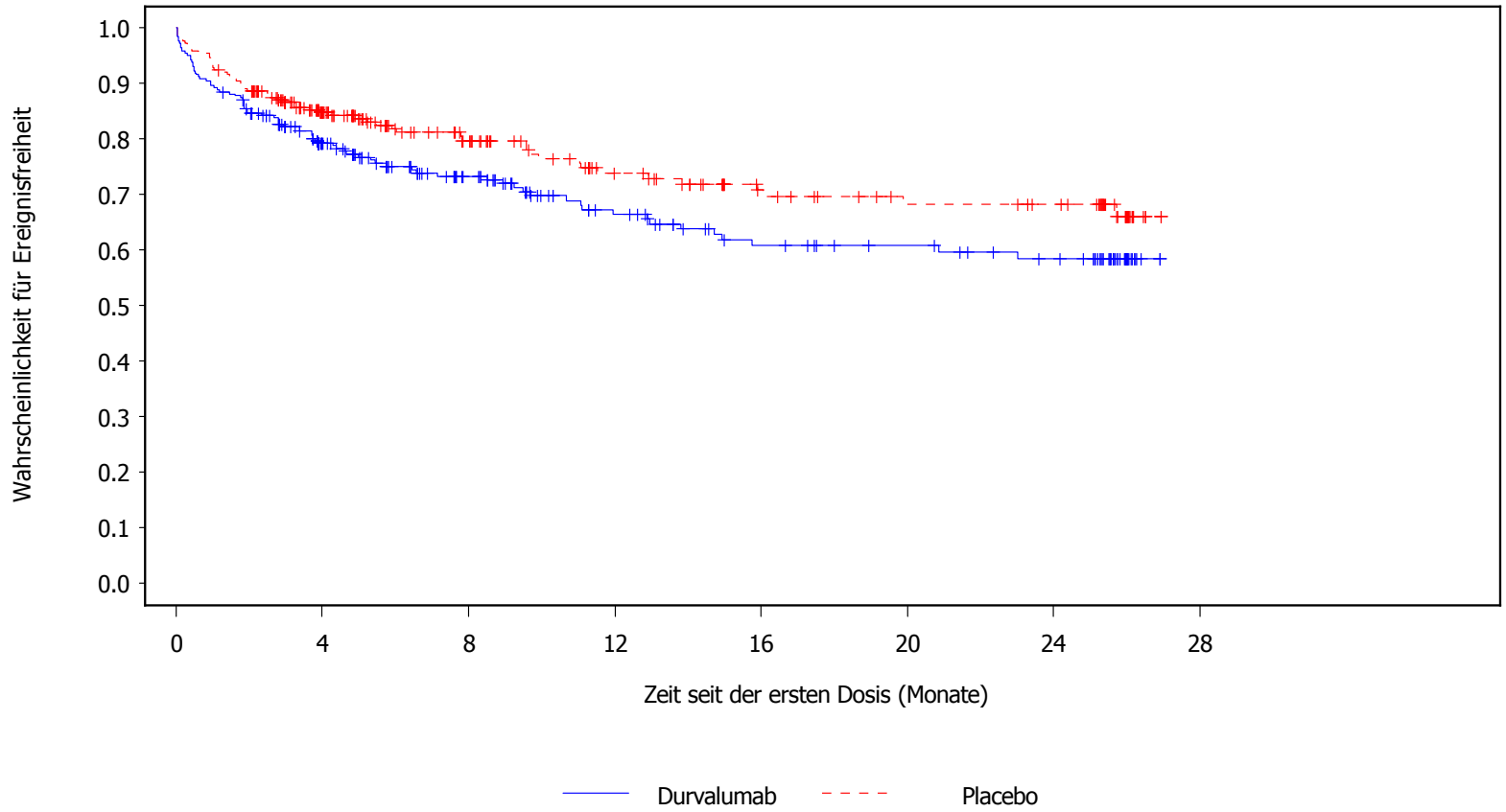
Anzahl an Patienten unter Risiko:

262	196	143	113	103	93	86	0	Durvalumab
265	194	141	107	86	75	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1ban 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.15 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Haut und des Unterhautgewebes
Safety Analysis Set, DCO 15JAN2024



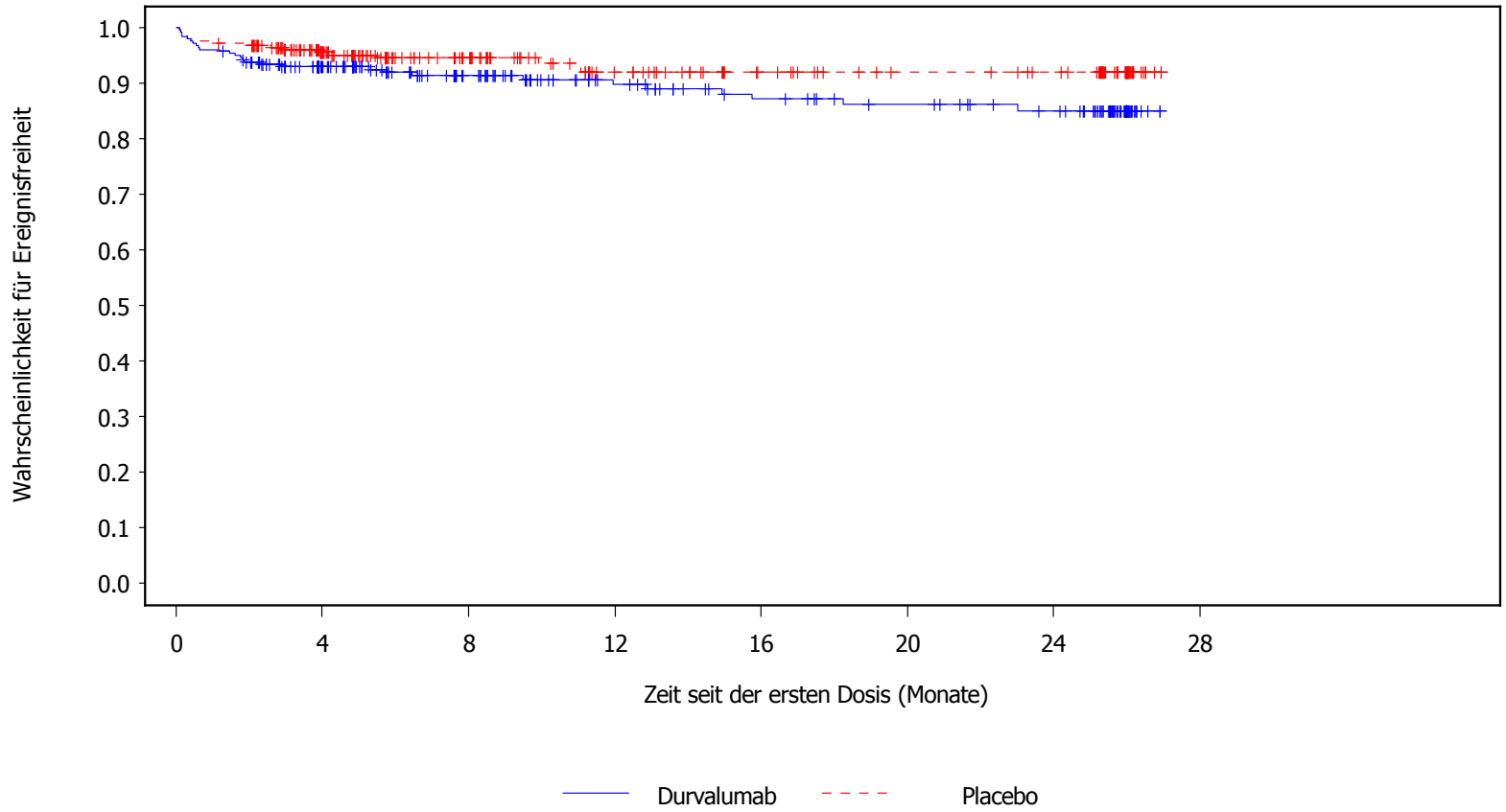
Anzahl an Patienten unter Risiko:

262	162	113	79	61	55	48	0	Durvalumab
265	167	111	79	59	50	47	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bao 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.16 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Ausschlag
Safety Analysis Set, DCO 15JAN2024



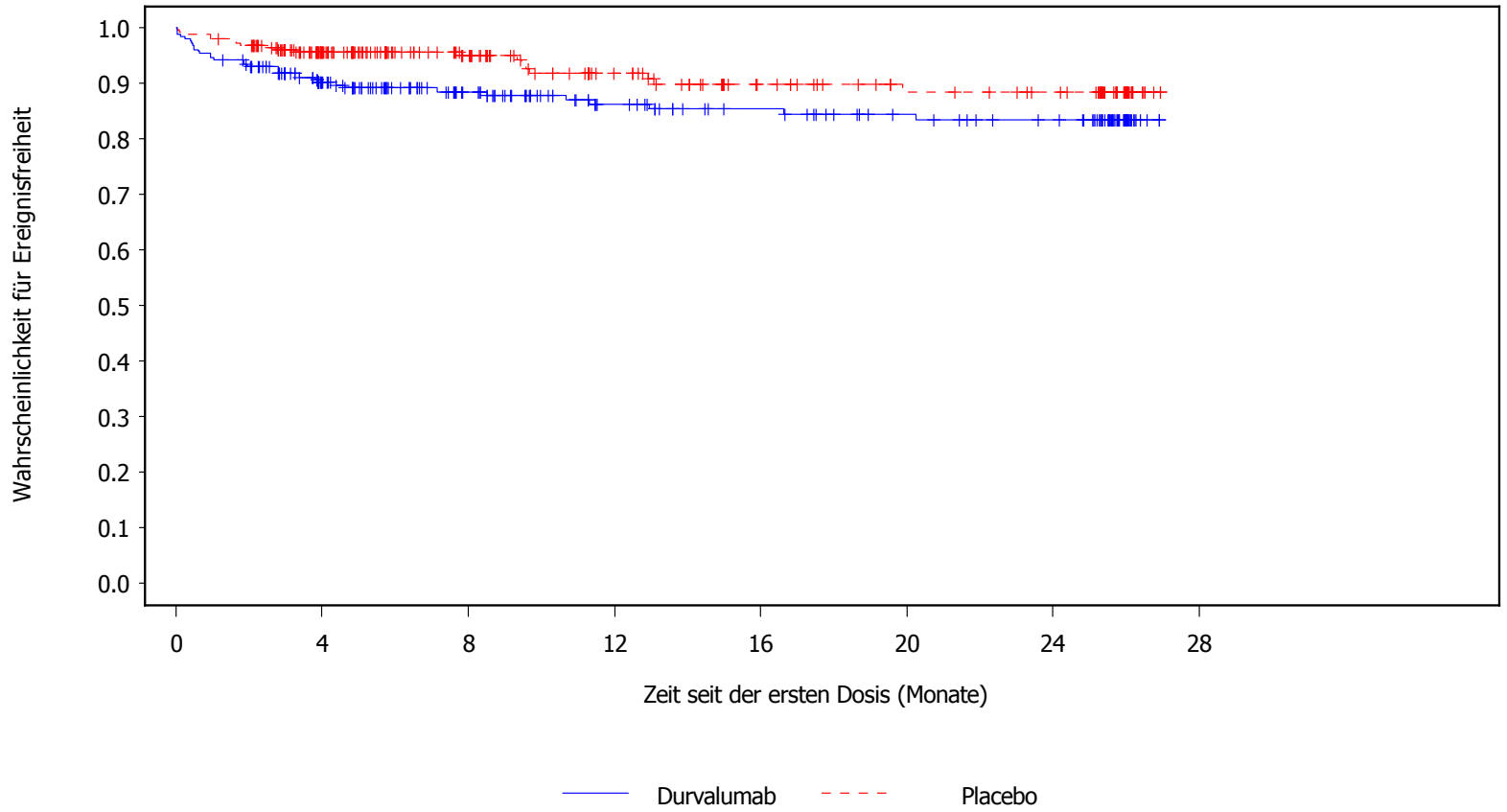
Anzahl an Patienten unter Risiko:

262	194	145	110	94	87	79	0	Durvalumab
265	194	135	100	80	70	66	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bap 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.17 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Pruritus
Safety Analysis Set, DCO 15JAN2024



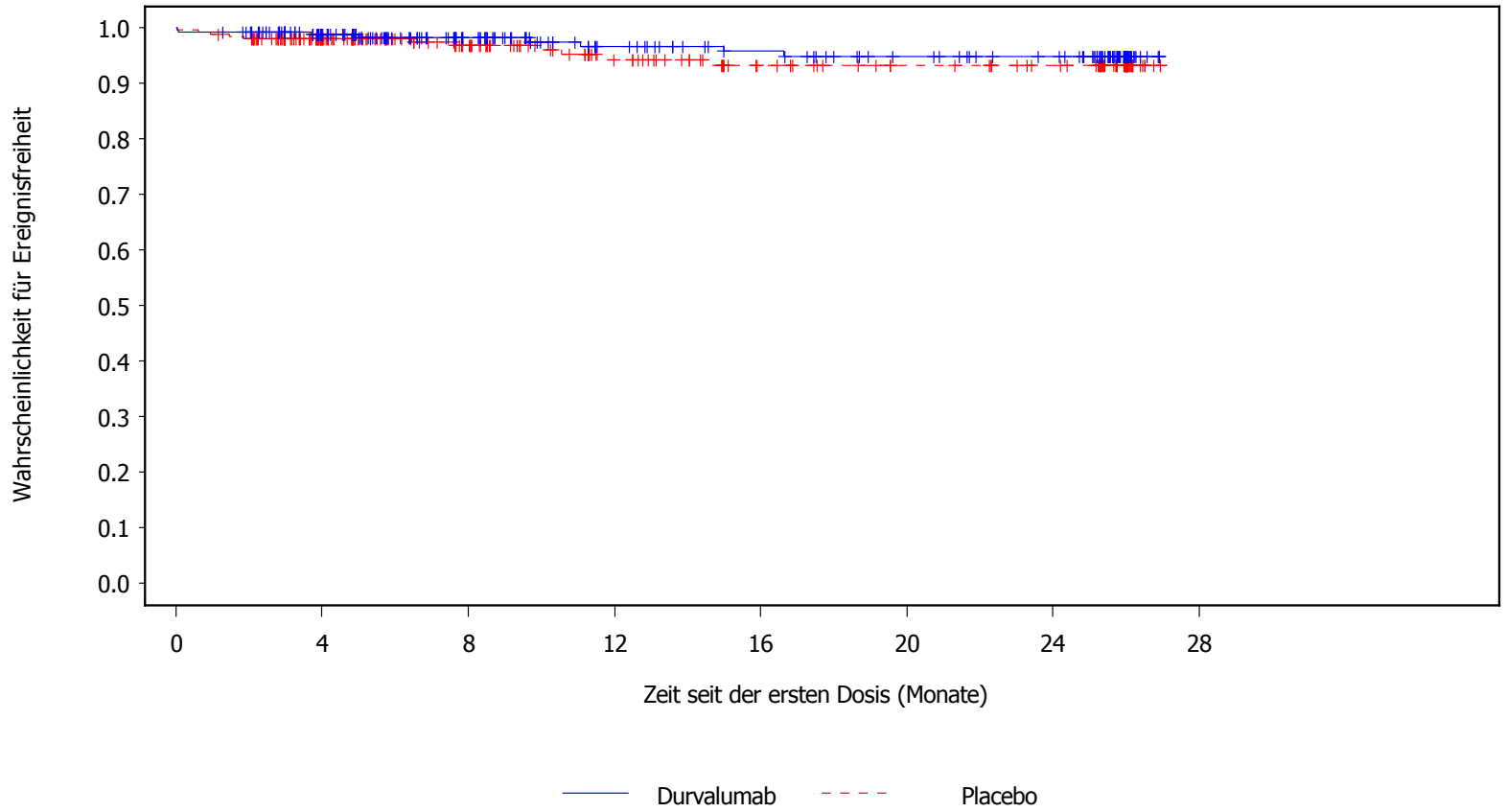
Anzahl an Patienten unter Risiko:

262	185	136	103	89	78	71	0	Durvalumab
265	194	135	100	77	65	60	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baq 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.18 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Trockene Haut
Safety Analysis Set, DCO 15JAN2024



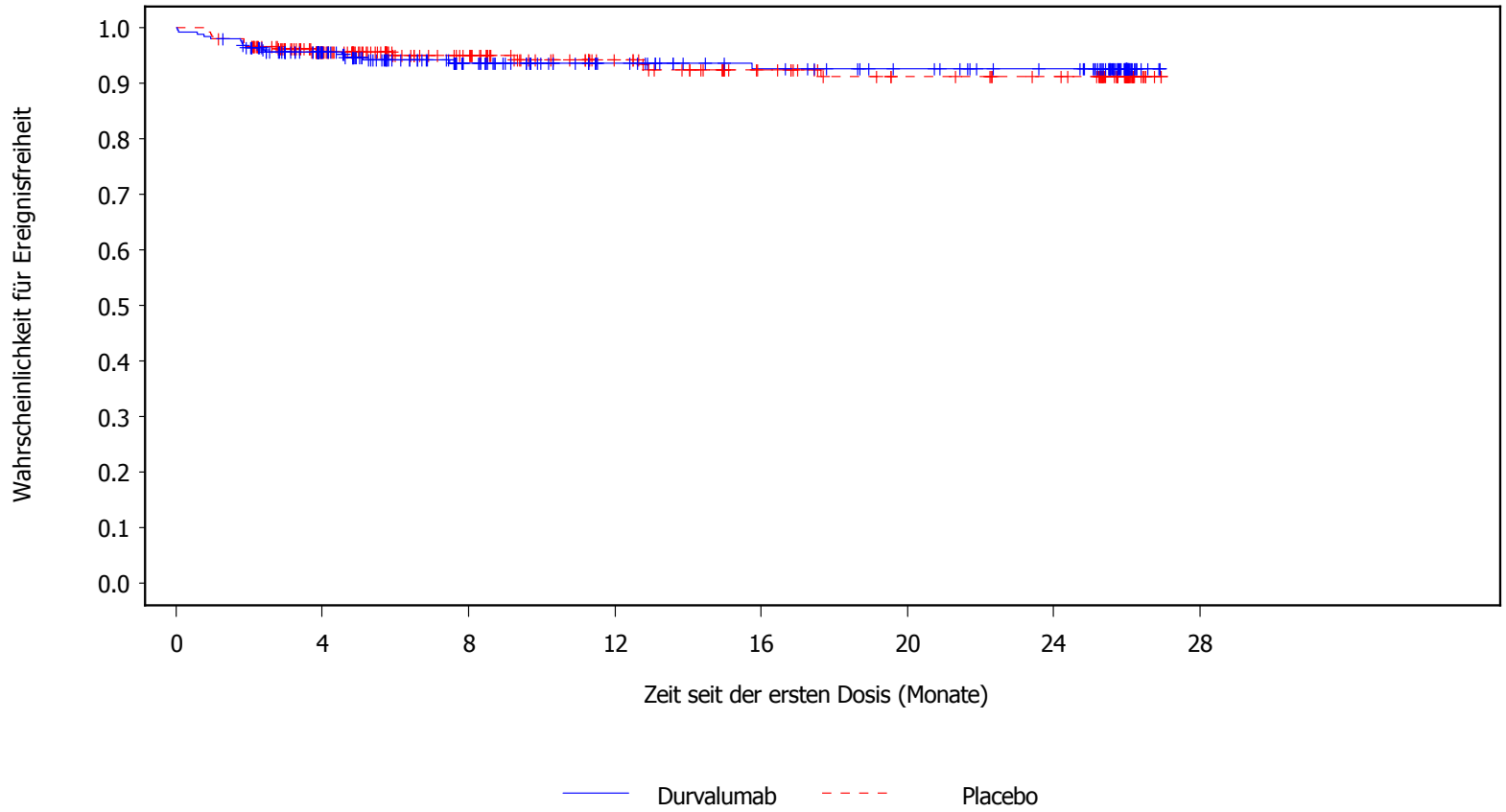
Anzahl an Patienten unter Risiko:

262	207	153	118	105	94	86	0	Durvalumab
265	201	144	107	84	73	66	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bar 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.19 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Nieren und Harnwege
Safety Analysis Set, DCO 15JAN2024



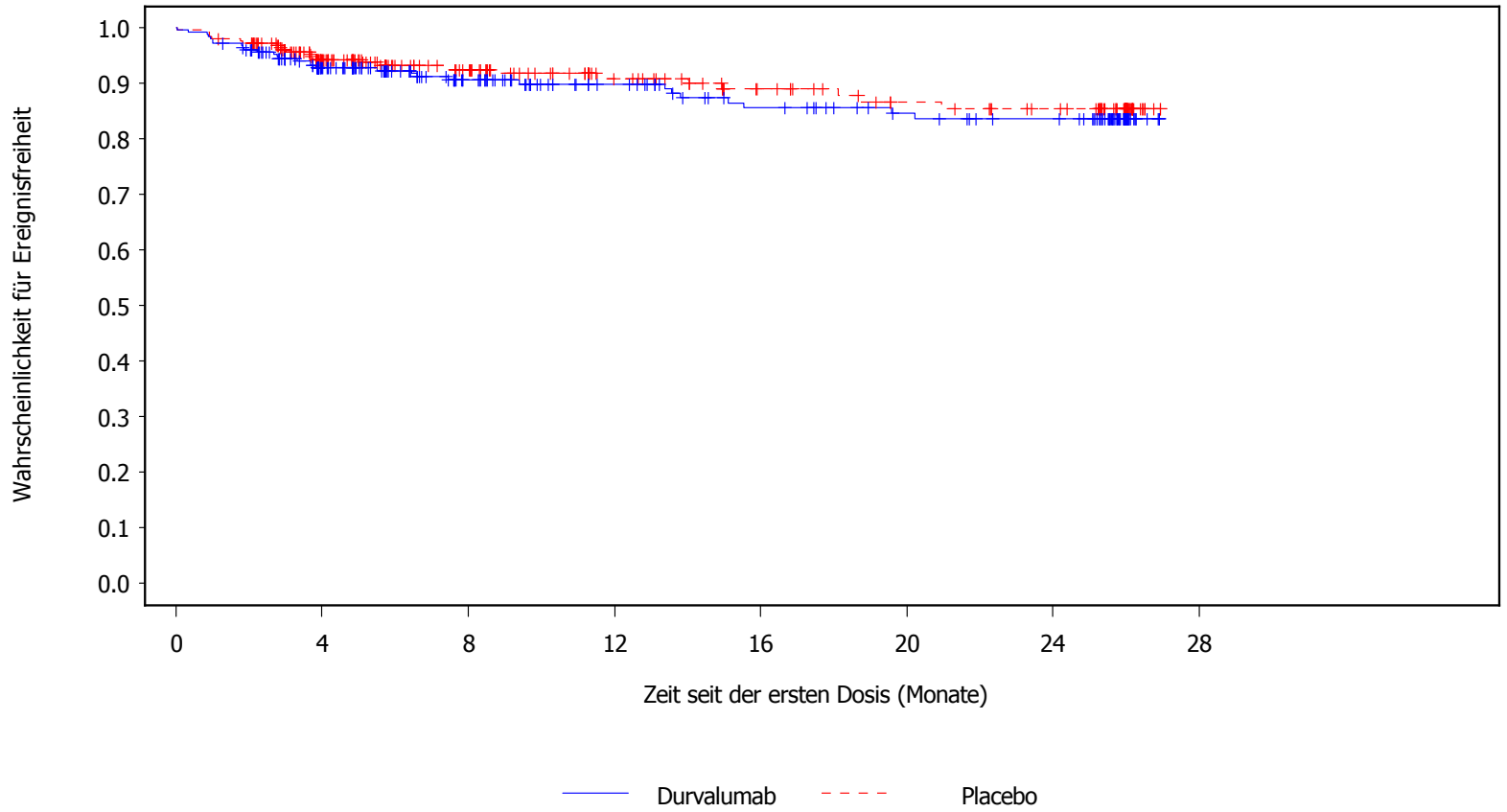
Anzahl an Patienten unter Risiko:

262	199	144	114	101	93	85	0	Durvalumab
265	195	139	103	81	69	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bas 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.20 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Blutes und des Lymphsystems
Safety Analysis Set, DCO 15JAN2024



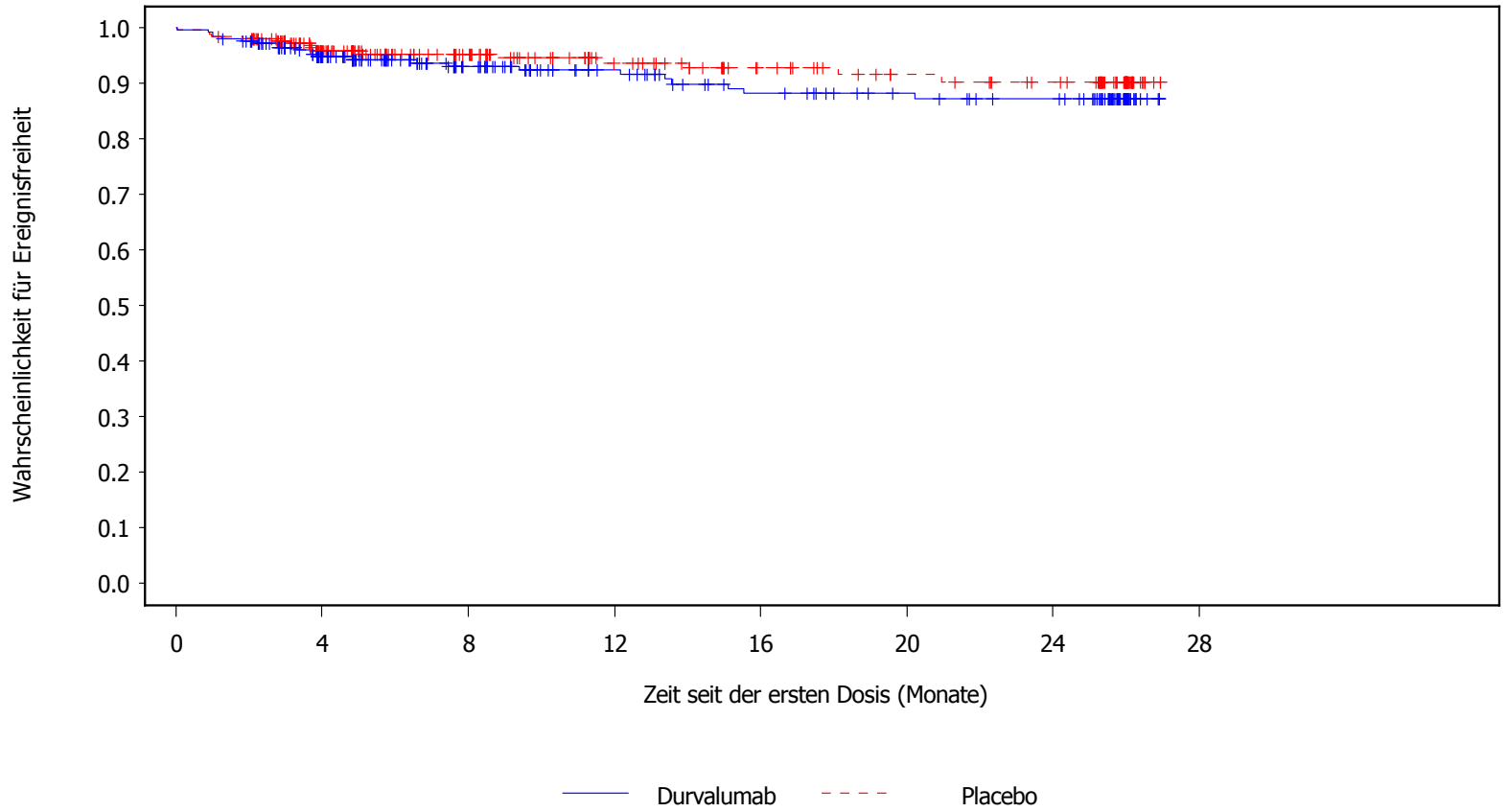
Anzahl an Patienten unter Risiko:

262	197	145	114	97	87	81	0	Durvalumab
265	192	137	102	82	70	63	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bat 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.21 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Anaemie
Safety Analysis Set, DCO 15JAN2024

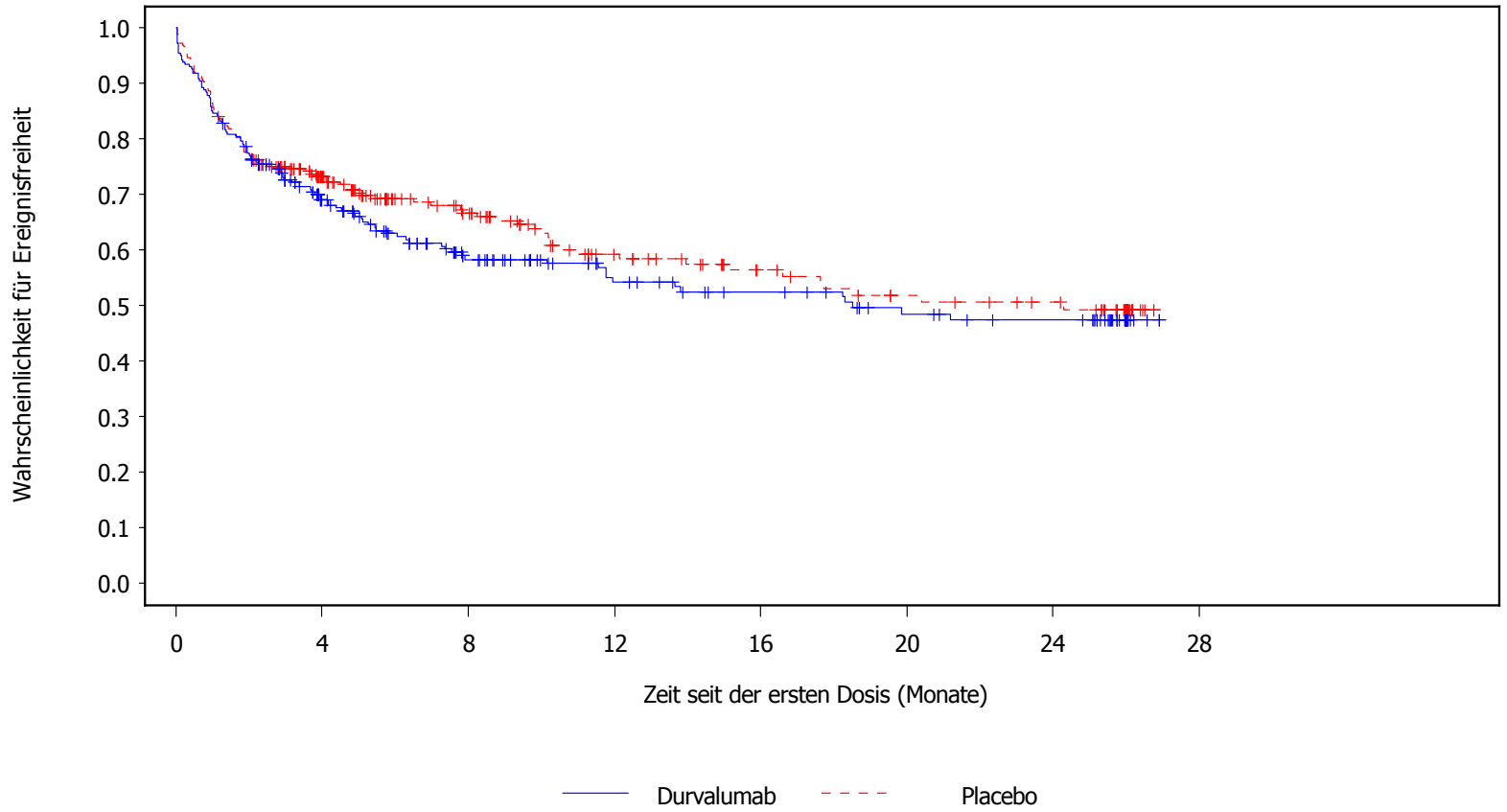


Anzahl an Patienten unter Risiko:

262	200	148	117	100	91	85	0	Durvalumab
265	196	141	105	85	73	66	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bau 05JUN2025:07:

Figure 2.3.22 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 15JAN2024



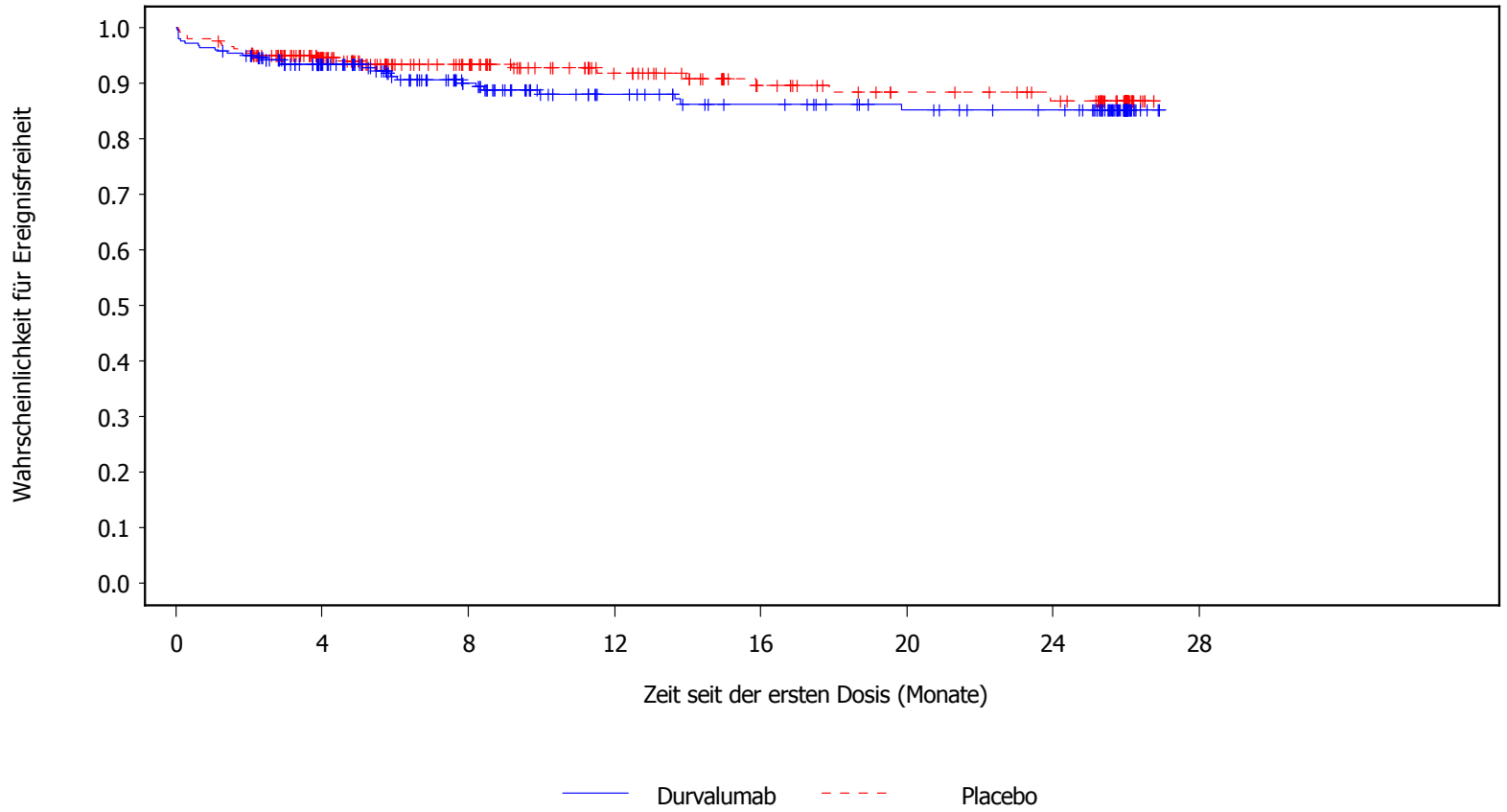
Anzahl an Patienten unter Risiko:

262	141	93	66	56	46	41	0	Durvalumab
265	156	102	68	52	43	38	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bav 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.23 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Diarrhoe
Safety Analysis Set, DCO 15JAN2024



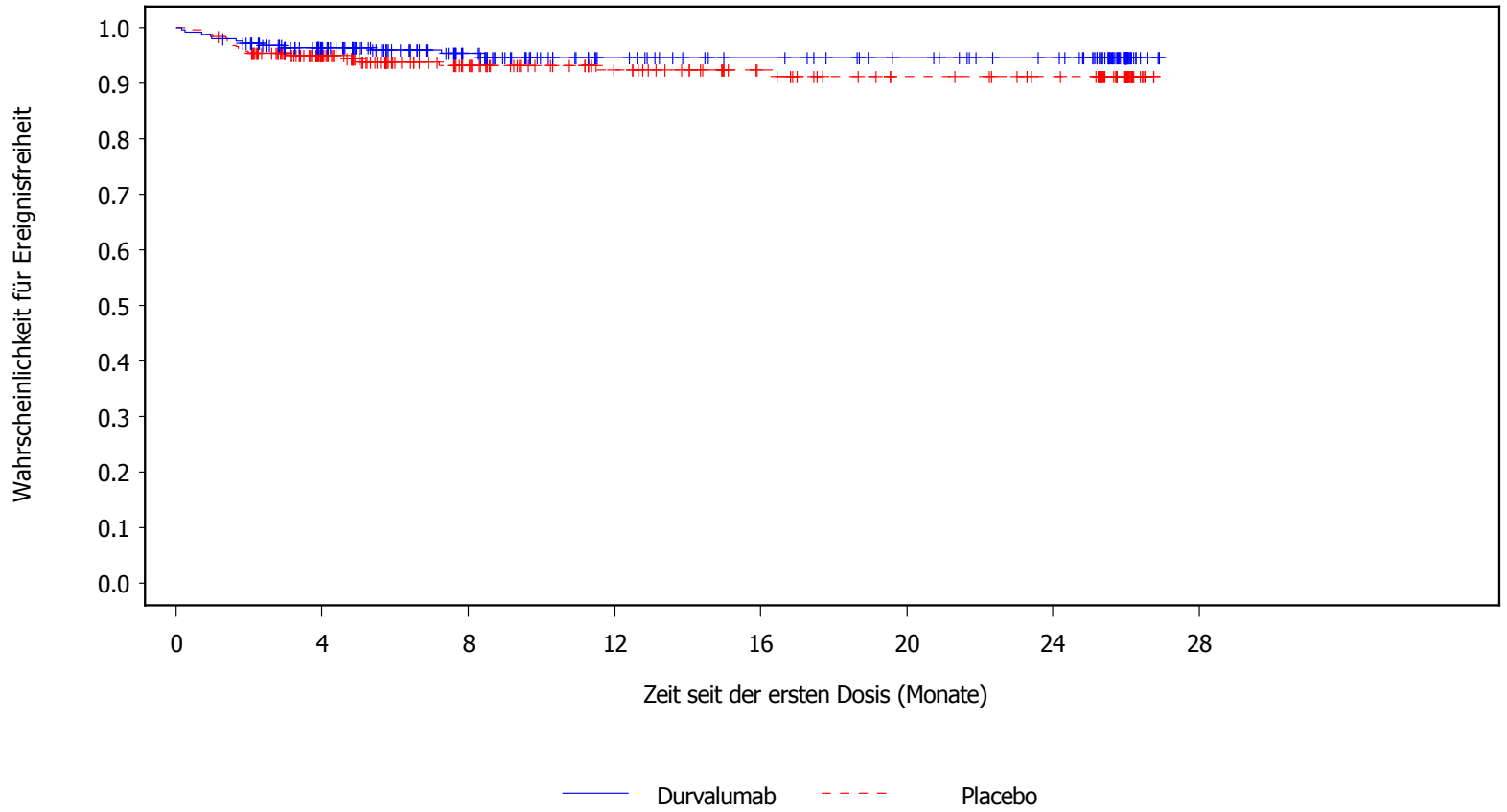
Anzahl an Patienten unter Risiko:

262	195	142	107	95	86	80	0	Durvalumab
265	195	137	100	76	64	58	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baw 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.24 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Erbrechen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	203	150	116	105	97	89	0	Durvalumab
265	193	137	105	85	72	66	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bax 05JUN2025:07:

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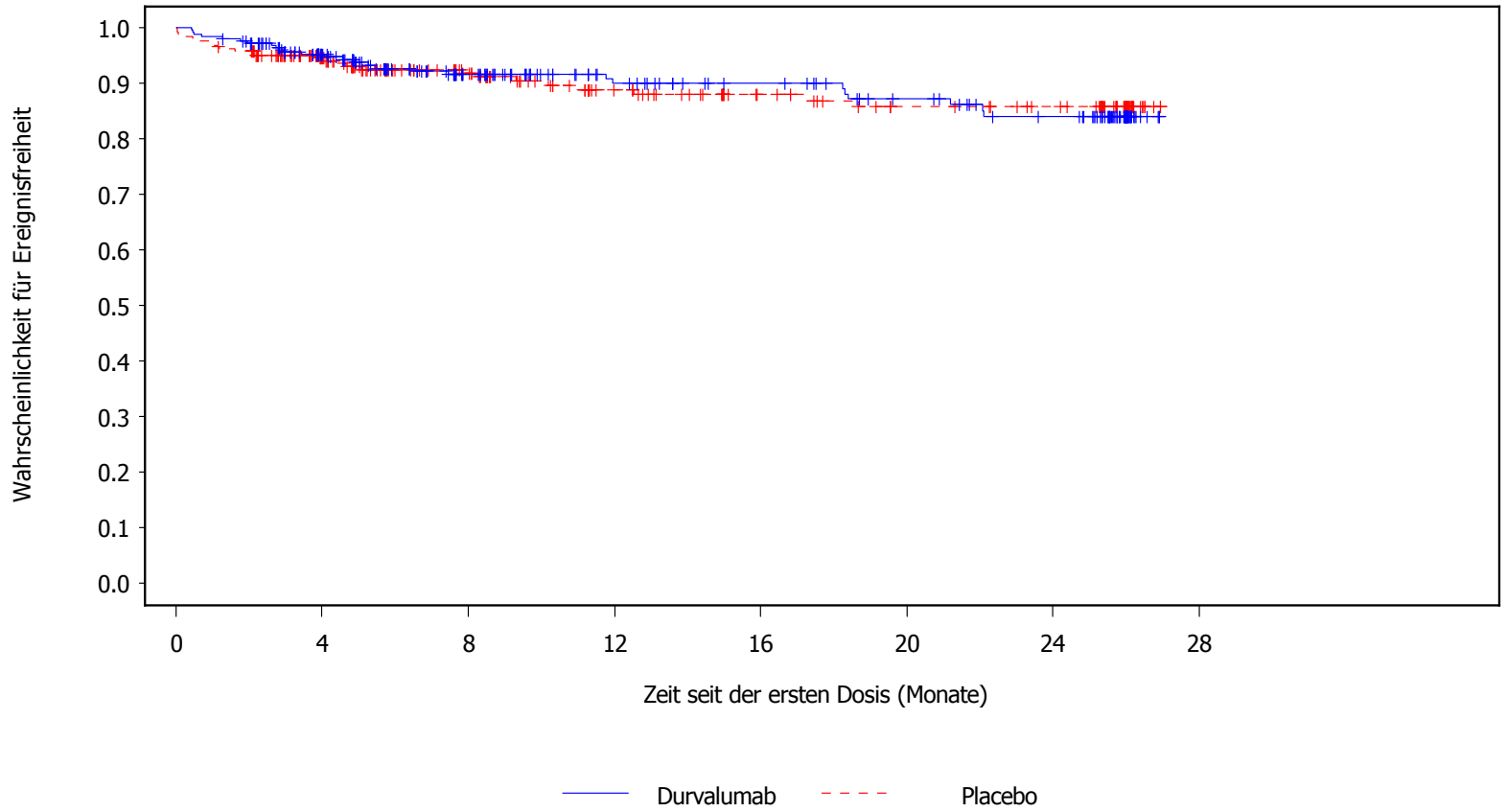
Figure 2.3.25 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Obstipation
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	201	148	113	101	89	78	0	Durvalumab
265	198	138	103	82	70	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bay 05JUN2025:07:

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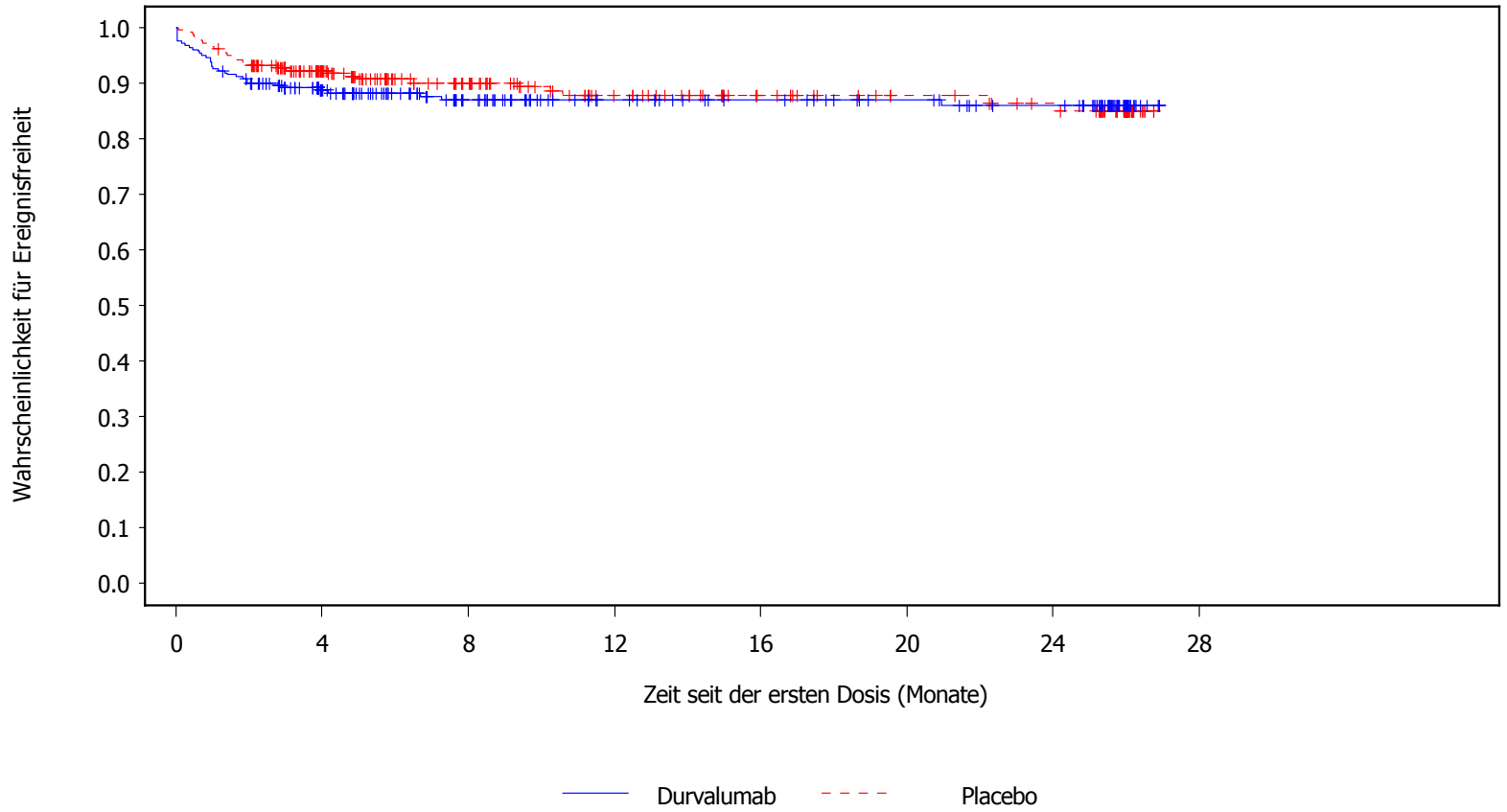
Figure 2.3.26 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Uebelkeit
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	185	136	106	96	88	80	0	Durvalumab
265	188	134	100	80	69	63	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1baz 05JUN2025:07:

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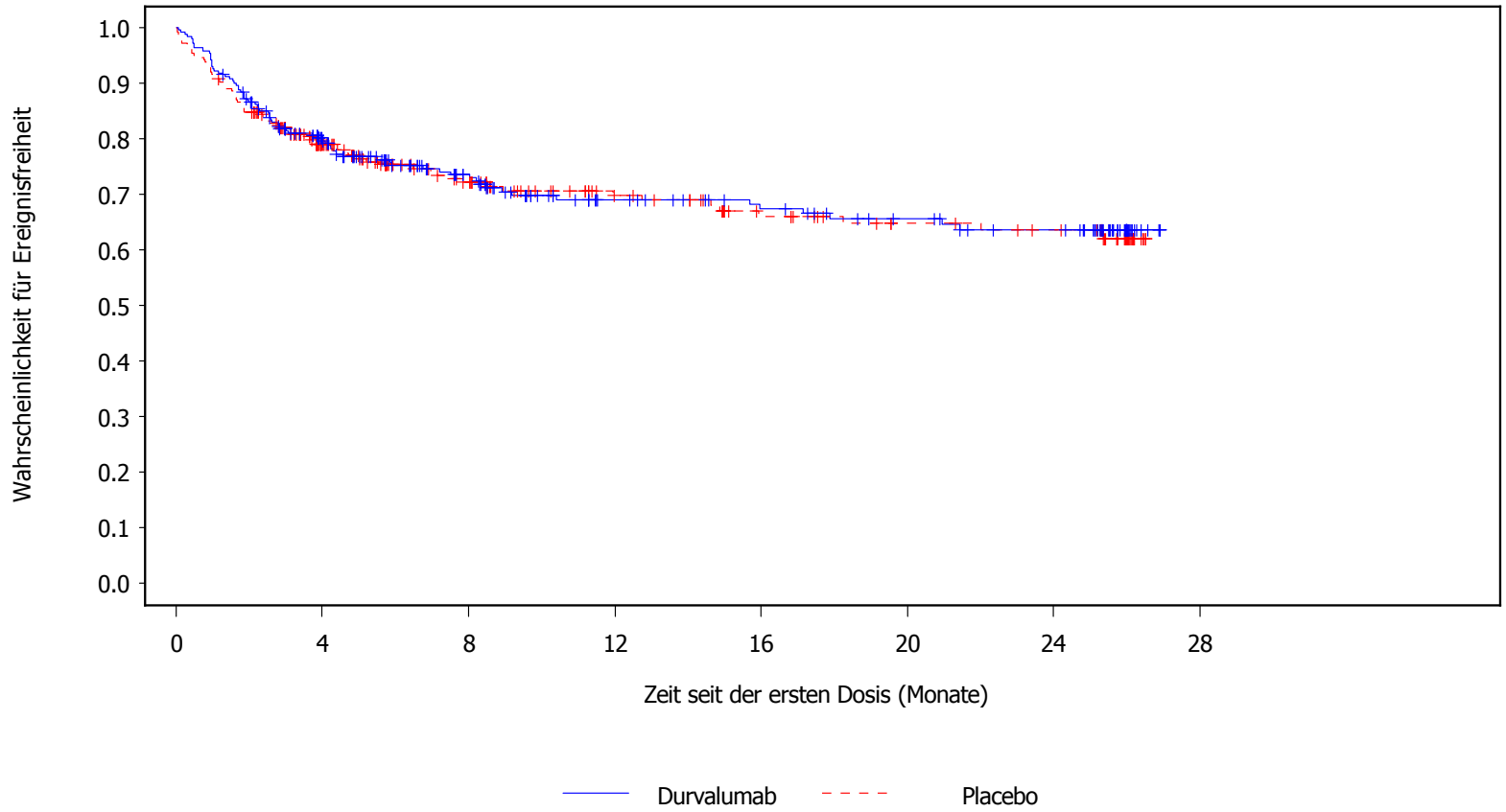
Figure 2.3.27 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Nervensystems
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	172	123	89	79	70	63	0	Durvalumab
265	165	109	80	62	52	48	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bba 05JUN2025:07:

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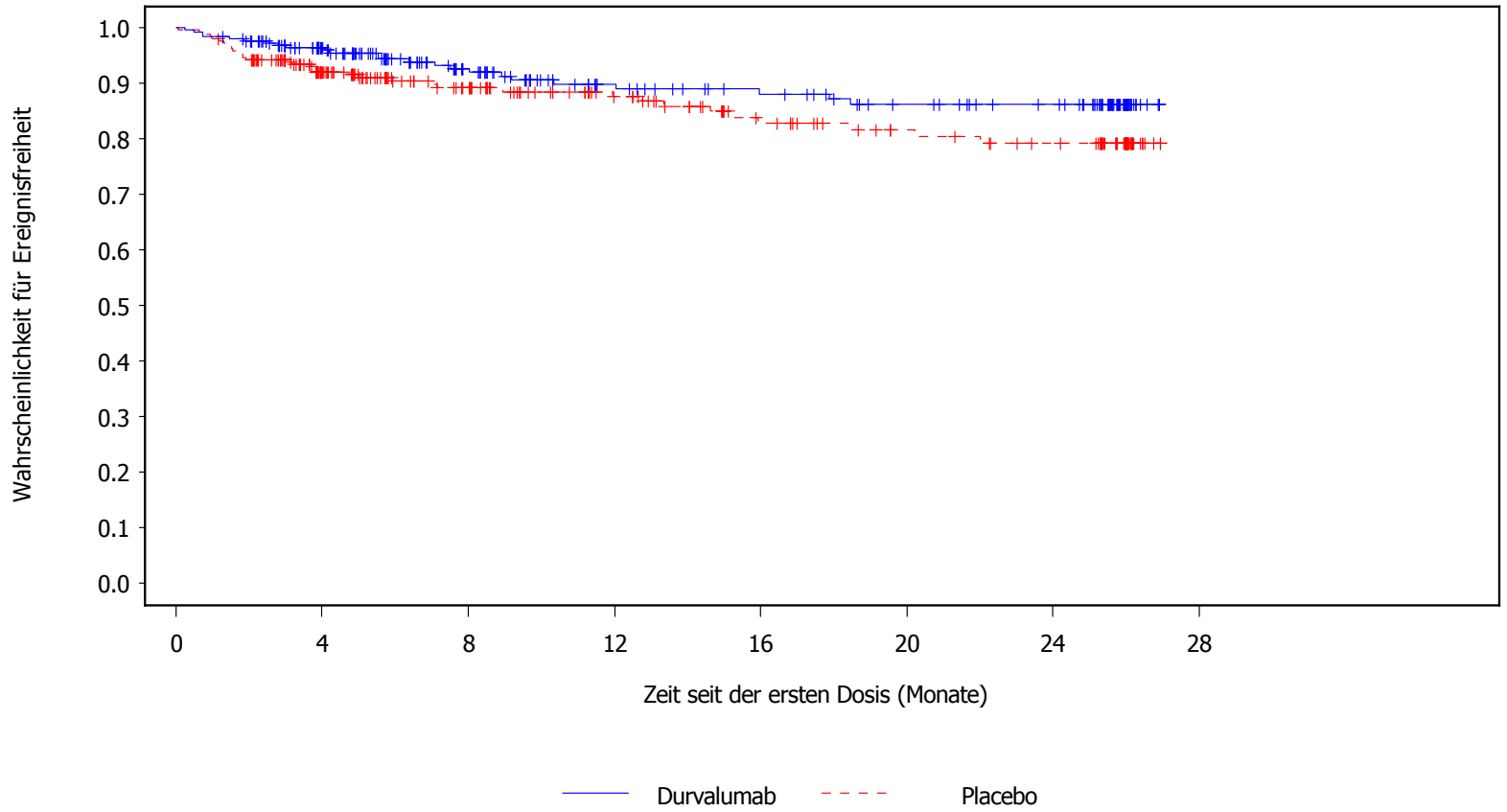
Figure 2.3.28 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Kopfschmerzen
Safety Analysis Set, DCO 15JAN2024



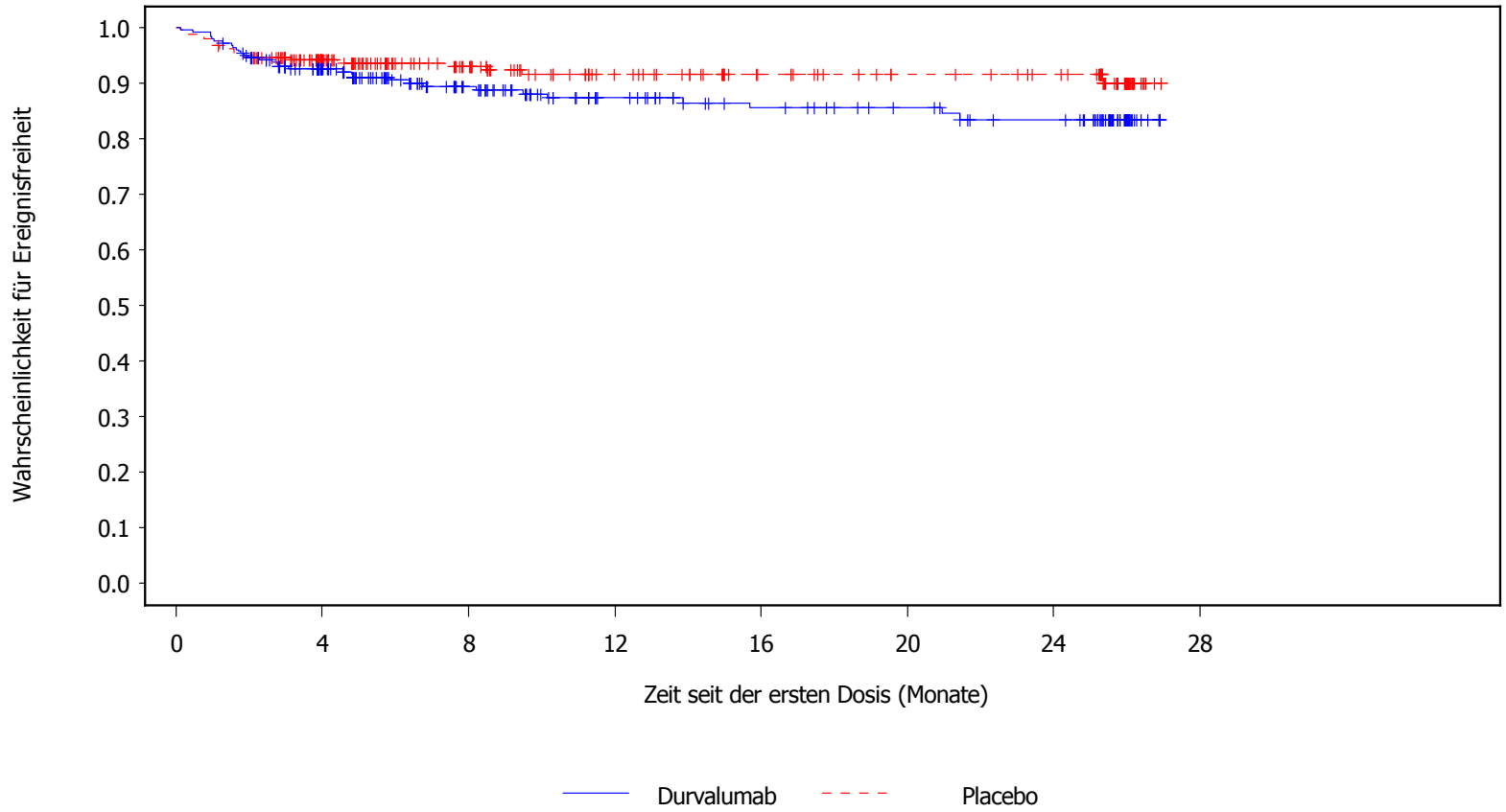
Anzahl an Patienten unter Risiko:

262	202	144	110	99	88	80	0	Durvalumab
265	191	137	105	80	67	60	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbb 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.29 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Schwindelgefuehl
Safety Analysis Set, DCO 15JAN2024

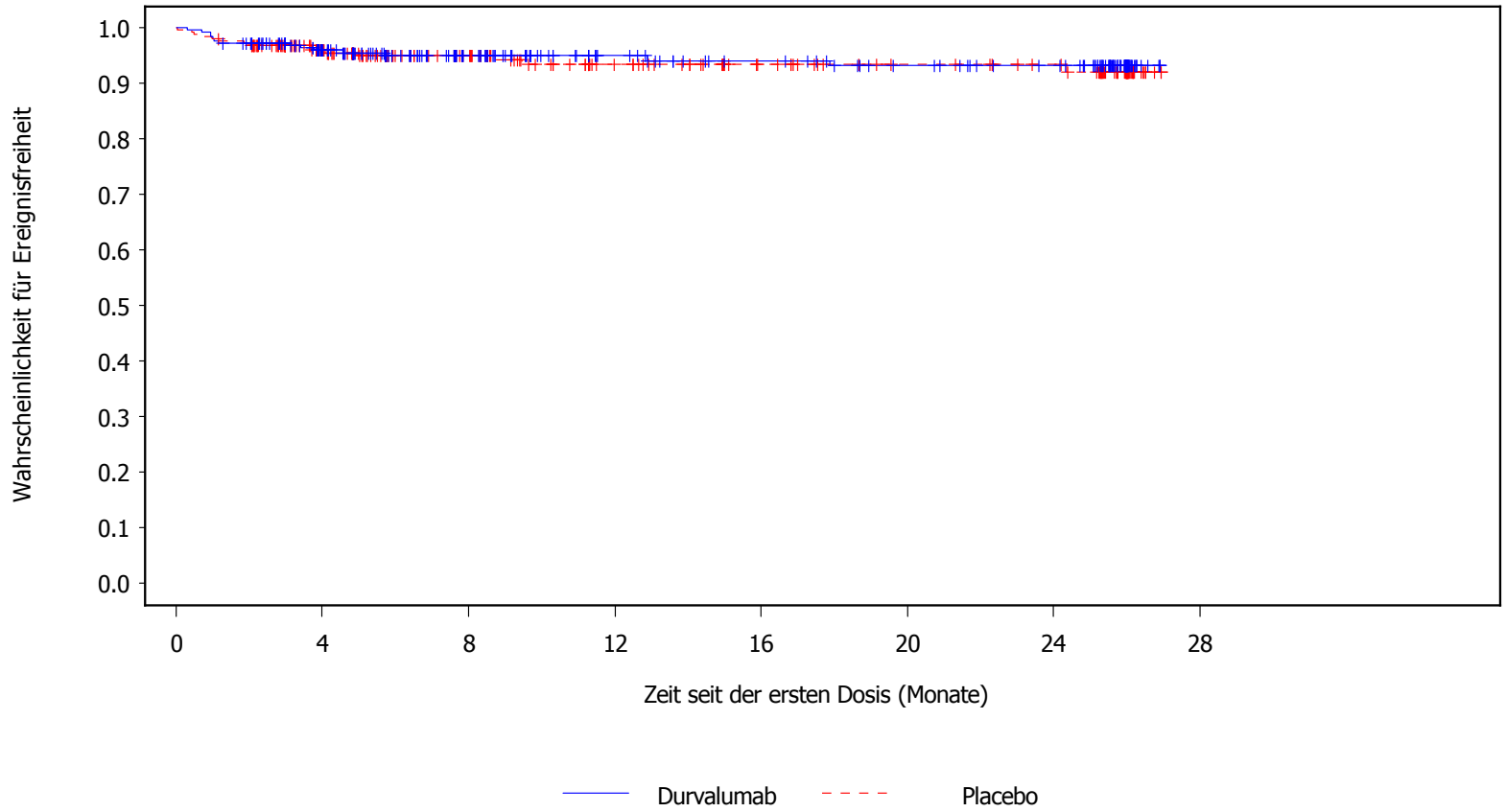


Anzahl an Patienten unter Risiko:

262	197	143	108	93	85	77	0	Durvalumab
265	194	137	103	84	74	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbc 05JUN2025:07:

Figure 2.3.30 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Ohrs und des Labyrinths
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	201	150	116	103	93	85	0	Durvalumab
265	196	140	104	84	73	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbd 05JUN2025:07:

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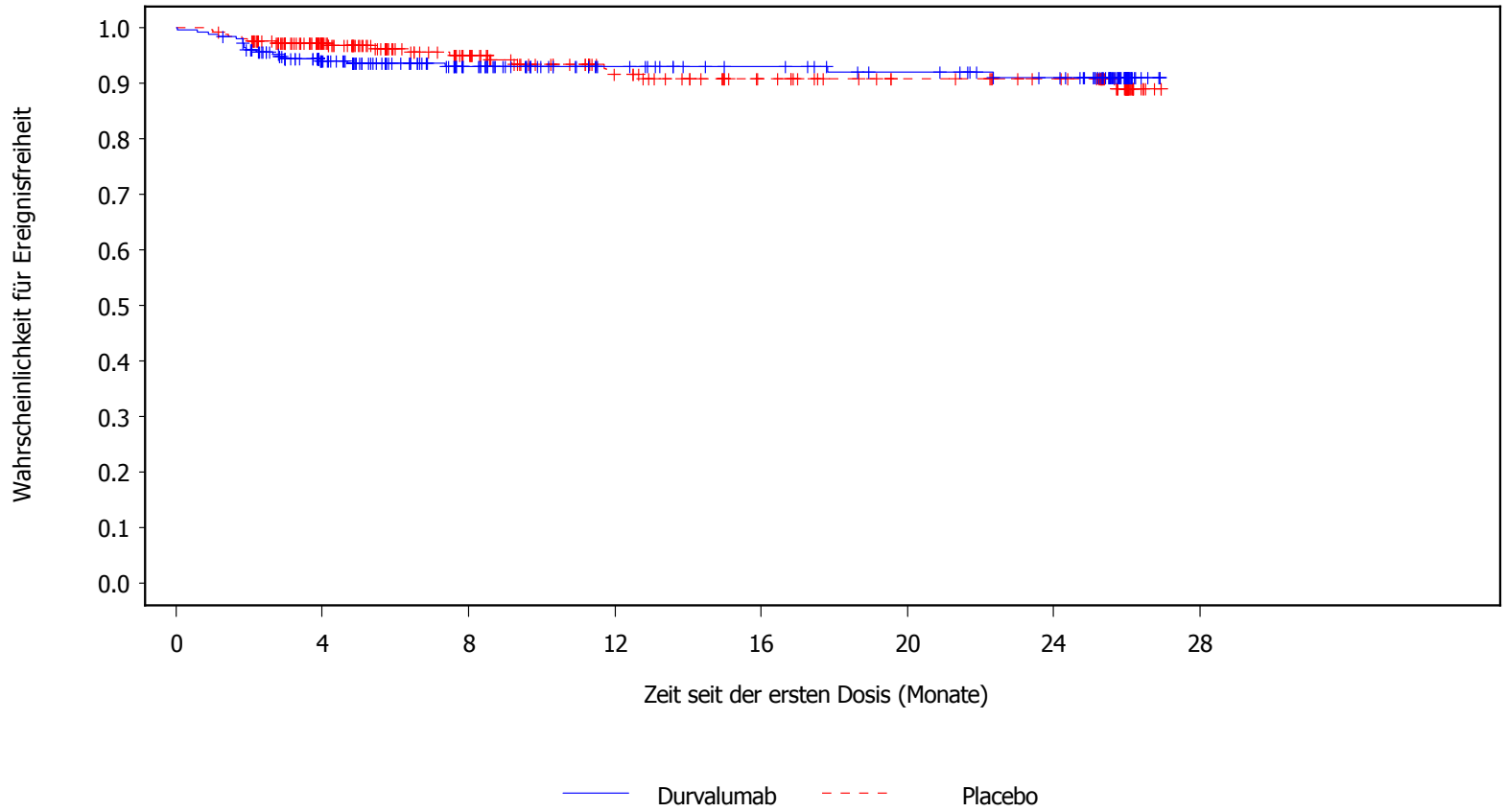
Figure 2.3.31 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Gefaesserkrankungen
Safety Analysis Set, DCO 15JAN2024



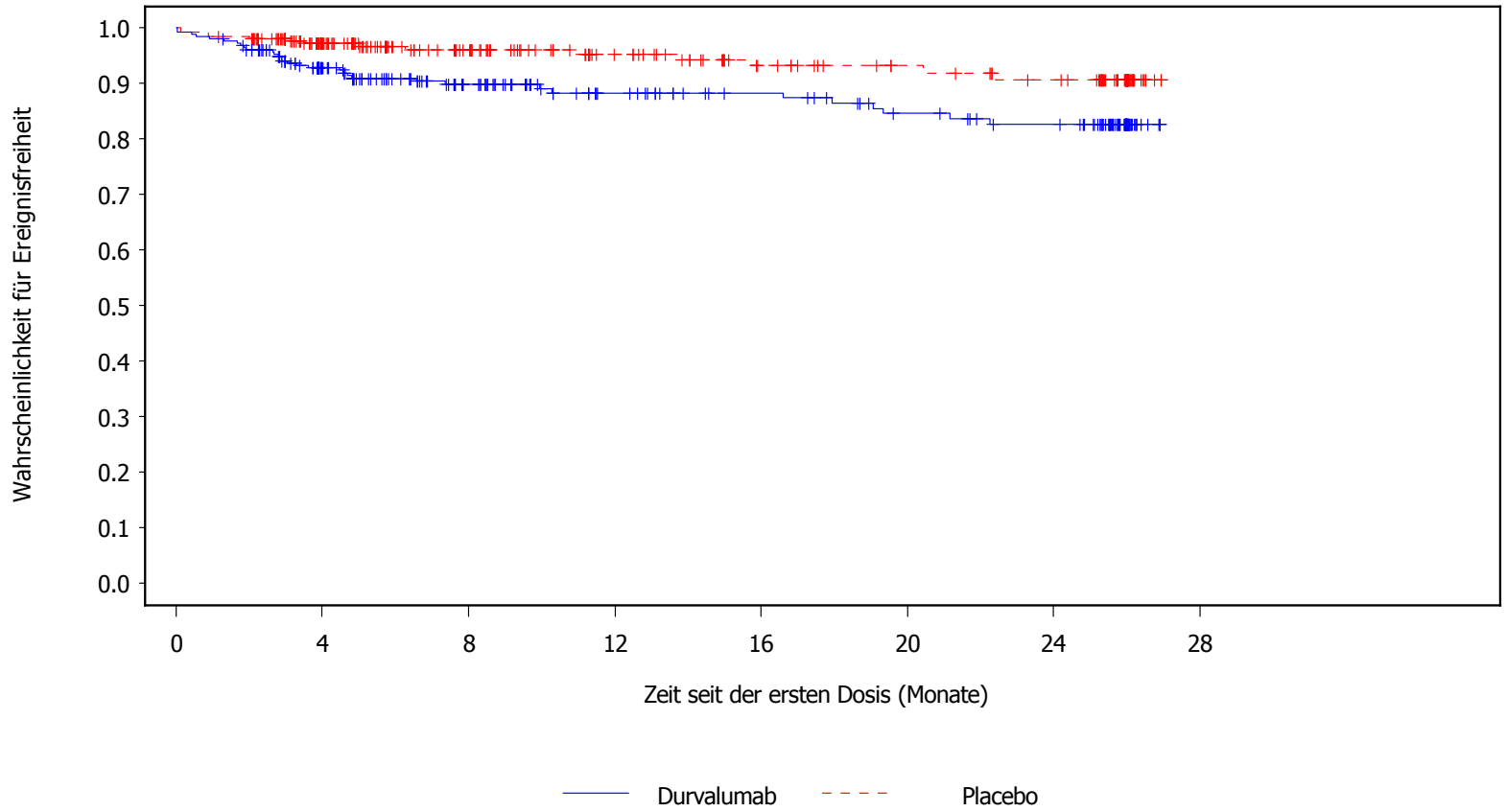
Anzahl an Patienten unter Risiko:

262	196	144	112	102	95	87	0	Durvalumab
265	201	141	103	83	71	65	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbe 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.32 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Herzerkrankungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	197	145	111	98	87	80	0	Durvalumab
265	199	142	107	84	74	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbf 05JUN2025:07:

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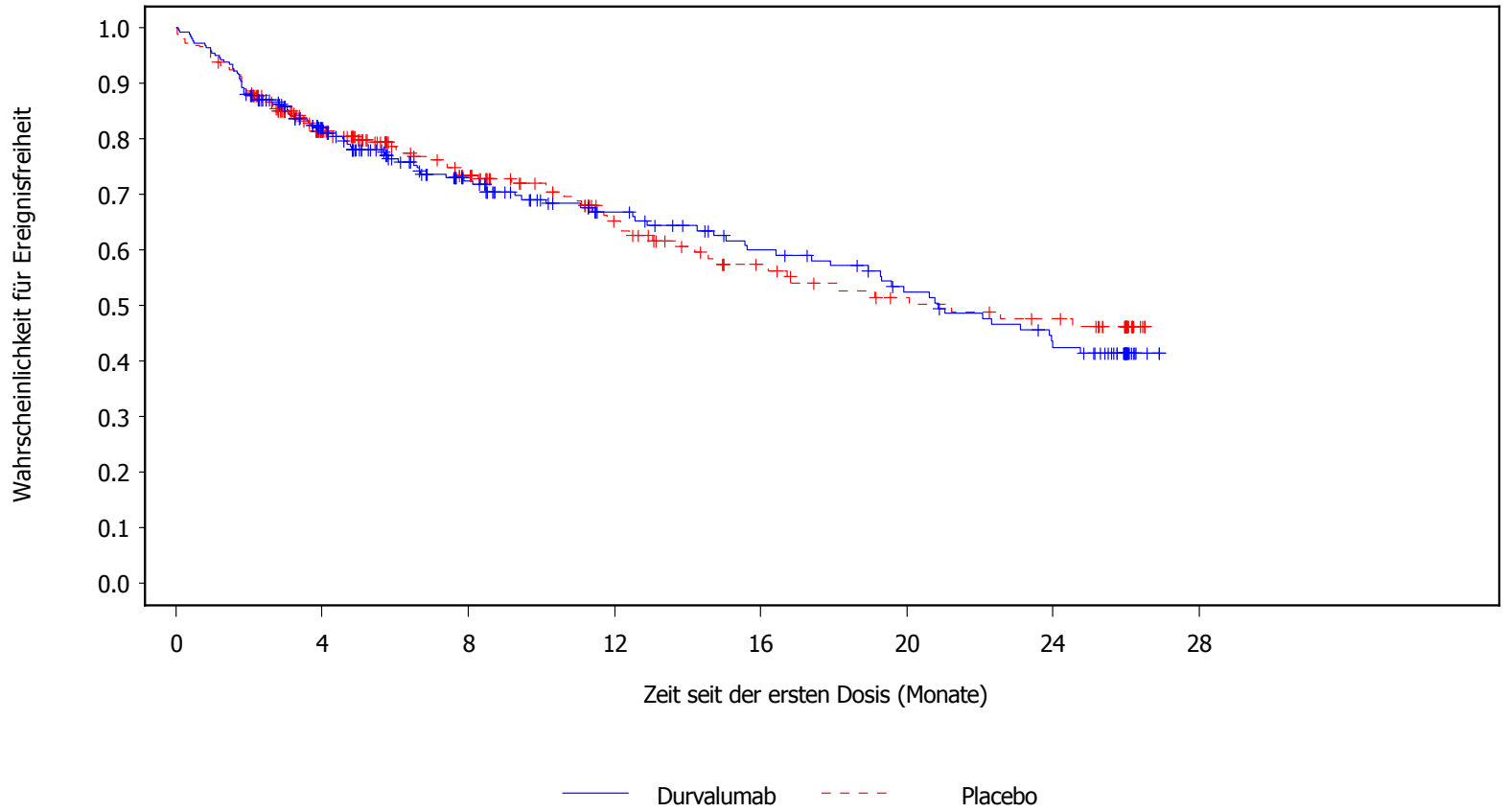
Figure 2.3.33 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 15JAN2024



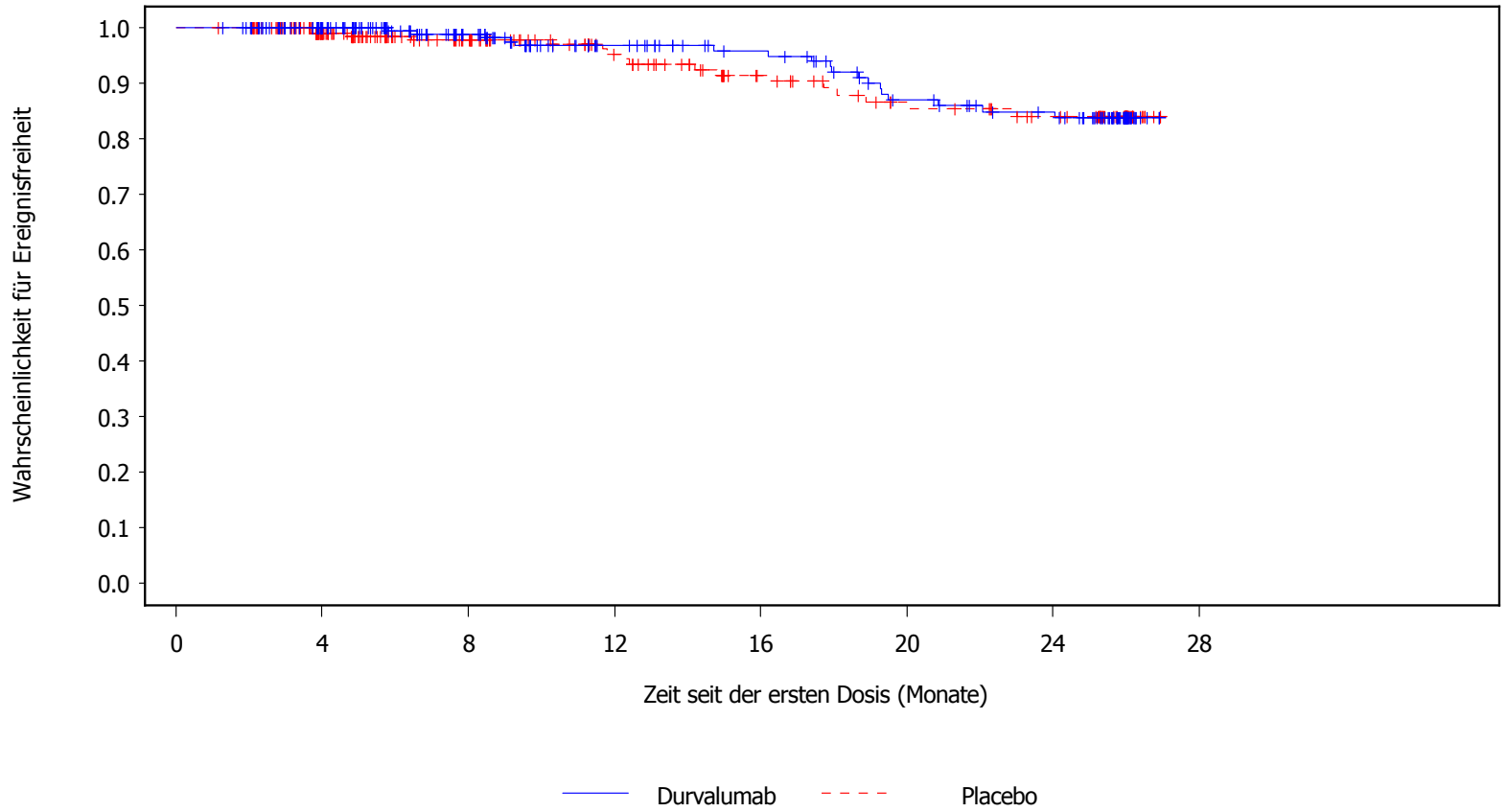
Anzahl an Patienten unter Risiko:

262	173	115	83	67	54	42	0	Durvalumab
265	165	108	71	50	40	35	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbg 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.34 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: COVID-19
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	154	118	104	85	76	0	Durvalumab
265	203	143	106	81	67	58	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbh 05JUN2025:07:

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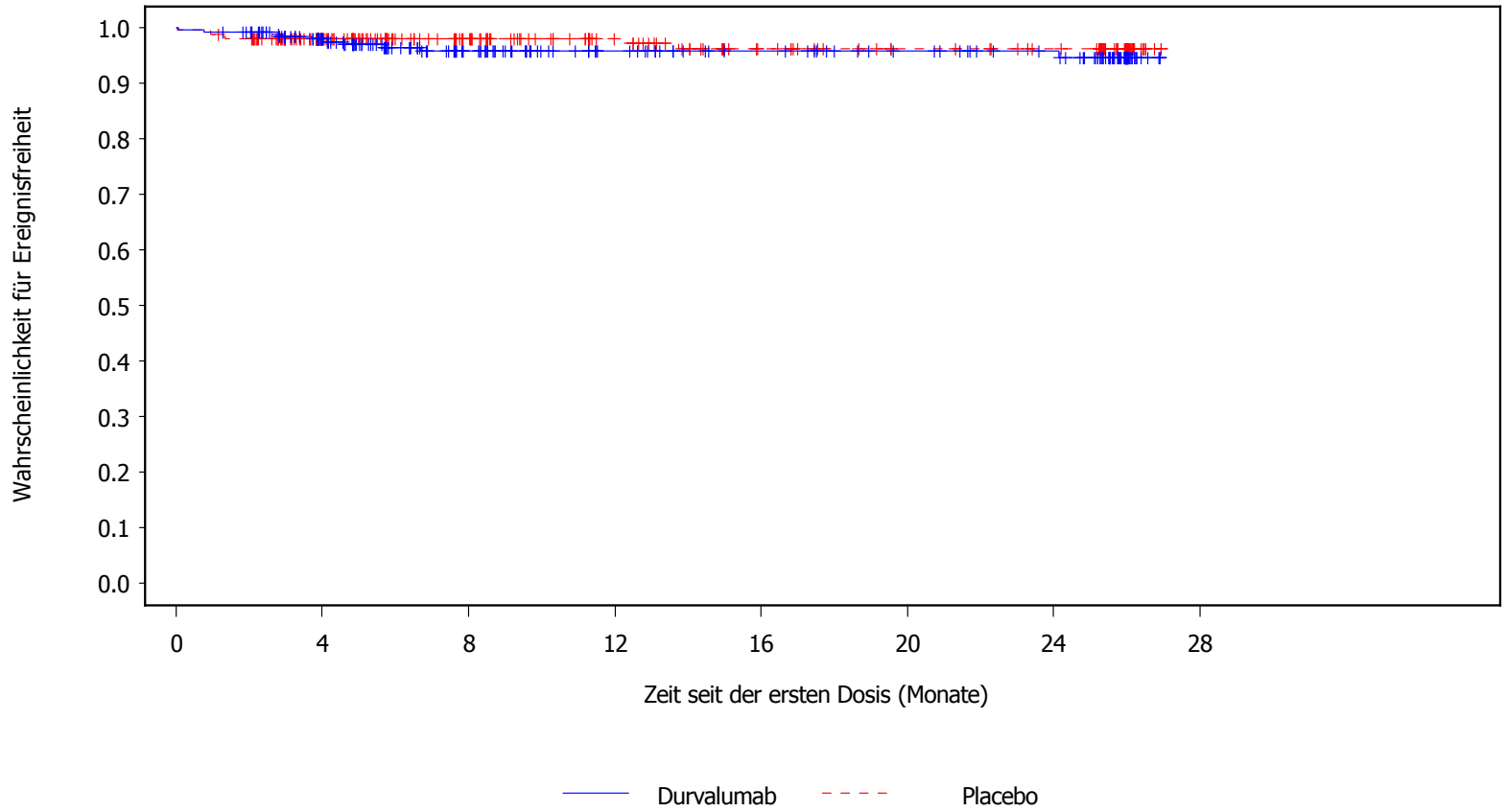
Figure 2.3.35 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Harnwegsinfektion
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	204	147	115	102	93	85	0	Durvalumab
265	202	144	109	85	73	67	0	Placebo

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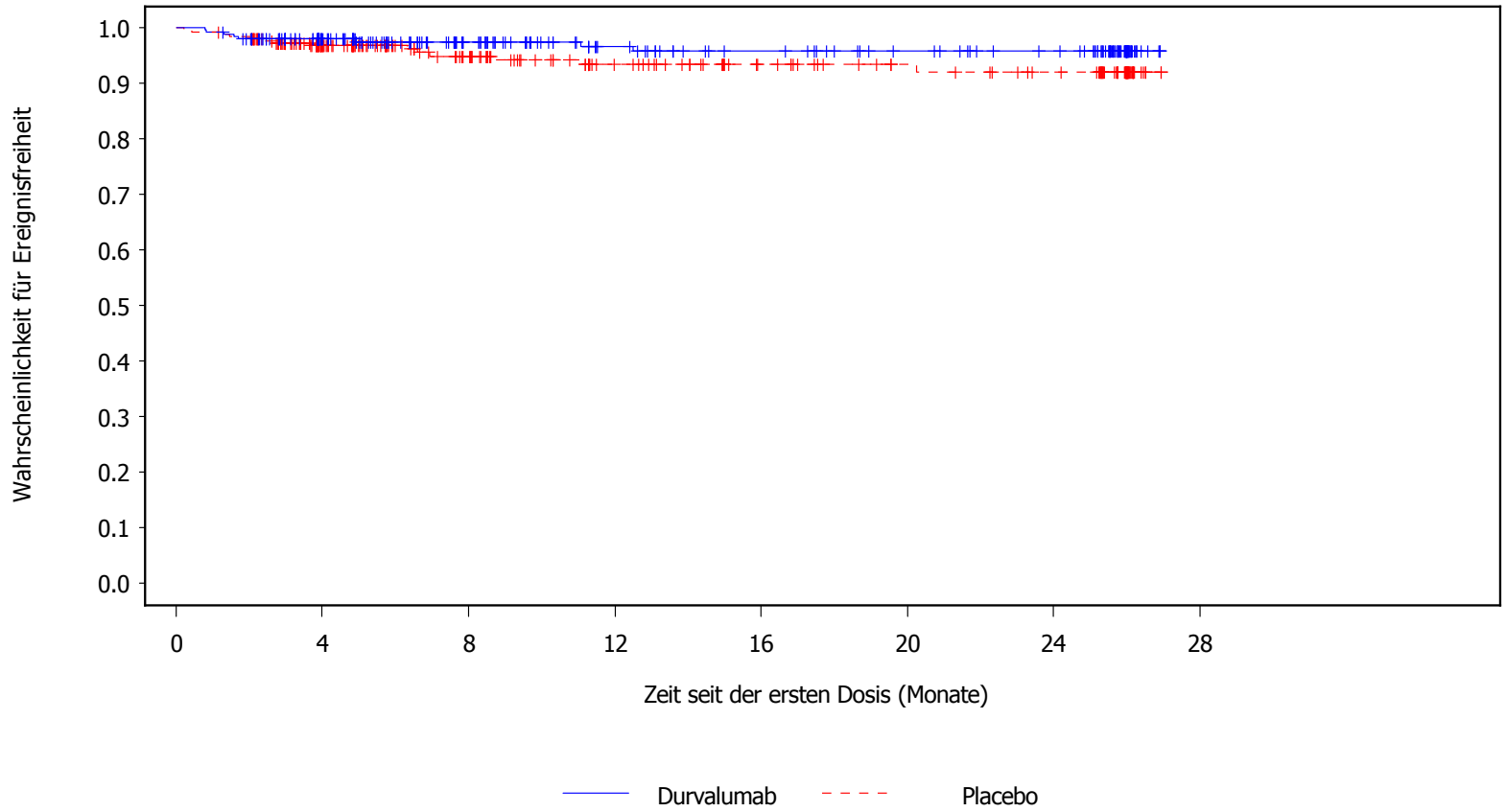
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.36 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Infektion der oberen Atemwege
Safety Analysis Set, DCO 15JAN2024



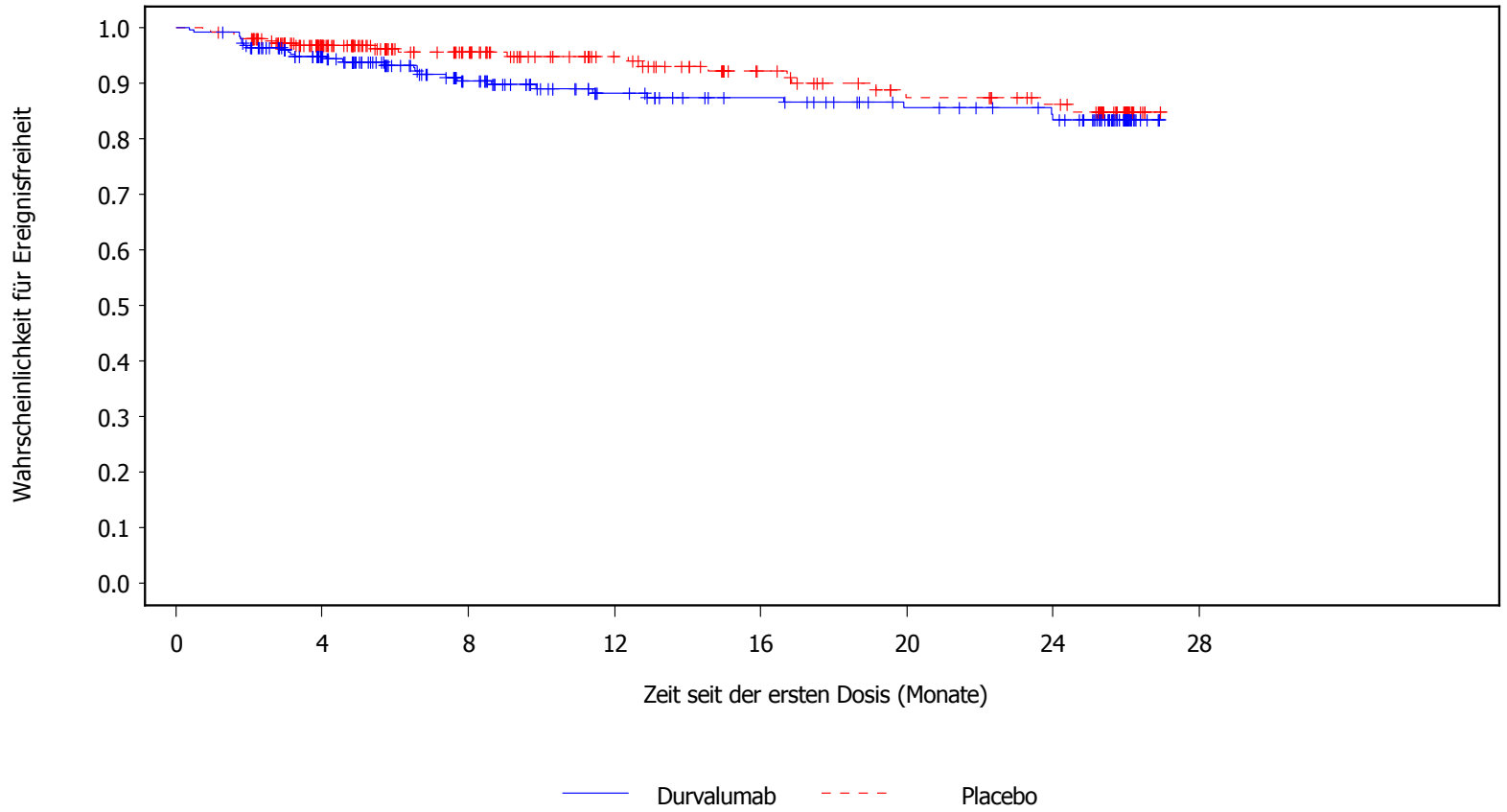
Anzahl an Patienten unter Risiko:

262	204	151	117	103	93	85	0	Durvalumab
265	197	141	105	84	72	65	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbj 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.37 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Pneumonie
Safety Analysis Set, DCO 15JAN2024



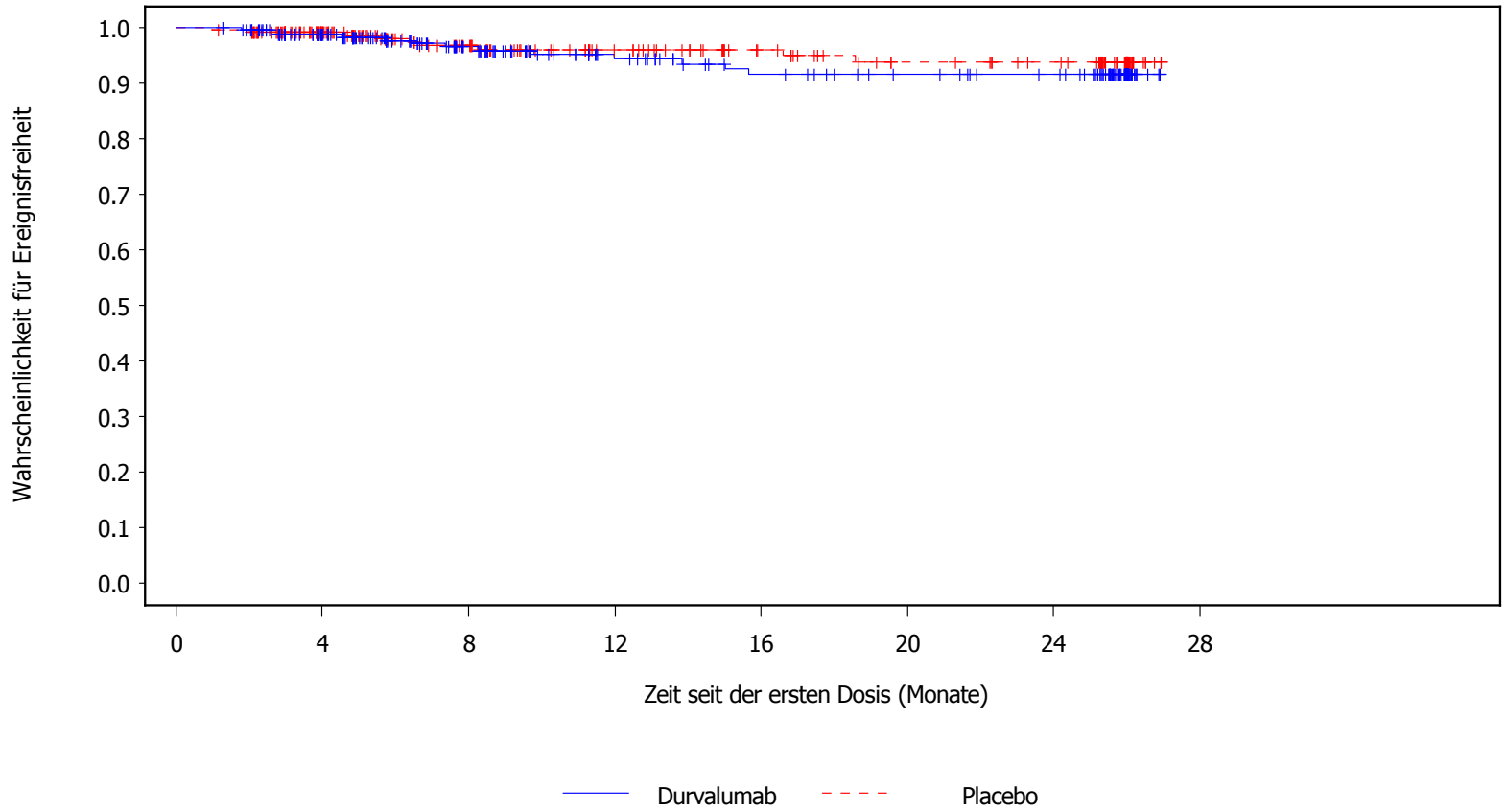
Anzahl an Patienten unter Risiko:

262	200	144	110	98	87	80	0	Durvalumab
265	199	143	108	85	71	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbk 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.38 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Leber- und Gallenerkrankungen
Safety Analysis Set, DCO 15JAN2024



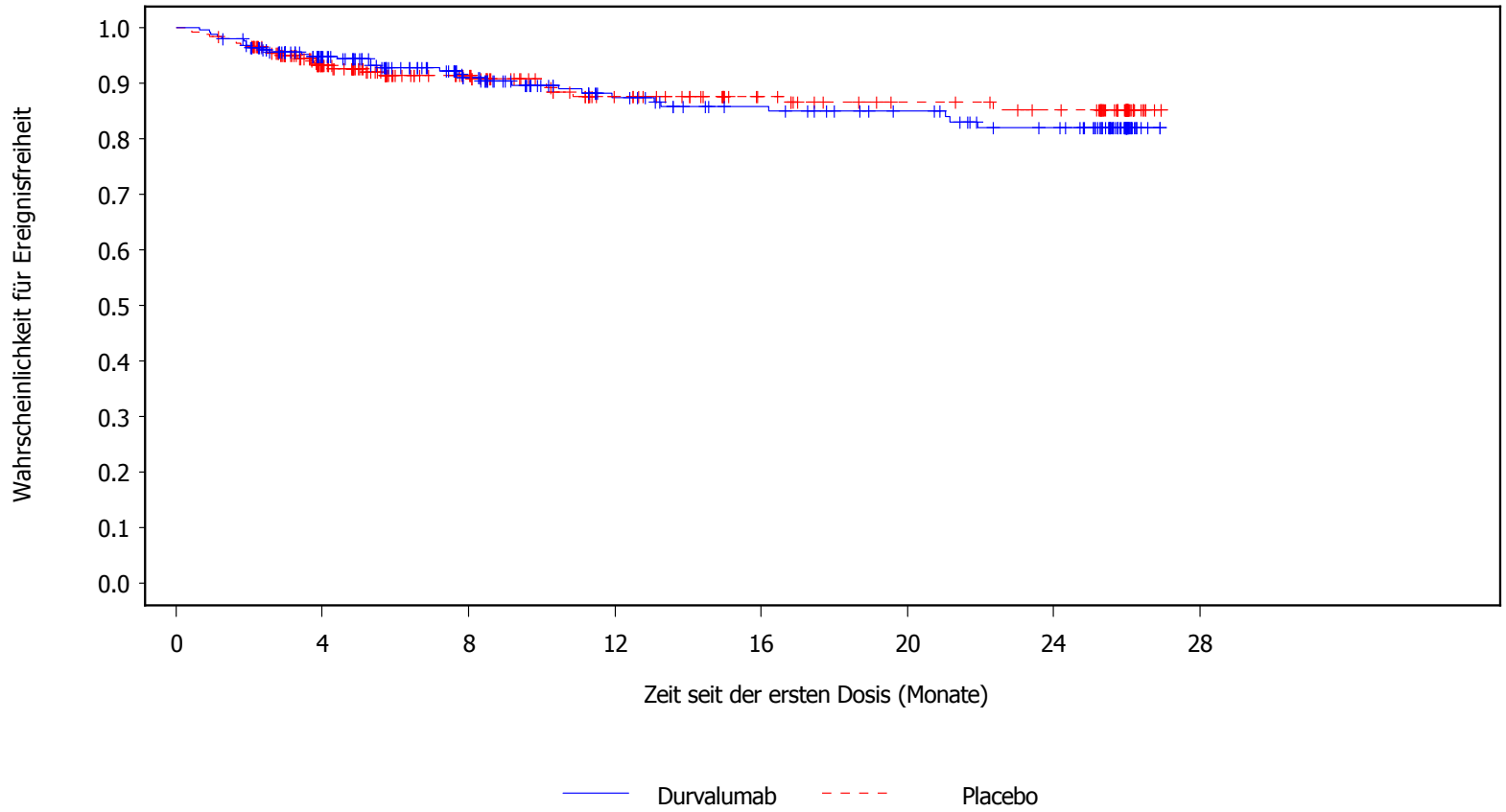
Anzahl an Patienten unter Risiko:

262	207	151	116	100	92	86	0	Durvalumab
265	203	142	108	86	72	66	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbl 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.39 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Psychiatrische Erkrankungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	197	148	113	100	91	80	0	Durvalumab
265	192	136	100	80	69	64	0	Placebo

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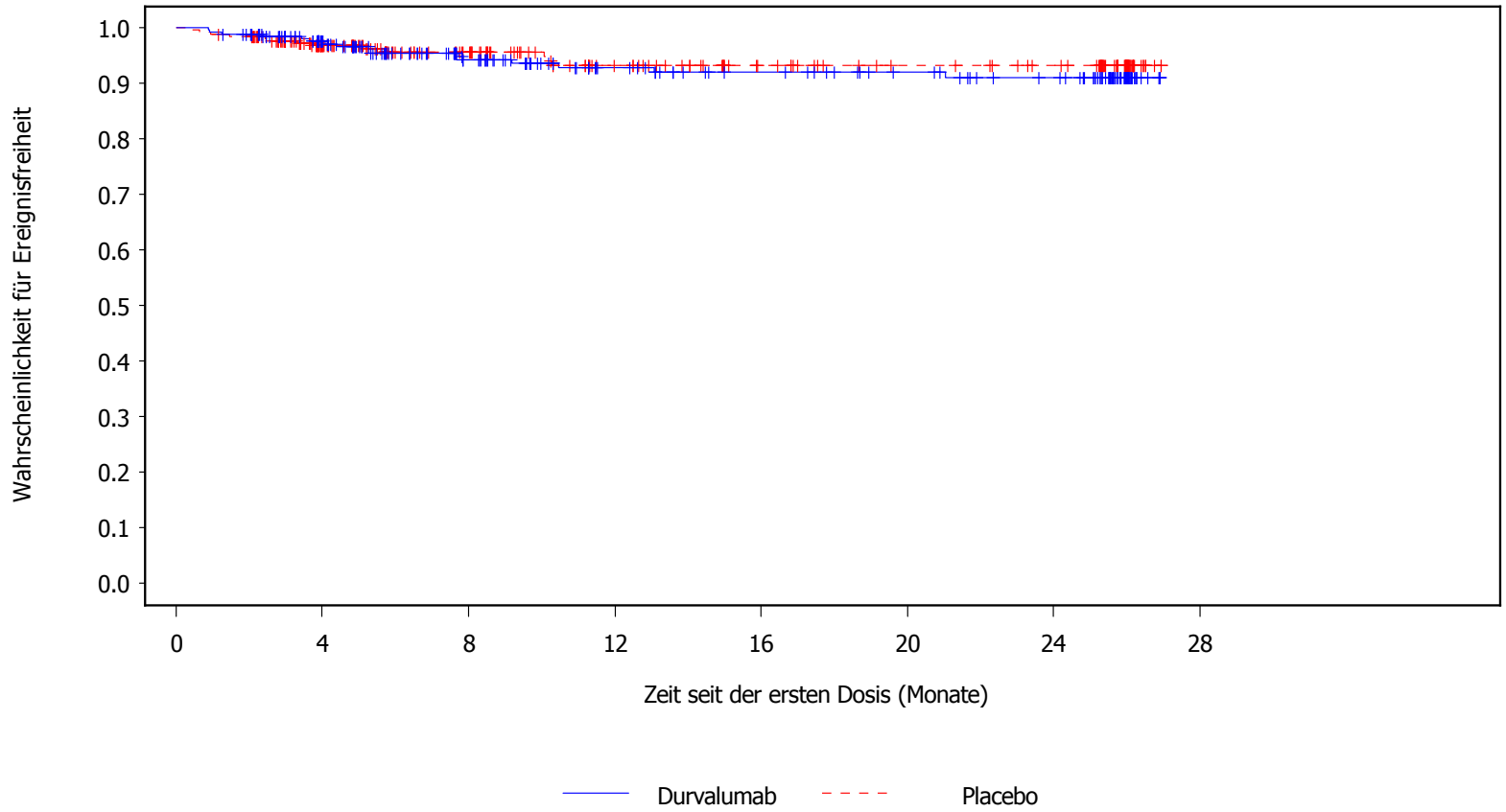
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.40 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Schlaflosigkeit
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	203	150	116	103	94	85	0	Durvalumab
265	199	144	107	86	75	69	0	Placebo

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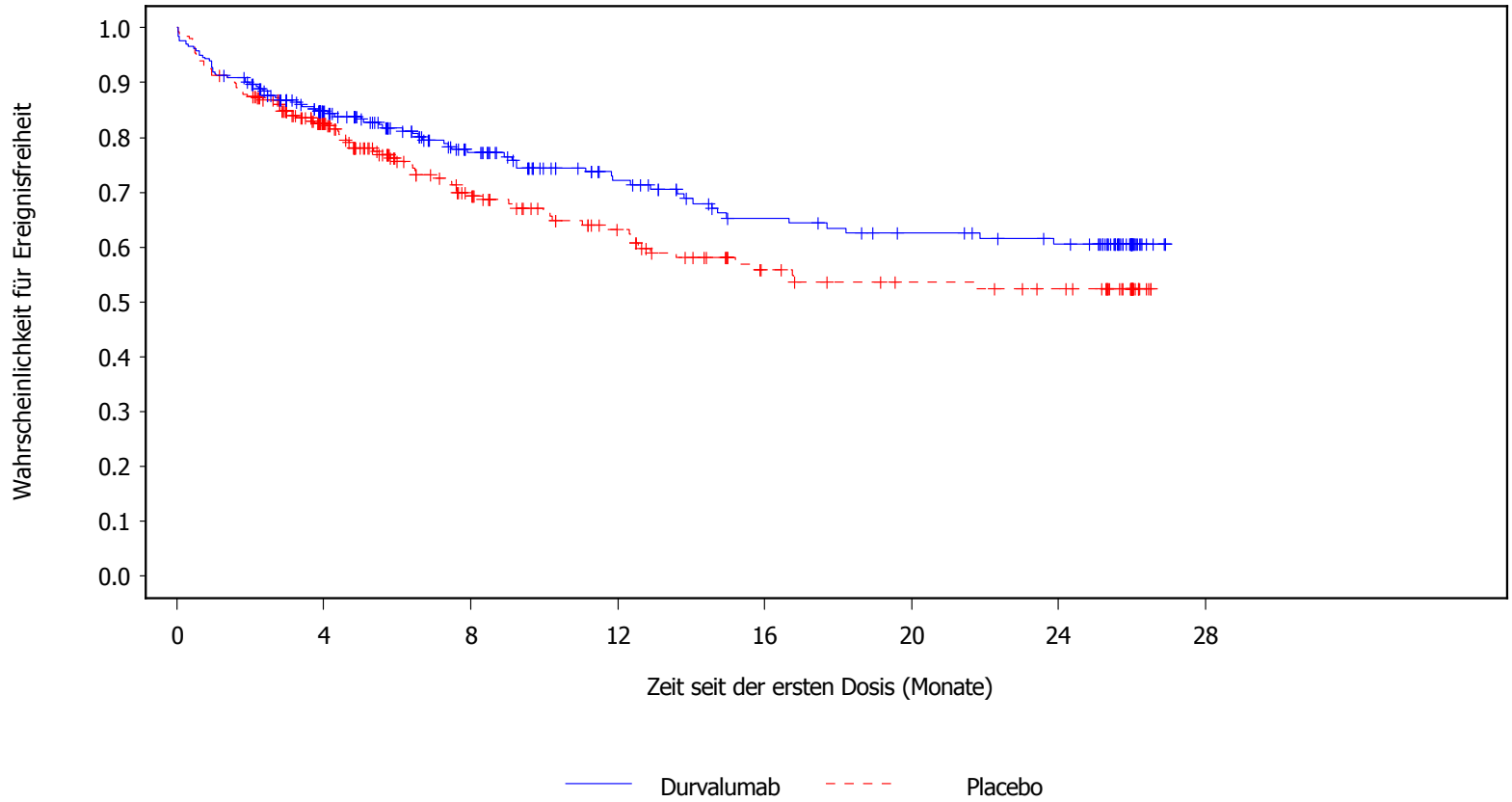
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.41 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen
Safety Analysis Set, DCO 15JAN2024



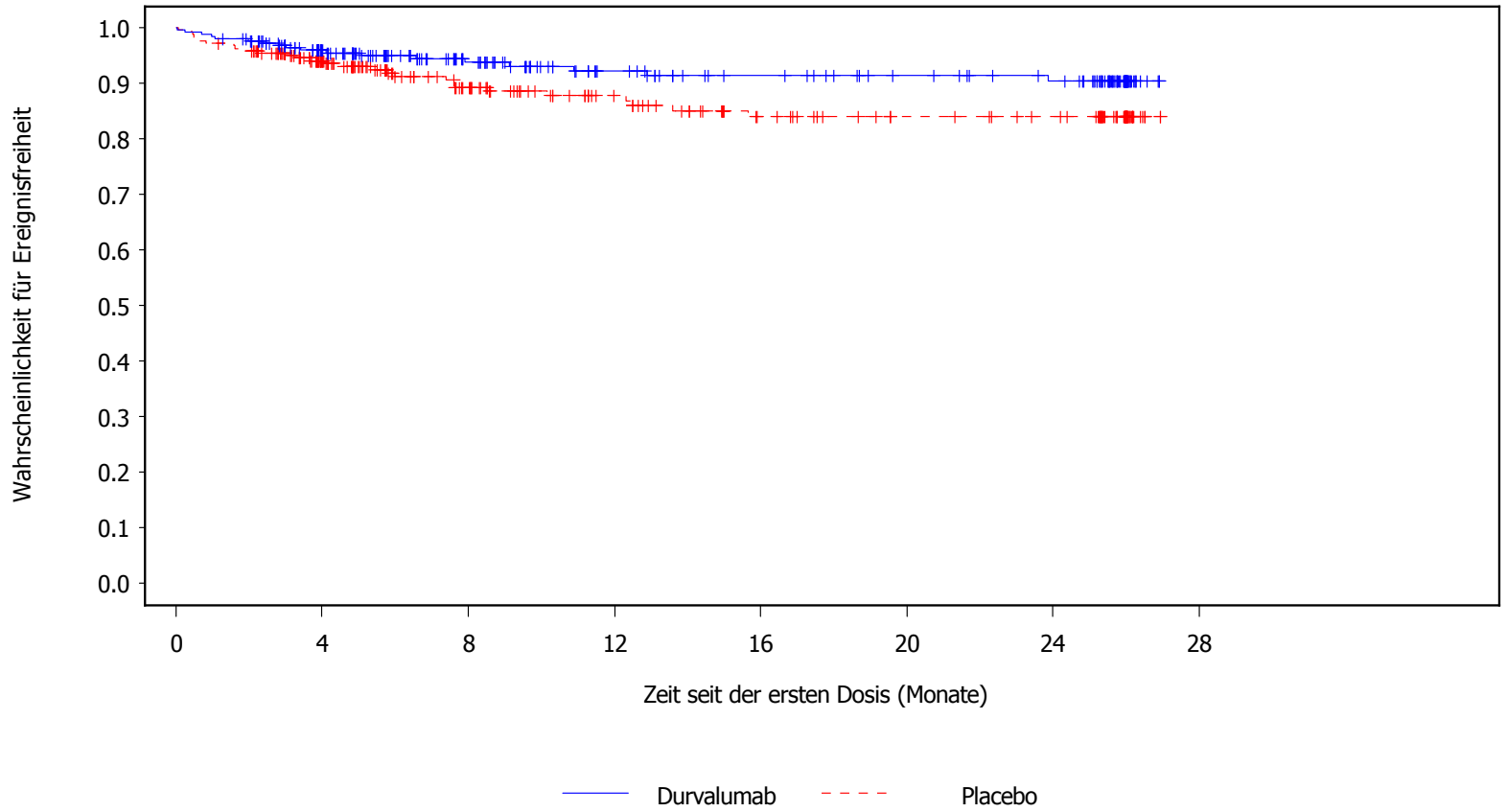
Anzahl an Patienten unter Risiko:

262	180	126	91	72	65	59	0	Durvalumab
265	171	103	75	51	44	40	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbo 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.42 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Arthralgie
Safety Analysis Set, DCO 15JAN2024



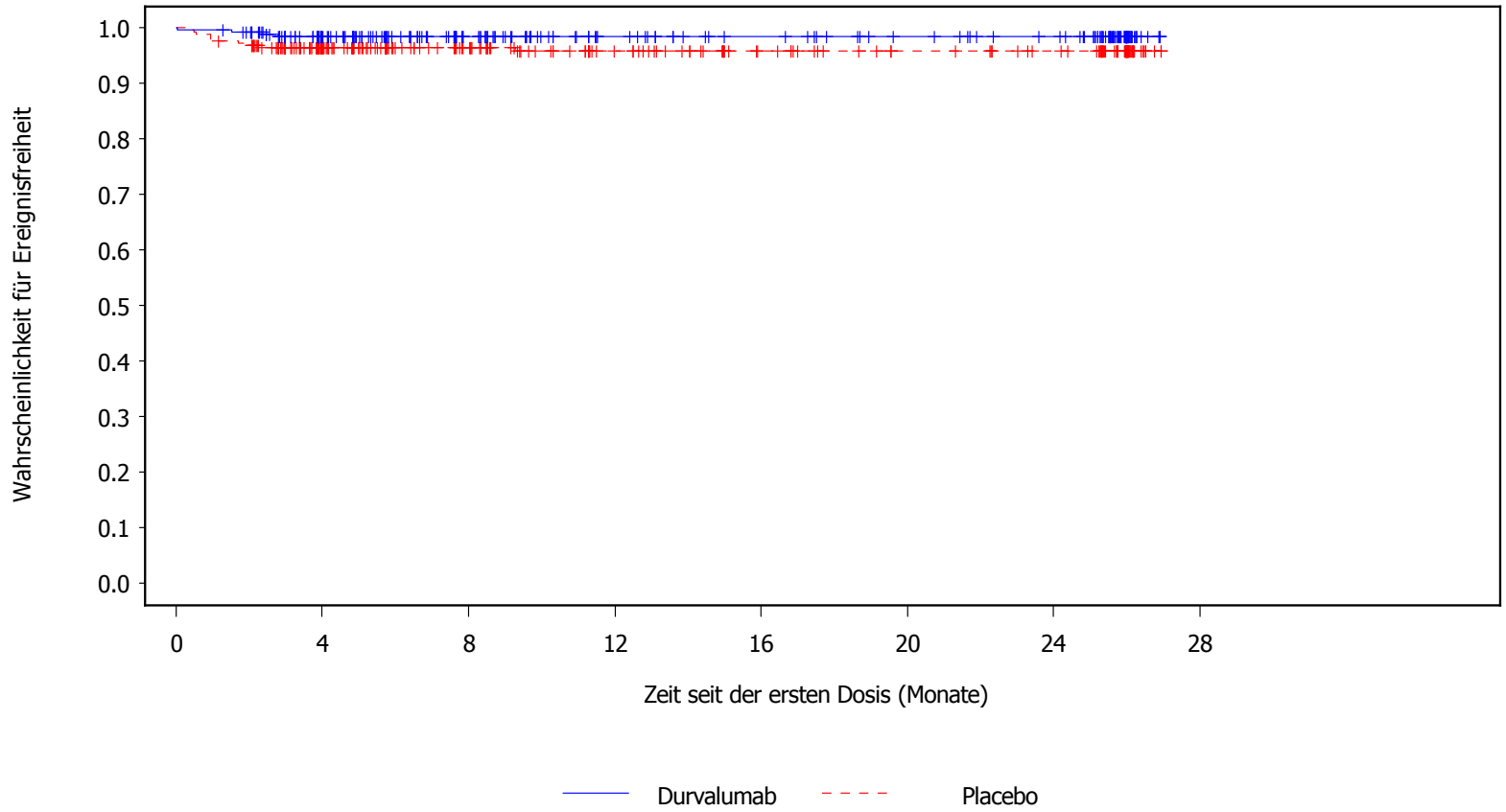
Anzahl an Patienten unter Risiko:

262	200	146	112	98	89	82	0	Durvalumab
265	194	131	98	75	64	59	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbp 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.43 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Brustschmerzen die Skelettmuskulatur betreffend
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	205	152	118	106	97	90	0	Durvalumab
265	199	143	108	86	74	67	0	Placebo

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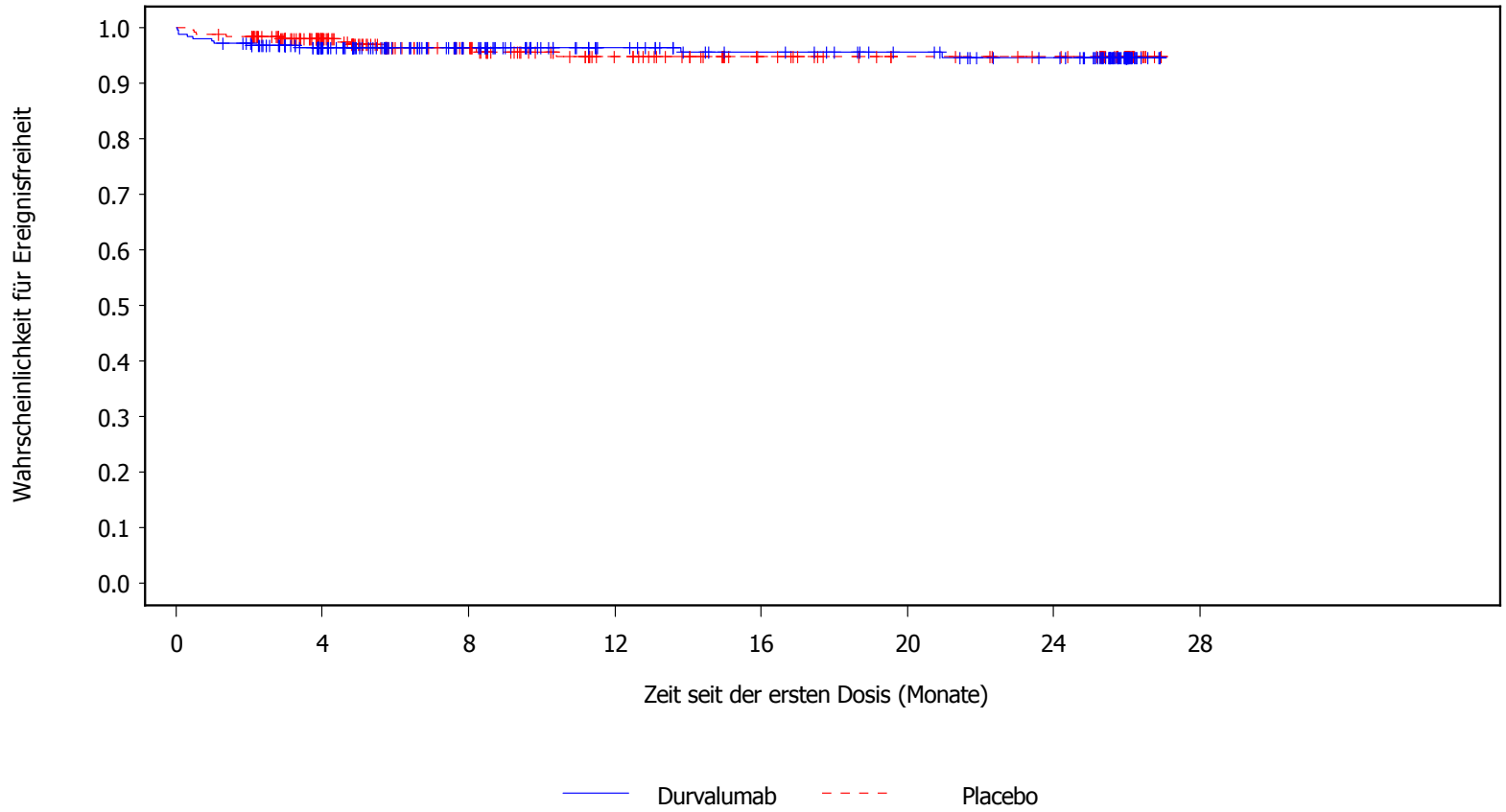
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.44 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Myalgie
Safety Analysis Set, DCO 15JAN2024



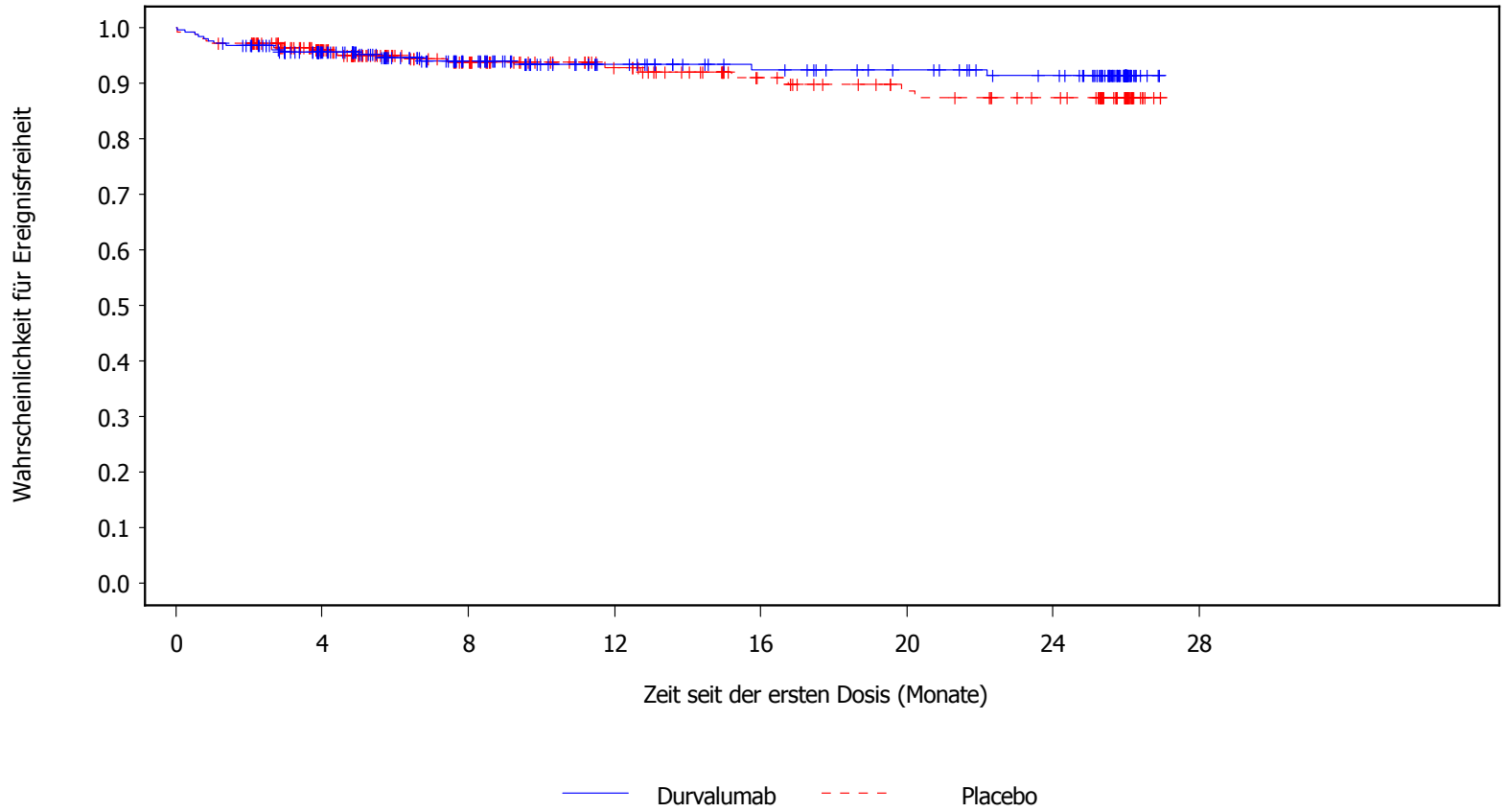
Anzahl an Patienten unter Risiko:

262	202	152	119	106	98	89	0	Durvalumab
265	202	143	107	85	74	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbr 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.45 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Rueckenschmerzen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	204	151	116	103	95	86	0	Durvalumab
265	198	139	107	84	71	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbs 05JUN2025:07:

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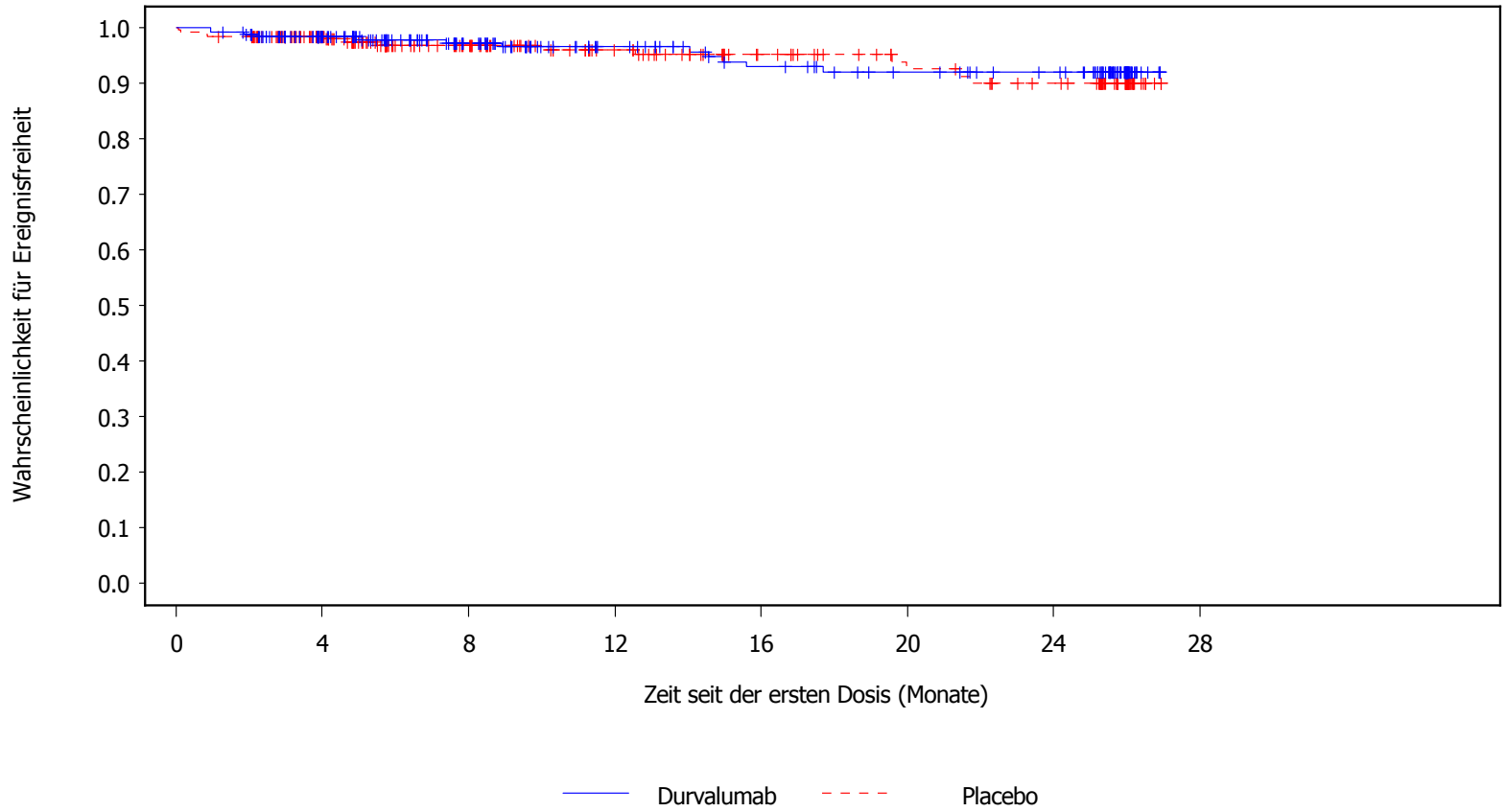
Figure 2.3.46 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Schmerz in einer Extremitaet
Safety Analysis Set, DCO 15JAN2024



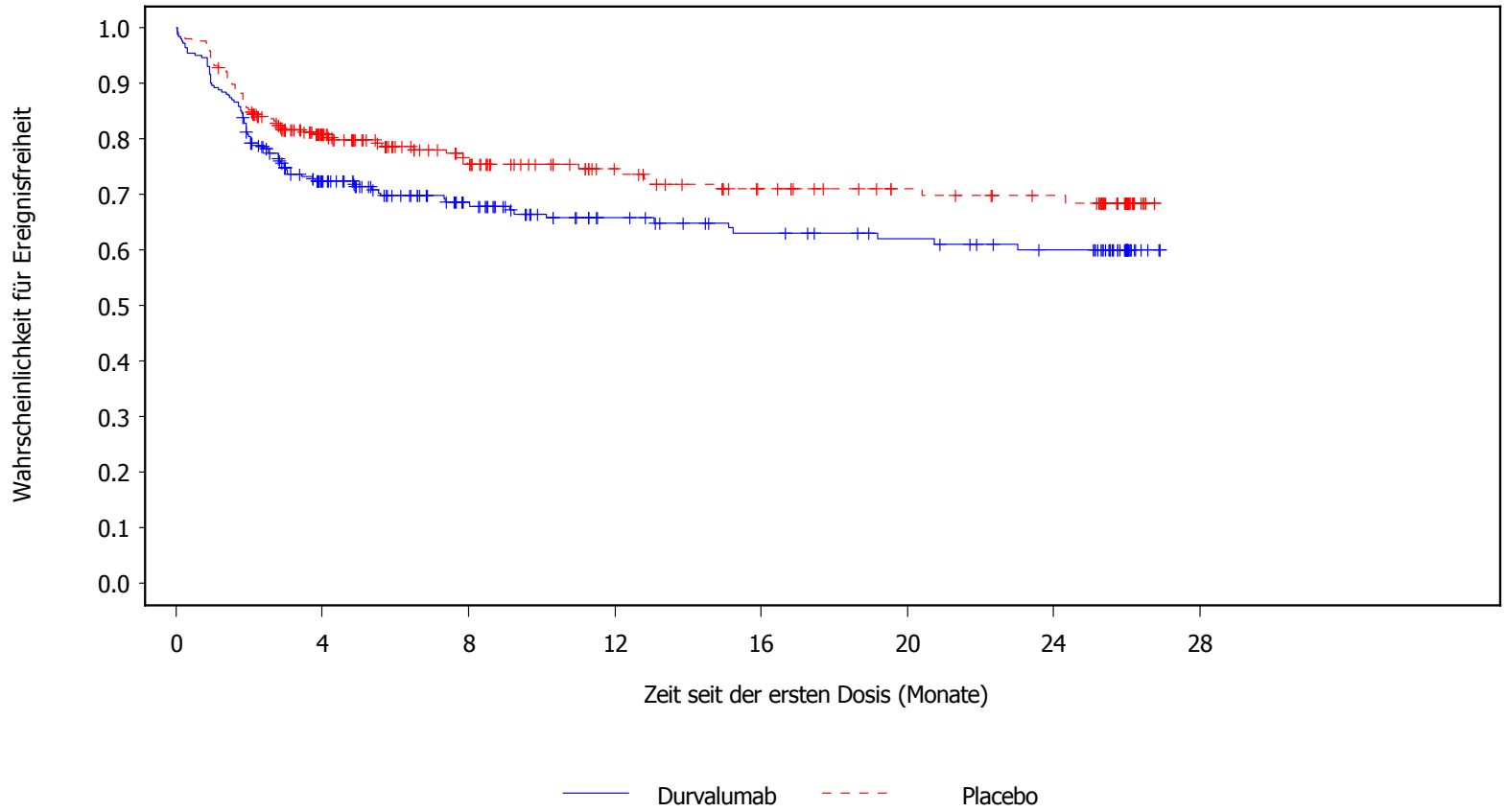
Anzahl an Patienten unter Risiko:

262	205	152	117	101	92	85	0	Durvalumab
265	202	144	108	86	72	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbt 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.47 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	152	109	79	69	63	56	0	Durvalumab
265	166	114	85	70	60	55	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbu 05JUN2025:07:

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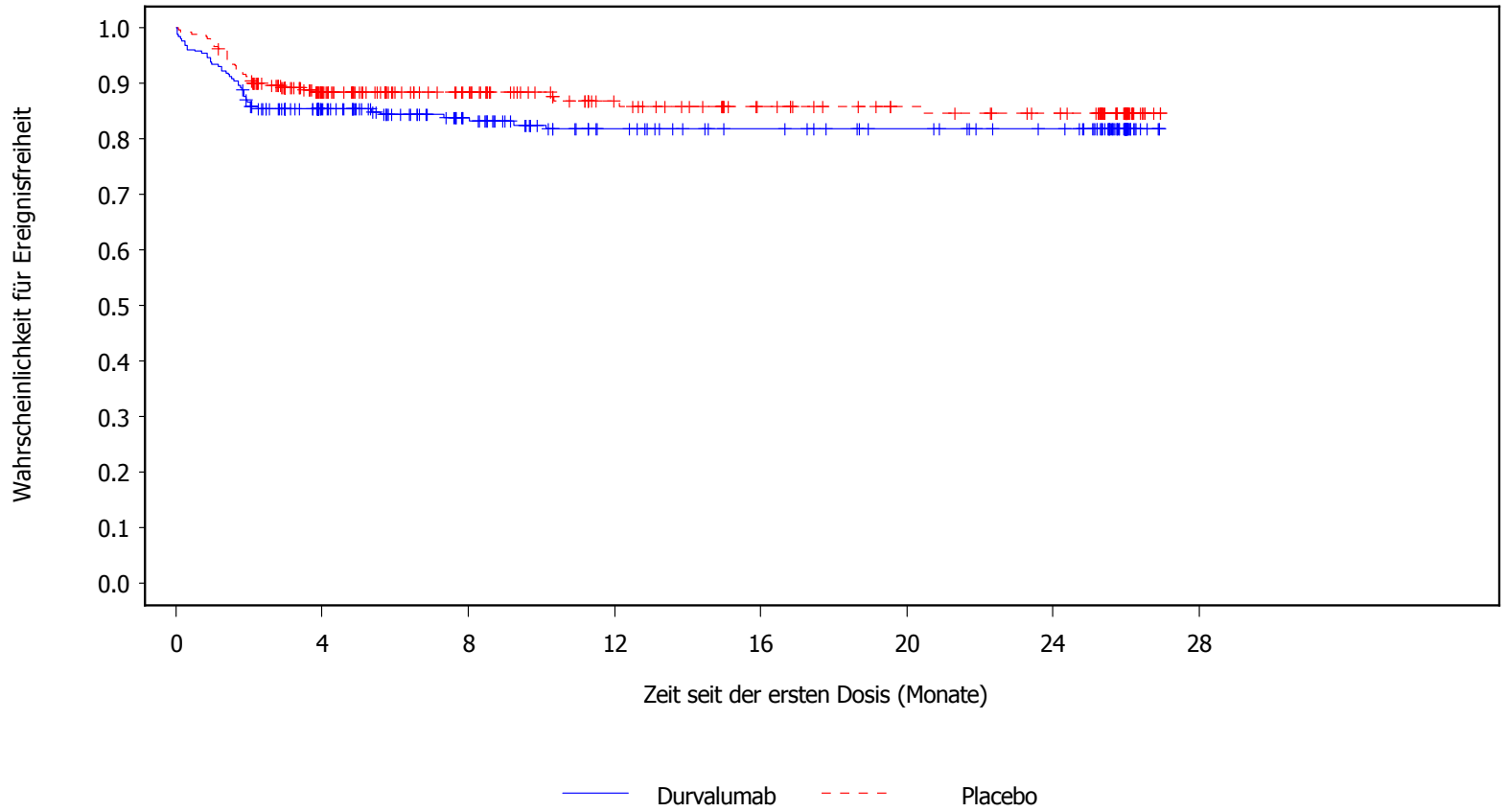
Figure 2.3.48 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Appetit vermindert
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	180	135	104	93	86	79	0	Durvalumab
265	180	131	98	80	70	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbv 05JUN2025:07:

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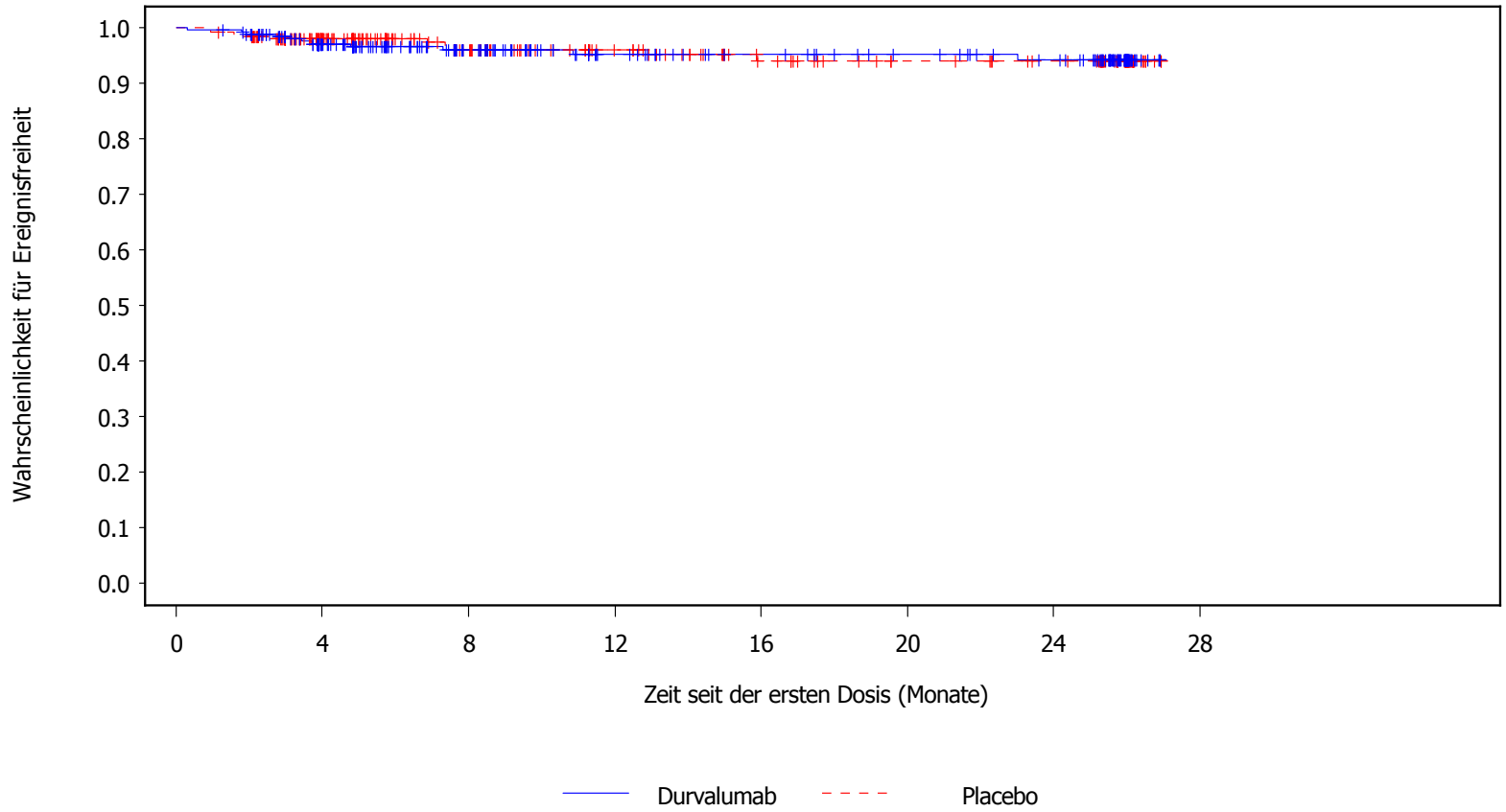
Figure 2.3.49 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Hyperglykaemie
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	205	150	116	104	96	88	0	Durvalumab
265	202	143	108	86	74	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbw 05JUN2025:07:

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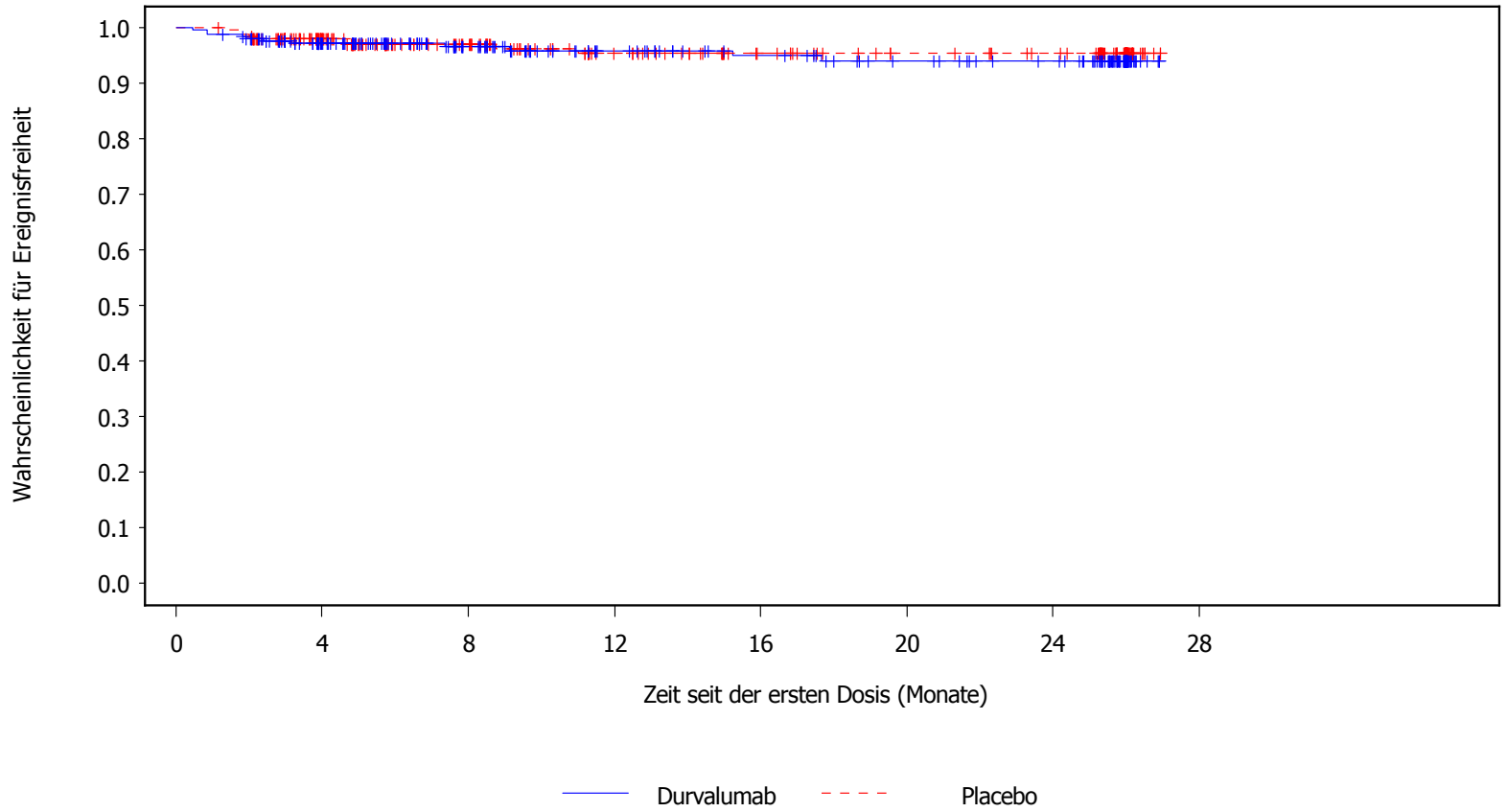
Figure 2.3.50 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Hyponatriaemie
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	203	151	117	103	92	84	0	Durvalumab
265	202	145	108	87	75	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbx 05JUN2025:07:

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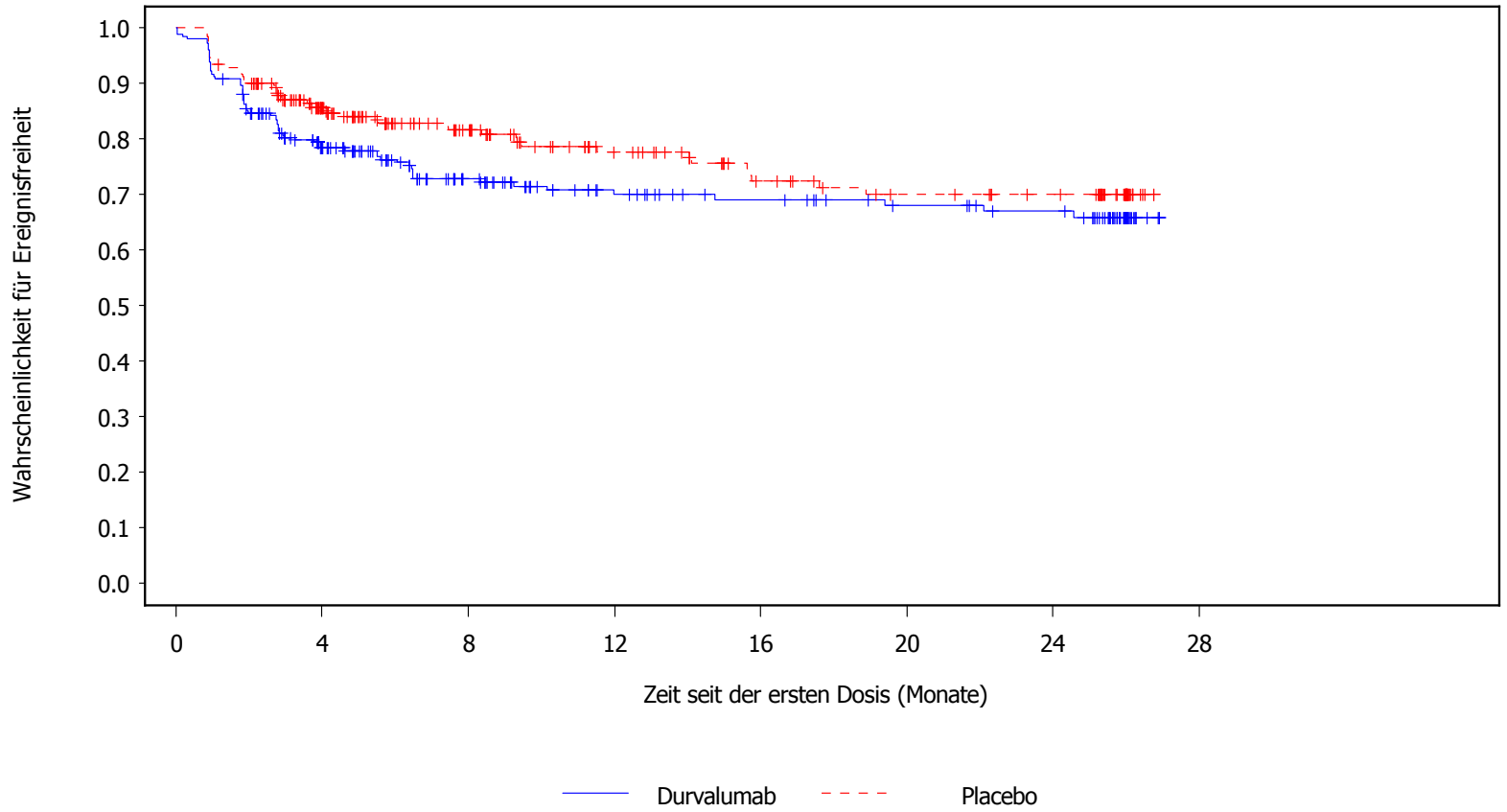
Figure 2.3.51 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Untersuchungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	166	114	85	75	67	62	0	Durvalumab
265	174	121	85	65	56	51	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bby 05JUN2025:07:

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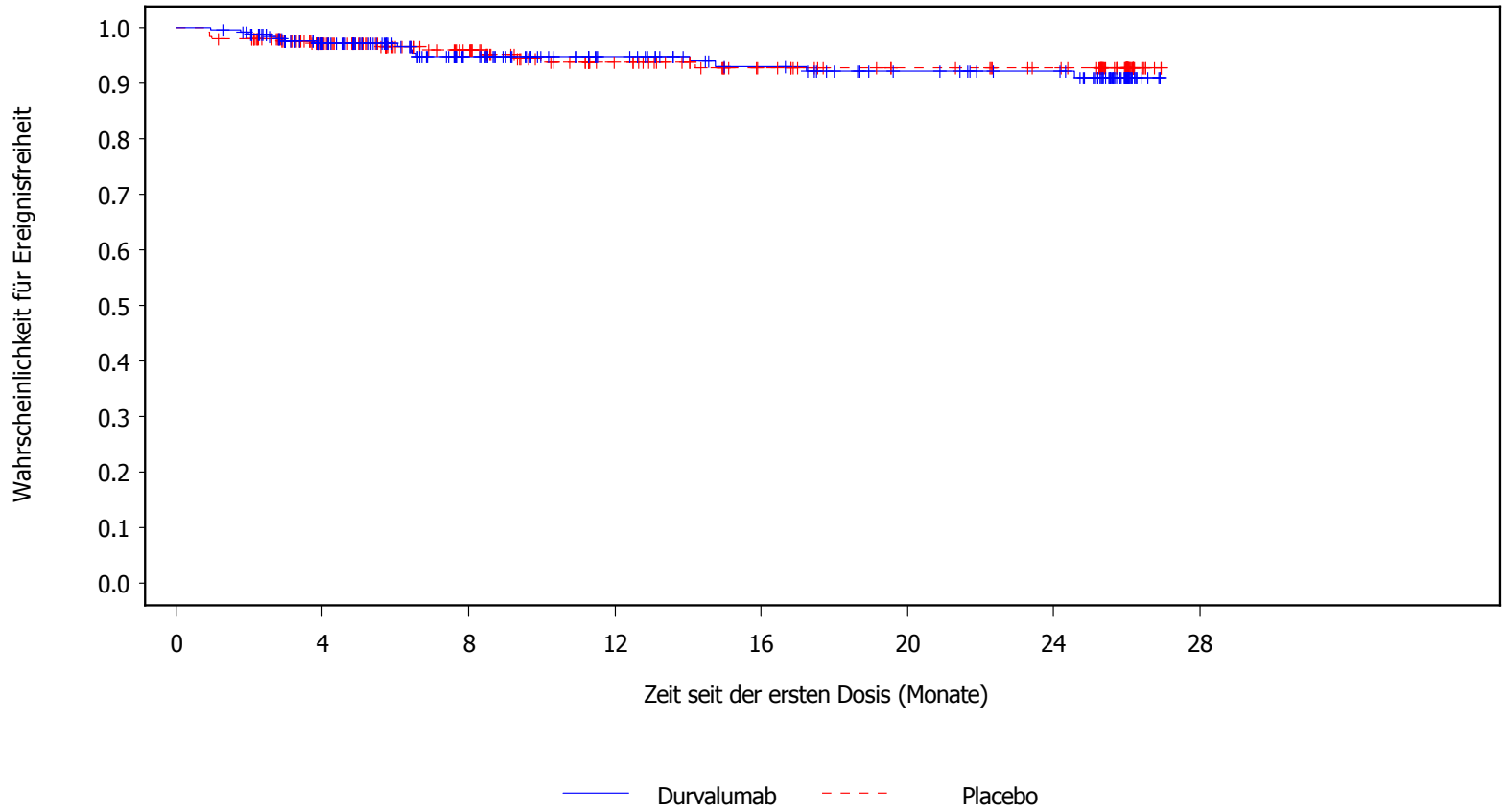
Figure 2.3.52 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Alaninaminotransferase erhoeht
Safety Analysis Set, DCO 15JAN2024



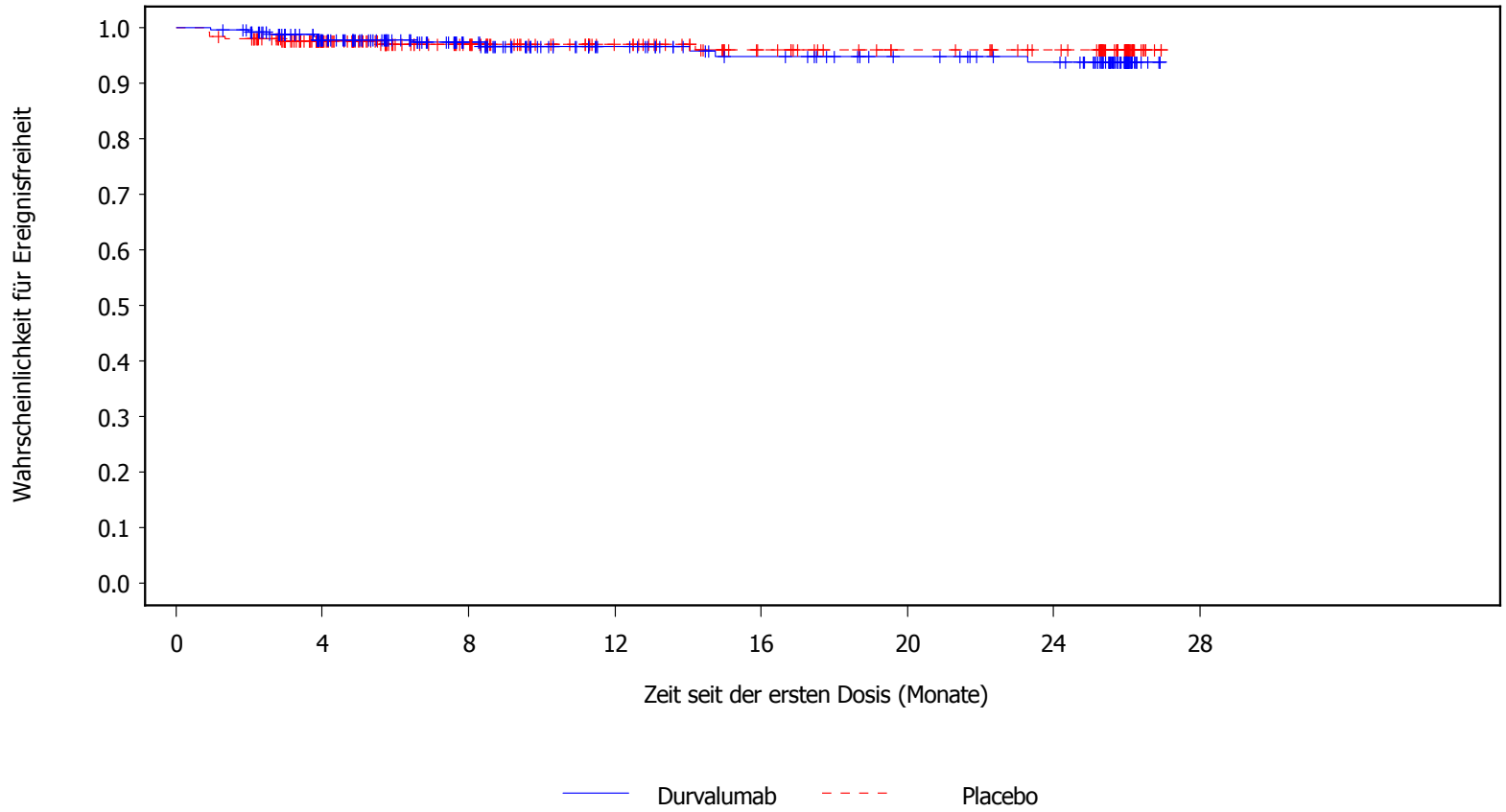
Anzahl an Patienten unter Risiko:

262	204	149	117	102	91	85	0	Durvalumab
265	199	143	106	85	74	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bbz 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.53 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Aspartataminotransferase erhoeht
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	205	153	118	103	93	86	0	Durvalumab
265	200	146	111	89	77	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bca 05JUN2025:07:

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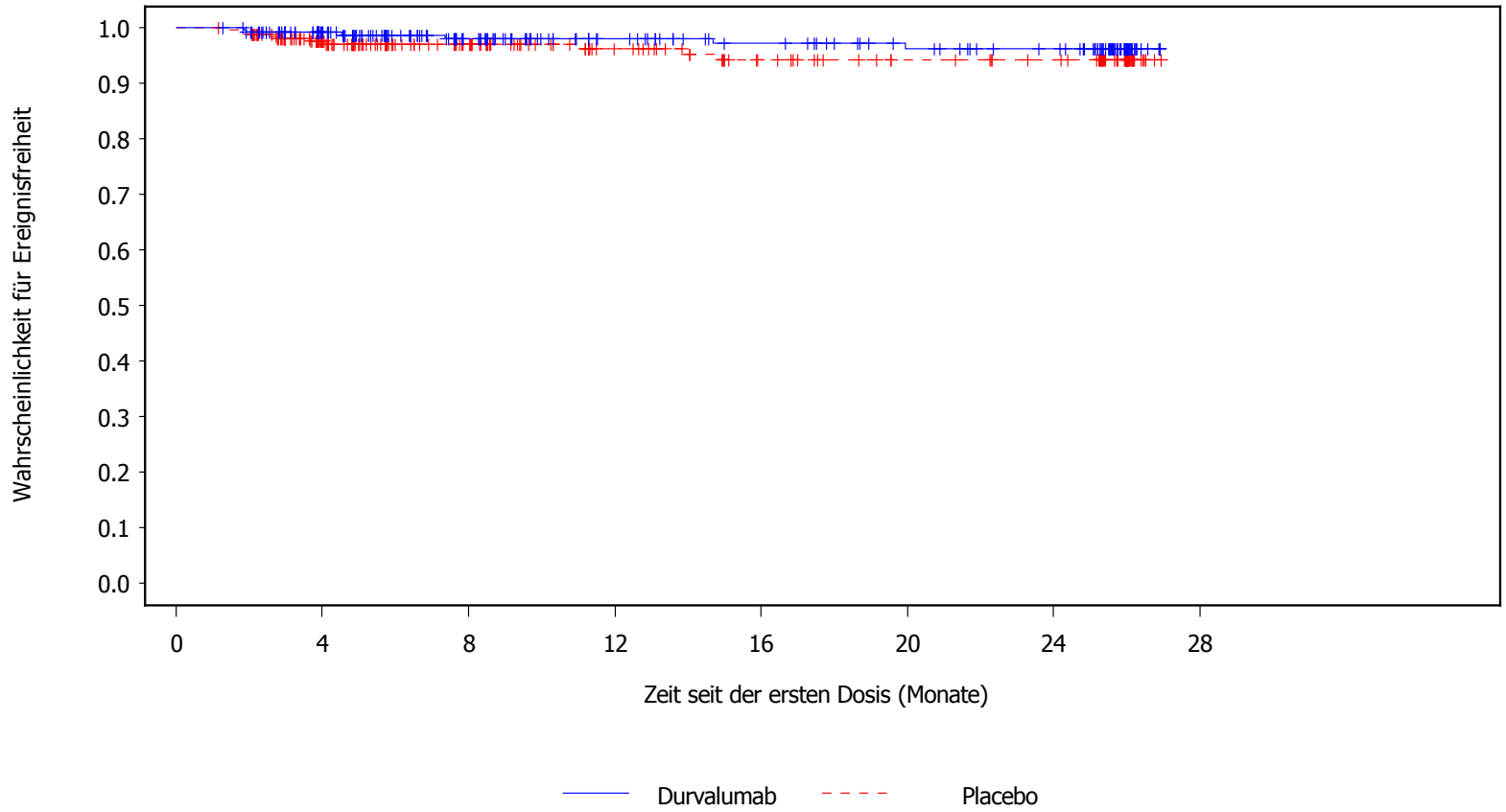
Figure 2.3.54 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Bilirubin im Blut erhoeht
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	153	120	106	95	87	0	Durvalumab
265	200	142	106	85	73	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcb 05JUN2025:07:

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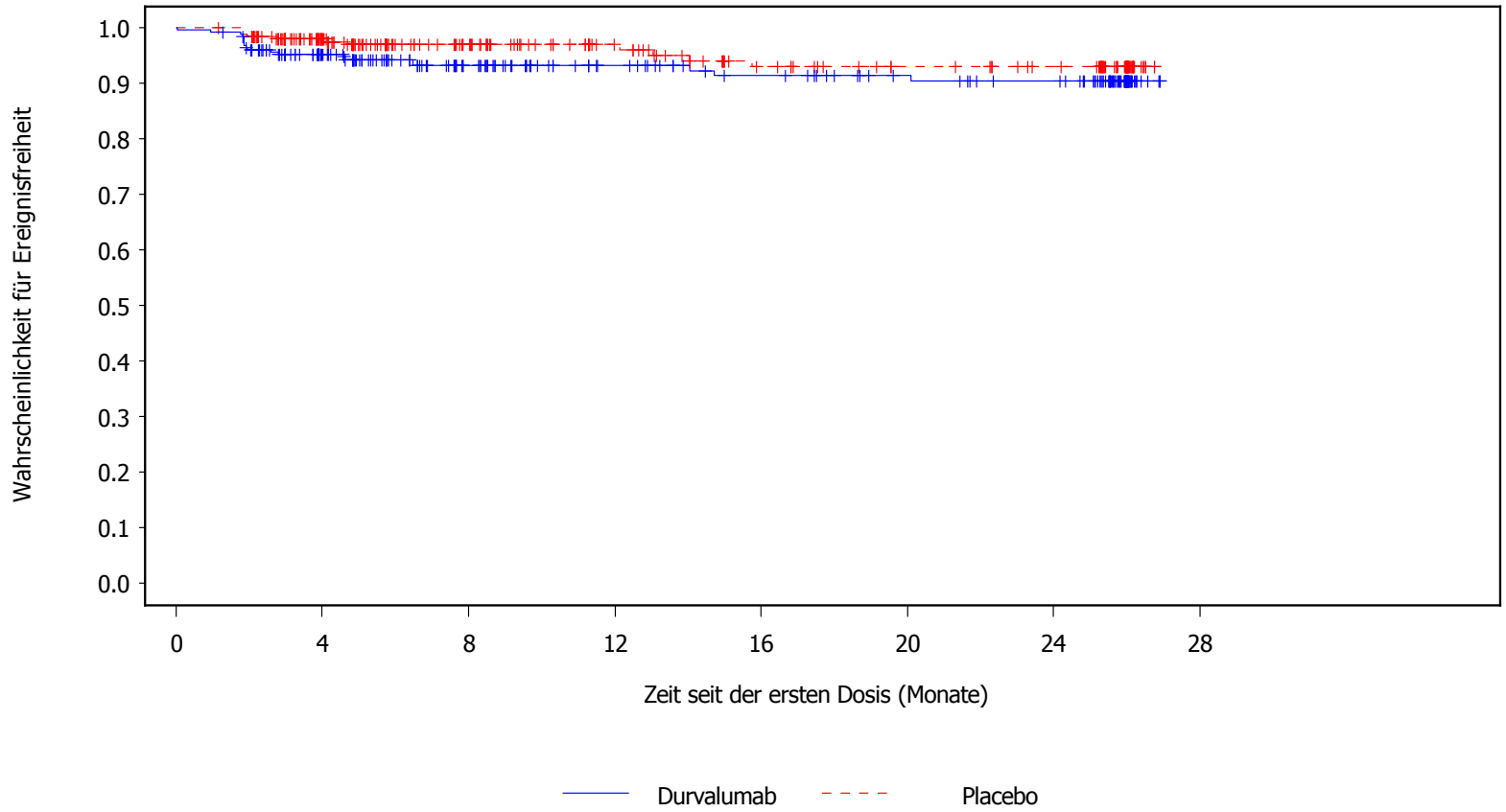
Figure 2.3.55 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Gewicht erniedrigt
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	199	145	114	101	91	85	0	Durvalumab
265	200	141	106	82	71	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcc 05JUN2025:07:

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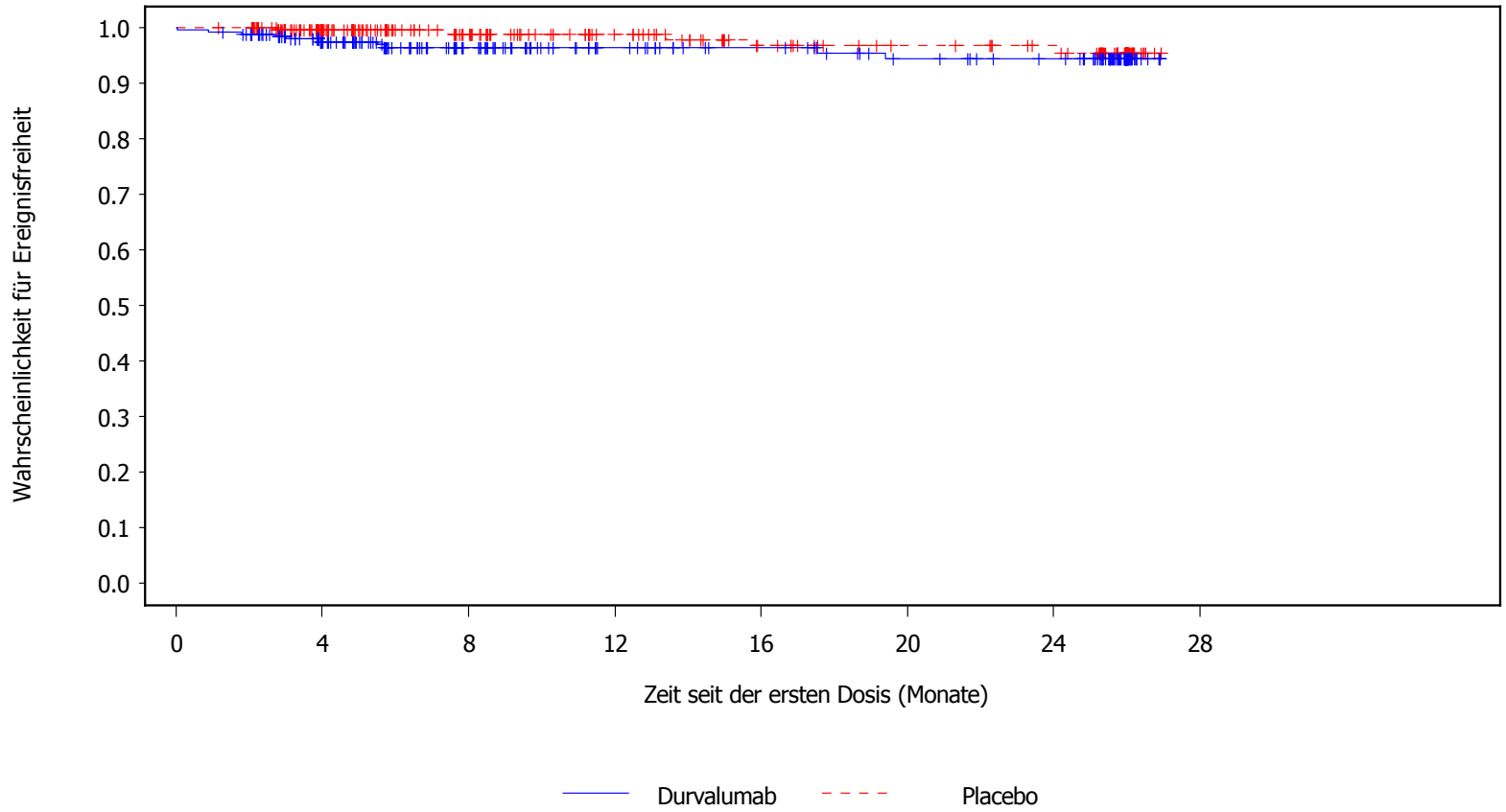
Figure 2.3.56 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Kreatinin im Blut erhoeht
Safety Analysis Set, DCO 15JAN2024



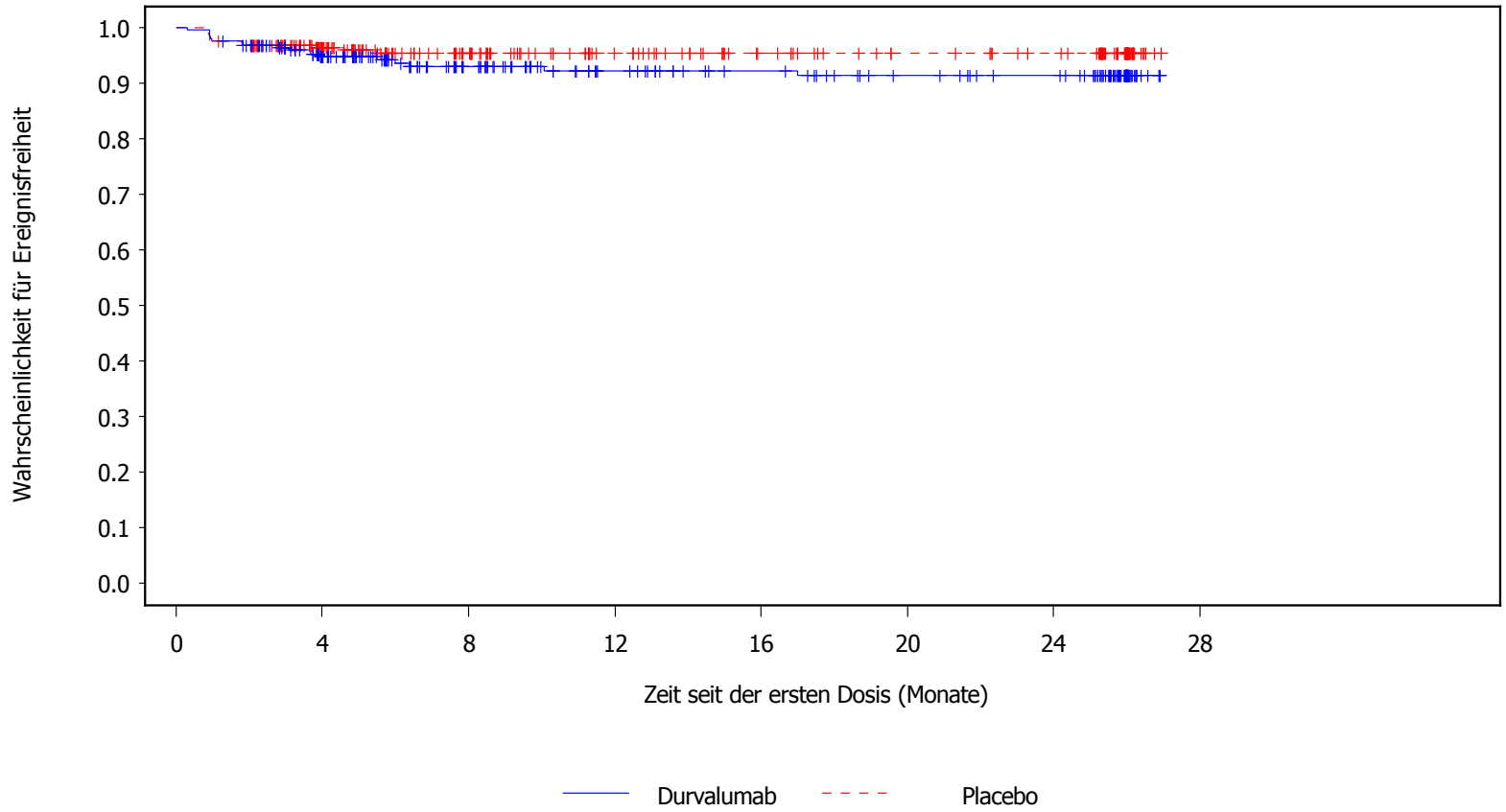
Anzahl an Patienten unter Risiko:

262	205	150	116	104	93	87	0	Durvalumab
265	204	146	111	87	76	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcd 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.57 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Leukozytenzahl erniedrigt
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	198	145	113	100	89	83	0	Durvalumab
265	196	141	106	86	74	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bce 05JUN2025:07:

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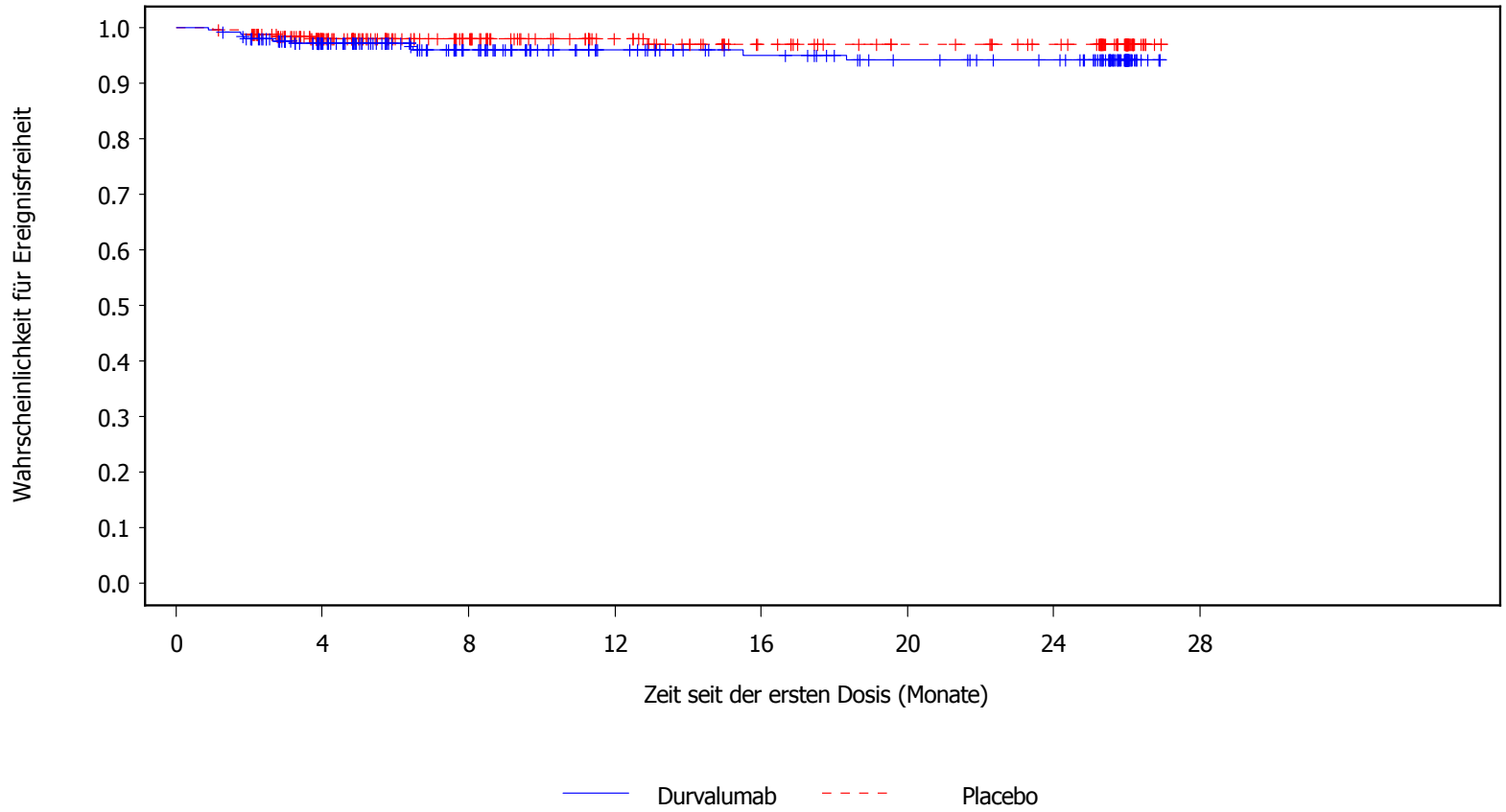
Figure 2.3.58 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Lymphozytenzahl erniedrigt
Safety Analysis Set, DCO 15JAN2024



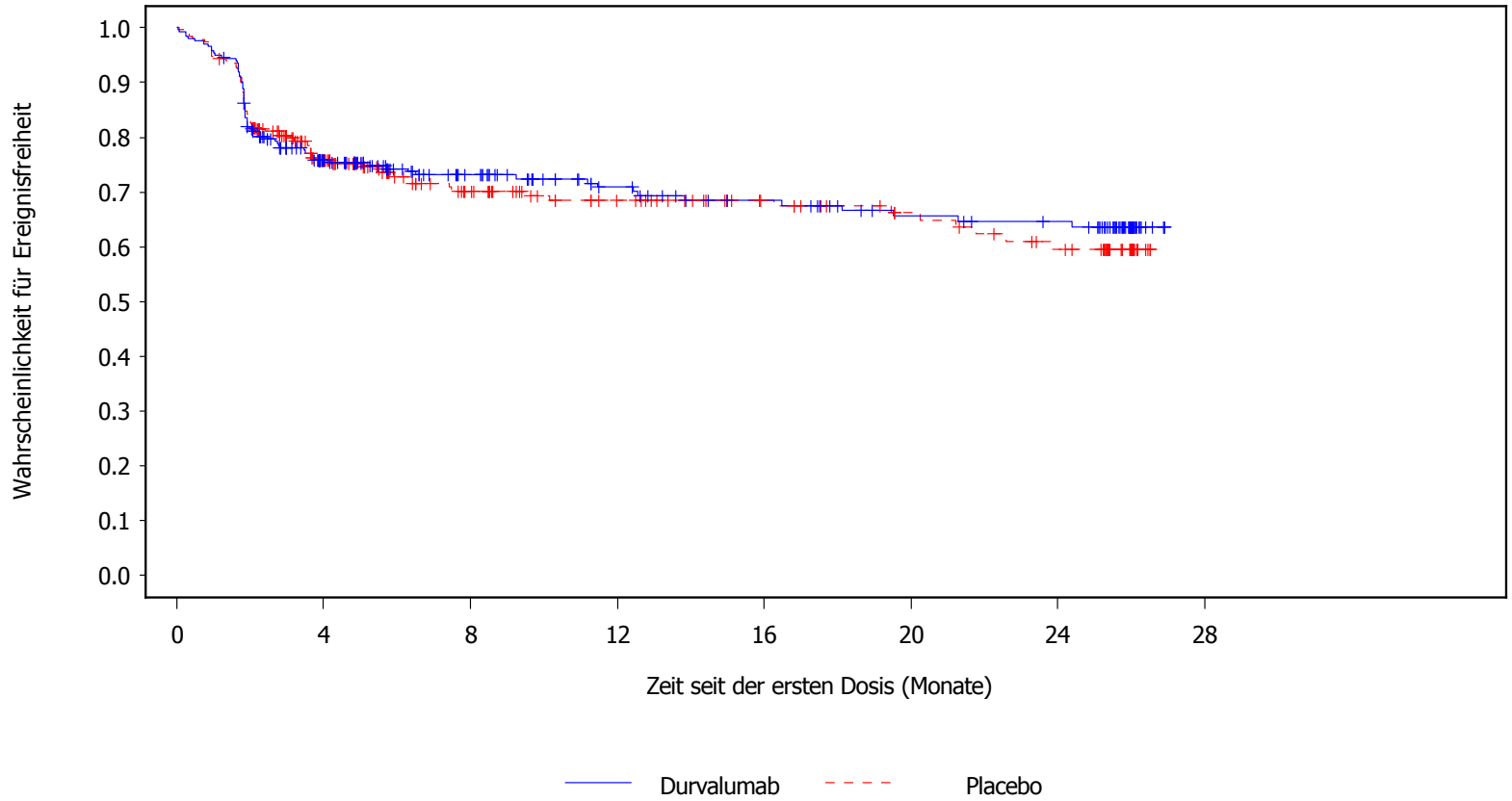
Anzahl an Patienten unter Risiko:

262	202	149	117	103	92	86	0	Durvalumab
265	201	145	110	88	76	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcf 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.59 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen
Safety Analysis Set, DCO 15JAN2024



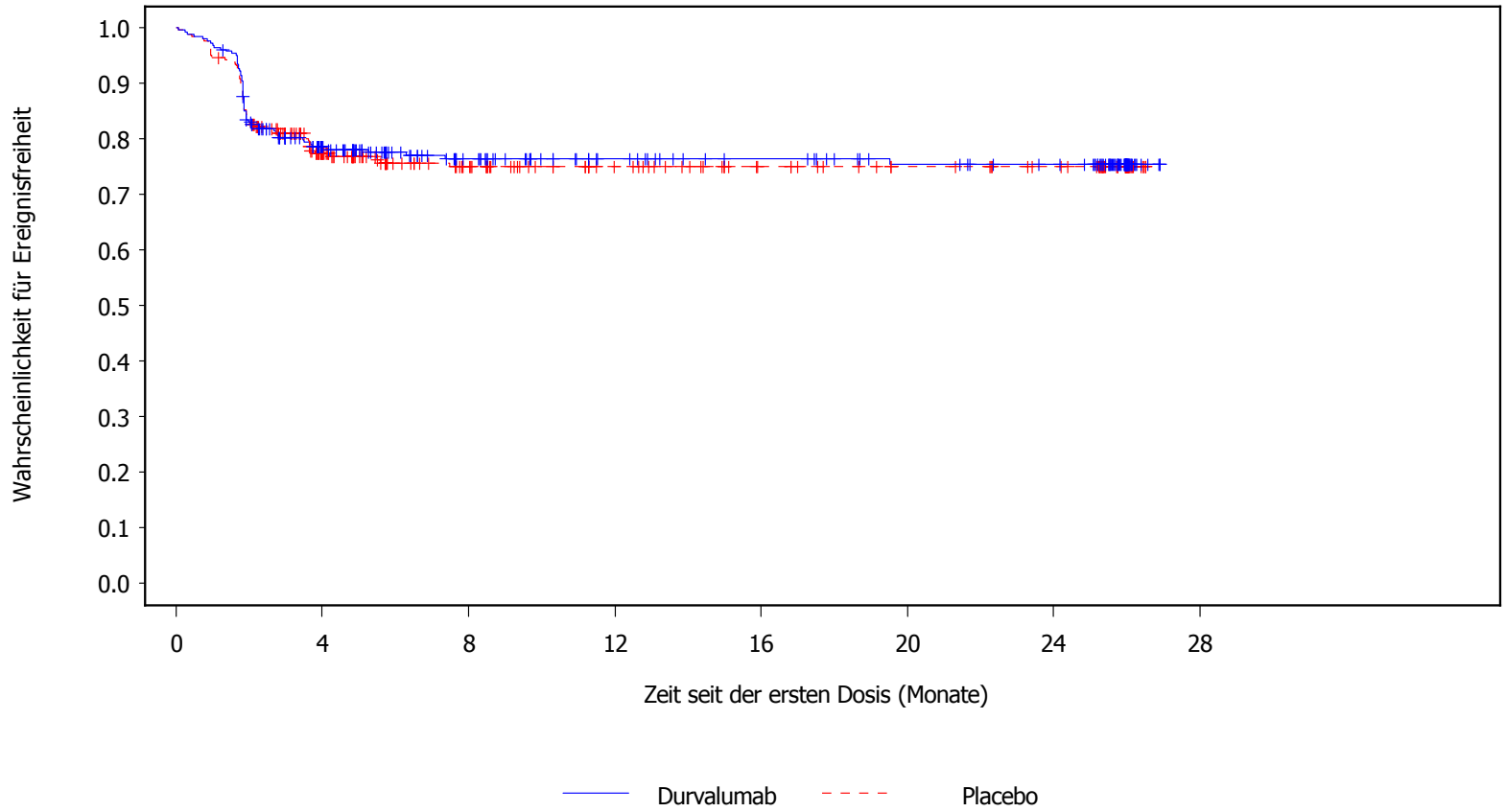
Anzahl an Patienten unter Risiko:

262	159	114	89	78	68	64	0	Durvalumab
265	155	99	77	61	51	42	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcg 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.60 ADRIATIC: Kaplan-Meier plot of time to first occurrence of PT: Strahlenbedingte Pneumonitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	163	118	95	85	76	71	0	Durvalumab
265	159	106	81	65	56	50	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bch 05JUN2025:07:

Anhang 4-G8.1.2: UE jeglichen Schweregrades - gesamt und nach SOC/PT - Subgruppenanalysen

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Table 5.1.1 ADRIATIC: Summary of subgroup analysis of time to first UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	32 (88,9)	1,0 [0,5; 1,9]	37	35 (94,6)	1,0 [0,8; 1,6]	0,79	[0,49; 1,28]	0,3458
Stadium III	226	215 (95,1)	1,0 [0,9; 1,0]	228	199 (87,3)	1,0 [1,0; 1,2]	1,26	[1,04; 1,53]	0,0177*
Interaktions p-Wert									0,0788
TNM Status (eCRF) - DEU									
Stadium I/II	33	29 (87,9)	1,1 [0,8; 1,9]	34	32 (94,1)	1,0 [0,7; 1,6]	0,73	[0,44; 1,20]	0,2155
Stadium III	229	218 (95,2)	1,0 [0,9; 1,0]	231	202 (87,4)	1,0 [1,0; 1,3]	1,28	[1,05; 1,55]	0,0131*
Interaktions p-Wert									0,0415*
Erhalt einer PCI (IVRS) - DEU									
Ja	141	135 (95,7)	1,0 [0,7; 1,0]	143	134 (93,7)	0,9 [0,9; 1,0]	0,97	[0,76; 1,23]	0,7900
Nein	121	112 (92,6)	1,0 [1,0; 1,5]	122	100 (82,0)	1,7 [1,0; 1,8]	1,44	[1,10; 1,89]	0,0086*
Interaktions p-Wert									0,0321*
Erhalt einer PCI (eCRF) - DEU									
Ja	141	135 (95,7)	1,0 [0,7; 1,0]	142	133 (93,7)	0,9 [0,8; 1,0]	0,97	[0,76; 1,23]	0,7796
Nein	121	112 (92,6)	1,0 [1,0; 1,5]	123	101 (82,1)	1,7 [1,0; 1,8]	1,43	[1,09; 1,88]	0,0090*
Interaktions p-Wert									0,0325*
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	29 (93,5)	1,7 [1,0; 1,8]	32	27 (84,4)	1,9 [1,0; 3,6]	1,37	[0,81; 2,34]	0,2352
>=14 bis <28 Tage	79	72 (91,1)	0,9 [0,7; 1,0]	80	71 (88,8)	1,5 [1,0; 1,8]	1,31	[0,94; 1,82]	0,1076
>=28 Tage	152	146 (96,1)	1,0 [0,9; 1,0]	153	136 (88,9)	1,0 [0,9; 1,0]	1,06	[0,84; 1,34]	0,6415
Interaktions p-Wert									0,4649
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	15 (93,8)	1,8 [1,0; 1,9]	24	21 (87,5)	1,9 [1,0; 3,1]	1,22	[0,62; 2,36]	0,5559
>=28 bis <56 Tage	103	97 (94,2)	1,0 [1,0; 1,4]	103	90 (87,4)	1,1 [1,0; 1,7]	1,28	[0,96; 1,71]	0,0929

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubae1.sas gttesubae1aaa
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Nutzenbewertung nach AMNOG

Table 5.1.1 ADRIATIC: Summary of subgroup analysis of time to first UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	93 (94,9)	0,9 [0,7; 1,0]	76	67 (88,2)	0,9 [0,6; 1,0]	0,97	[0,71; 1,34]	0,8638
>=84 Tage	45	42 (93,3)	0,9 [0,4; 1,0]	62	56 (90,3)	1,0 [0,5; 1,7]	1,13	[0,75; 1,69]	0,5491
Interaktions p-Wert									0,6528
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	86 (96,6)	1,0 [0,9; 1,1]	88	74 (84,1)	1,0 [0,9; 1,7]	1,43	[1,04; 1,95]	0,0254*
Cisplatin	173	161 (93,1)	1,0 [0,9; 1,0]	177	160 (90,4)	1,0 [0,9; 1,3]	1,07	[0,86; 1,34]	0,5336
Interaktions p-Wert									0,1422
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	180 (93,3)	1,0 [1,0; 1,2]	186	163 (87,6)	1,0 [1,0; 1,5]	1,18	[0,95; 1,46]	0,1254
Zweimal täglich	69	67 (97,1)	0,9 [0,6; 1,0]	79	71 (89,9)	0,9 [0,5; 1,0]	1,20	[0,86; 1,68]	0,2795
Interaktions p-Wert									0,9252
Bestes Ansprechen auf cCRT - DEU									
CR	31	29 (93,5)	1,0 [0,5; 1,7]	34	33 (97,1)	1,0 [0,5; 1,3]	0,76	[0,46; 1,26]	0,2910
PR	189	179 (94,7)	1,0 [0,9; 1,1]	199	174 (87,4)	1,0 [0,9; 1,2]	1,26	[1,02; 1,55]	0,0316*
SD	42	39 (92,9)	1,0 [0,9; 1,0]	32	27 (84,4)	1,5 [1,0; 1,8]	1,23	[0,76; 2,04]	0,3983
Interaktions p-Wert									0,1929
Geschlecht - DEU									
Männer	178	165 (92,7)	1,0 [0,9; 1,2]	187	158 (84,5)	1,2 [1,0; 1,7]	1,28	[1,03; 1,59]	0,0273*
Frauen	84	82 (97,6)	1,0 [0,7; 1,0]	78	76 (97,4)	0,9 [0,8; 1,0]	0,92	[0,67; 1,25]	0,5832
Interaktions p-Wert									0,0868
Altersgruppe - DEU									
<65 Jahre	159	152 (95,6)	1,0 [0,9; 1,0]	161	143 (88,8)	1,0 [0,9; 1,2]	1,21	[0,96; 1,52]	0,1046
>=65 Jahre	103	95 (92,2)	1,0 [0,8; 1,3]	104	91 (87,5)	1,0 [0,9; 1,7]	1,14	[0,85; 1,52]	0,3801
Interaktions p-Wert									0,7454

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubae1.sas gttesubae1aaa
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Nutzenbewertung nach AMNOG

Table 5.1.1 ADRIATIC: Summary of subgroup analysis of time to first UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	75 (96,2)	1,0 [0,9; 1,0]	72	64 (88,9)	1,0 [0,9; 1,8]	1,53	[1,09; 2,14]	0,0138*
TC or IC >=1%	84	77 (91,7)	1,4 [0,9; 1,8]	98	84 (85,7)	1,1 [1,0; 1,6]	0,99	[0,72; 1,35]	0,9374
Interaktions p-Wert									0,0626
Raucherstatus - DEU									
Raucher	239	225 (94,1)	1,0 [0,9; 1,0]	239	210 (87,9)	1,0 [1,0; 1,4]	1,20	[0,996; 1,45]	0,0549
Nichtraucher	23	22 (95,7)	1,0 [0,9; 1,8]	26	24 (92,3)	1,0 [0,9; 1,2]	0,98	[0,55; 1,75]	0,9500
Interaktions p-Wert									0,5131
Abstammung - DEU									
Weiß	128	123 (96,1)	1,0 [0,9; 1,1]	137	120 (87,6)	1,0 [1,0; 1,3]	1,22	[0,95; 1,57]	0,1201
Schwarz/Afroamerikanisch	1	1 (100)	0,0 [NE; NE]	3	2 (66,7)	1,0 [1,0; NE]	NC	[NC]	NC
Asiatisch	131	121 (92,4)	1,0 [0,9; 1,1]	121	108 (89,3)	1,0 [0,9; 1,5]	1,15	[0,89; 1,50]	0,2850
Andere	2	2 (100)	2,5 [0,7; NE]	4	4 (100)	0,5 [0,1; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7520
Geographische Region - DEU									
Asien	129	119 (92,2)	1,0 [0,9; 1,2]	120	107 (89,2)	1,0 [0,9; 1,6]	1,15	[0,89; 1,50]	0,2909
Europa	94	90 (95,7)	1,1 [1,0; 1,8]	112	95 (84,8)	1,2 [1,0; 1,7]	1,21	[0,90; 1,61]	0,2020
Nordamerika	39	38 (97,4)	0,6 [0,2; 1,0]	33	32 (97,0)	0,7 [0,5; 1,0]	1,05	[0,66; 1,69]	0,8355
Interaktions p-Wert									0,8854
ECOG-Status zu Baseline - DEU									
0	131	122 (93,1)	1,0 [0,9; 1,4]	131	117 (89,3)	1,0 [1,0; 1,6]	1,10	[0,85; 1,41]	0,4779
1	131	125 (95,4)	1,0 [0,8; 1,0]	134	117 (87,3)	1,0 [0,9; 1,2]	1,28	[0,99; 1,65]	0,0556
Interaktions p-Wert									0,3967

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Table 5.1.2 ADRIATIC: Summary of subgroup analysis of time to first SOC: Endokrine Erkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	4 (11,1)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	4,59	[0,68; 89,80]	0,1241
Stadium III	226	61 (27,0)	NE [NE; NE]	228	14 (6,1)	NE [NE; NE]	4,93	[2,84; 9,17]	<0,0001*
Interaktions p-Wert									0,9517
TNM Status (eCRF) - DEU									
Stadium I/II	33	4 (12,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	4,51	[0,67; 88,28]	0,1287
Stadium III	229	61 (26,6)	NE [NE; NE]	231	14 (6,1)	NE [NE; NE]	4,94	[2,85; 9,20]	<0,0001*
Interaktions p-Wert									0,9380
Erhalt einer PCI (IVRS) - DEU									
Ja	141	34 (24,1)	NE [NE; NE]	143	9 (6,3)	NE [NE; NE]	4,24	[2,13; 9,41]	<0,0001*
Nein	121	31 (25,6)	NE [NE; NE]	122	6 (4,9)	NE [NE; NE]	5,93	[2,66; 15,77]	<0,0001*
Interaktions p-Wert									0,5627
Erhalt einer PCI (eCRF) - DEU									
Ja	141	34 (24,1)	NE [NE; NE]	142	8 (5,6)	NE [NE; NE]	4,76	[2,32; 11,06]	<0,0001*
Nein	121	31 (25,6)	NE [NE; NE]	123	7 (5,7)	NE [NE; NE]	5,10	[2,38; 12,62]	<0,0001*
Interaktions p-Wert									0,9033
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	10 (32,3)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	12,12	[2,32;222,40]	0,0013*
>=14 bis <28 Tage	79	17 (21,5)	NE [NE; NE]	80	7 (8,8)	NE [NE; NE]	2,72	[1,17; 7,03]	0,0191*
>=28 Tage	152	38 (25,0)	NE [NE; NE]	153	7 (4,6)	NE [NE; NE]	6,12	[2,91; 14,98]	<0,0001*
Interaktions p-Wert									0,2421
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	5 (31,3)	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	7,38	[1,19;141,44]	0,0303*
>=28 bis <56 Tage	103	24 (23,3)	NE [NE; NE]	103	4 (3,9)	NE [NE; NE]	6,65	[2,57; 22,63]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.2 ADRIATIC: Summary of subgroup analysis of time to first SOC: Endokrine Erkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	26 (26,5)	NE [NE; NE]	76	7 (9,2)	NE [NE; NE]	3,13	[1,43; 7,82]	0,0033*
>=84 Tage	45	10 (22,2)	NE [NE; NE]	62	3 (4,8)	NE [NE; NE]	5,73	[1,75; 25,57]	0,0032*
Interaktions p-Wert									0,6669
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	21 (23,6)	NE [NE; NE]	88	7 (8,0)	NE [NE; NE]	3,05	[1,36; 7,74]	0,0060*
Cisplatin	173	44 (25,4)	NE [NE; NE]	177	8 (4,5)	NE [NE; NE]	6,59	[3,28; 15,14]	<0,0001*
Interaktions p-Wert									0,1886
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	45 (23,3)	NE [NE; NE]	186	11 (5,9)	NE [NE; NE]	4,26	[2,29; 8,68]	<0,0001*
Zweimal täglich	69	20 (29,0)	NE [NE; NE]	79	4 (5,1)	NE [NE; NE]	6,97	[2,64; 23,98]	<0,0001*
Interaktions p-Wert									0,4338
Bestes Ansprechen auf cCRT - DEU									
CR	31	4 (12,9)	NE [NE; NE]	34	3 (8,8)	NE [NE; NE]	1,49	[0,33; 7,57]	0,5988
PR	189	48 (25,4)	NE [NE; NE]	199	9 (4,5)	NE [NE; NE]	6,43	[3,32; 14,03]	<0,0001*
SD	42	13 (31,0)	NE [NE; NE]	32	3 (9,4)	NE [NE; NE]	3,60	[1,16; 15,70]	0,0251*
Interaktions p-Wert									0,2238
Geschlecht - DEU									
Männer	178	39 (21,9)	NE [NE; NE]	187	8 (4,3)	NE [NE; NE]	5,59	[2,76; 12,91]	<0,0001*
Frauen	84	26 (31,0)	NE [NE; NE]	78	7 (9,0)	NE [NE; NE]	4,09	[1,88; 10,23]	0,0002*
Interaktions p-Wert									0,5888
Altersgruppe - DEU									
<65 Jahre	159	43 (27,0)	NE [NE; NE]	161	8 (5,0)	NE [NE; NE]	6,32	[3,14; 14,52]	<0,0001*
>=65 Jahre	103	22 (21,4)	NE [NE; NE]	104	7 (6,7)	NE [NE; NE]	3,37	[1,51; 8,53]	0,0024*
Interaktions p-Wert									0,2817

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.2 ADRIATIC: Summary of subgroup analysis of time to first SOC: Endokrine Erkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	22 (28,2)	NE [NE; NE]	72	4 (5,6)	NE [NE; NE]	5,86	[2,24; 20,04]	0,0001*
TC or IC >=1%	84	19 (22,6)	NE [NE; NE]	98	5 (5,1)	NE [NE; NE]	4,76	[1,91; 14,36]	0,0005*
Interaktions p-Wert									0,7782
Raucherstatus - DEU									
Raucher	239	56 (23,4)	NE [NE; NE]	239	14 (5,9)	NE [NE; NE]	4,44	[2,54; 8,29]	<0,0001*
Nichtraucher	23	9 (39,1)	NE [NE; NE]	26	1 (3,8)	NE [NE; NE]	12,71	[2,39;234,33]	0,0013*
Interaktions p-Wert									0,2819
Abstammung - DEU									
Weiß	128	35 (27,3)	NE [NE; NE]	137	9 (6,6)	NE [NE; NE]	4,76	[2,39; 10,55]	<0,0001*
Schwarz/Afroamerikanisch	1	1 (100)	2,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	29 (22,1)	NE [NE; NE]	121	6 (5,0)	NE [NE; NE]	5,00	[2,23; 13,35]	<0,0001*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9319
Geographische Region - DEU									
Asien	129	29 (22,5)	NE [NE; NE]	120	5 (4,2)	NE [NE; NE]	6,03	[2,55; 17,73]	<0,0001*
Europa	94	26 (27,7)	NE [NE; NE]	112	6 (5,4)	NE [NE; NE]	5,63	[2,48; 15,11]	<0,0001*
Nordamerika	39	10 (25,6)	NE [NE; NE]	33	4 (12,1)	NE [NE; NE]	2,60	[0,87; 9,48]	0,0896
Interaktions p-Wert									0,5148
ECOG-Status zu Baseline - DEU									
0	131	28 (21,4)	NE [NE; NE]	131	8 (6,1)	NE [NE; NE]	3,69	[1,76; 8,68]	0,0003*
1	131	37 (28,2)	NE [NE; NE]	134	7 (5,2)	NE [NE; NE]	6,46	[3,06; 15,83]	<0,0001*
Interaktions p-Wert									0,3298

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.3 ADRIATIC: Summary of subgroup analysis of time to first PT: Hyperthyroidismus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	2 (5,6)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	2,14	[0,20; 45,96]	0,5223
Stadium III	226	25 (11,1)	NE [NE; NE]	228	3 (1,3)	NE [NE; NE]	8,70	[3,05; 36,54]	<0,0001*
Interaktions p-Wert									0,3358
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	2,12	[0,20; 45,56]	0,5272
Stadium III	229	25 (10,9)	NE [NE; NE]	231	3 (1,3)	NE [NE; NE]	8,71	[3,06; 36,60]	<0,0001*
Interaktions p-Wert									0,3326
Erhalt einer PCI (IVRS) - DEU									
Ja	141	13 (9,2)	NE [NE; NE]	143	3 (2,1)	NE [NE; NE]	4,51	[1,45; 19,68]	0,0075*
Nein	121	14 (11,6)	NE [NE; NE]	122	1 (0,8)	NE [NE; NE]	14,76	[2,97;267,43]	0,0002*
Interaktions p-Wert									0,2999
Erhalt einer PCI (eCRF) - DEU									
Ja	141	13 (9,2)	NE [NE; NE]	142	3 (2,1)	NE [NE; NE]	4,48	[1,44; 19,53]	0,0078*
Nein	121	14 (11,6)	NE [NE; NE]	123	1 (0,8)	NE [NE; NE]	14,90	[3,00;270,02]	0,0002*
Interaktions p-Wert									0,2925
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	8 (25,8)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	9,00	[1,65;166,97]	0,0080*
>=14 bis <28 Tage	79	7 (8,9)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	12 (7,9)	NE [NE; NE]	153	3 (2,0)	NE [NE; NE]	4,11	[1,31; 18,03]	0,0141*
Interaktions p-Wert									0,5106
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	4 (25,0)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	12 (11,7)	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	12,43	[2,45;226,30]	0,0008*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.3 ADRIATIC: Summary of subgroup analysis of time to first PT: Hyperthyroidismus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	7 (7,1)	NE [NE; NE]	76	2 (2,6)	NE [NE; NE]	2,69	[0,65; 18,04]	0,1823
>=84 Tage	45	4 (8,9)	NE [NE; NE]	62	1 (1,6)	NE [NE; NE]	6,14	[0,91;120,14]	0,0636
Interaktions p-Wert									0,4824
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	8 (9,0)	NE [NE; NE]	88	2 (2,3)	NE [NE; NE]	3,93	[0,98; 26,04]	0,0529
Cisplatin	173	19 (11,0)	NE [NE; NE]	177	2 (1,1)	NE [NE; NE]	10,28	[2,99; 64,54]	<0,0001*
Interaktions p-Wert									0,3803
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	20 (10,4)	NE [NE; NE]	186	3 (1,6)	NE [NE; NE]	6,61	[2,27; 28,07]	0,0002*
Zweimal täglich	69	7 (10,1)	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	8,40	[1,49;156,93]	0,0126*
Interaktions p-Wert									0,8447
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	1,10	[0,04; 27,75]	0,9472
PR	189	22 (11,6)	NE [NE; NE]	199	3 (1,5)	NE [NE; NE]	8,13	[2,82; 34,36]	<0,0001*
SD	42	4 (9,5)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2135
Geschlecht - DEU									
Männer	178	19 (10,7)	NE [NE; NE]	187	3 (1,6)	NE [NE; NE]	6,81	[2,32; 28,99]	0,0002*
Frauen	84	8 (9,5)	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	7,90	[1,45;146,48]	0,0135*
Interaktions p-Wert									0,9034
Altersgruppe - DEU									
<65 Jahre	159	19 (11,9)	NE [NE; NE]	161	2 (1,2)	NE [NE; NE]	10,10	[2,93; 63,39]	<0,0001*
>=65 Jahre	103	8 (7,8)	NE [NE; NE]	104	2 (1,9)	NE [NE; NE]	4,10	[1,03; 27,14]	0,0455*
Interaktions p-Wert									0,4097

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.3 ADRIATIC: Summary of subgroup analysis of time to first PT: Hyperthyroidismus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	10 (12,8)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	9,59	[1,84;175,98]	0,0042*
TC or IC >=1%	84	6 (7,1)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	3,51	[0,81; 23,96]	0,0959
Interaktions p-Wert									0,4363
Raucherstatus - DEU									
Raucher	239	24 (10,0)	NE [NE; NE]	239	4 (1,7)	NE [NE; NE]	6,20	[2,40; 21,12]	<0,0001*
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	13 (10,2)	NE [NE; NE]	137	3 (2,2)	NE [NE; NE]	4,79	[1,54; 20,88]	0,0053*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	14 (10,7)	NE [NE; NE]	121	1 (0,8)	NE [NE; NE]	13,59	[2,73;246,34]	0,0003*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,3638
Geographische Region - DEU									
Asien	129	14 (10,9)	NE [NE; NE]	120	1 (0,8)	NE [NE; NE]	13,65	[2,75;247,41]	0,0003*
Europa	94	10 (10,6)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	3,99	[1,22; 17,81]	0,0208*
Nordamerika	39	3 (7,7)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2856
ECOG-Status zu Baseline - DEU									
0	131	10 (7,6)	NE [NE; NE]	131	4 (3,1)	NE [NE; NE]	2,50	[0,84; 9,11]	0,1033
1	131	17 (13,0)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Table 5.1.4 ADRIATIC: Summary of subgroup analysis of time to first PT: Hypothyreose
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	3 (8,3)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	3,49	[0,45; 70,48]	0,2418
Stadium III	226	39 (17,3)	NE [NE; NE]	228	9 (3,9)	NE [NE; NE]	4,49	[2,28; 9,89]	<0,0001*
Interaktions p-Wert									0,8375
TNM Status (eCRF) - DEU									
Stadium I/II	33	3 (9,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	3,39	[0,43; 68,57]	0,2528
Stadium III	229	39 (17,0)	NE [NE; NE]	231	9 (3,9)	NE [NE; NE]	4,52	[2,29; 9,94]	<0,0001*
Interaktions p-Wert									0,8172
Erhalt einer PCI (IVRS) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	143	5 (3,5)	NE [NE; NE]	5,19	[2,15; 15,42]	0,0001*
Nein	121	18 (14,9)	NE [NE; NE]	122	5 (4,1)	NE [NE; NE]	3,67	[1,47; 11,13]	0,0045*
Interaktions p-Wert									0,6246
Erhalt einer PCI (eCRF) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	142	4 (2,8)	NE [NE; NE]	6,48	[2,50; 22,04]	<0,0001*
Nein	121	18 (14,9)	NE [NE; NE]	123	6 (4,9)	NE [NE; NE]	3,07	[1,29; 8,46]	0,0105*
Interaktions p-Wert									0,2920
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	4 (12,9)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	11 (13,9)	NE [NE; NE]	80	6 (7,5)	NE [NE; NE]	1,89	[0,72; 5,48]	0,2002
>=28 Tage	152	27 (17,8)	NE [NE; NE]	153	4 (2,6)	NE [NE; NE]	7,22	[2,82; 24,42]	<0,0001*
Interaktions p-Wert									0,0652
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	2,38	[0,23; 51,23]	0,4638
>=28 bis <56 Tage	103	15 (14,6)	NE [NE; NE]	103	3 (2,9)	NE [NE; NE]	5,07	[1,67; 21,89]	0,0029*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.4 ADRIATIC: Summary of subgroup analysis of time to first PT: Hypothyreose
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	18 (18,4)	NE [NE; NE]	76	4 (5,3)	NE [NE; NE]	3,69	[1,38; 12,77]	0,0079*
>=84 Tage	45	7 (15,6)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	5,57	[1,35; 37,39]	0,0166*
Interaktions p-Wert									0,9255
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	14 (15,7)	NE [NE; NE]	88	6 (6,8)	NE [NE; NE]	2,19	[0,88; 6,18]	0,0947
Cisplatin	173	28 (16,2)	NE [NE; NE]	177	4 (2,3)	NE [NE; NE]	7,85	[3,08; 26,50]	<0,0001*
Interaktions p-Wert									0,0738
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	28 (14,5)	NE [NE; NE]	186	7 (3,8)	NE [NE; NE]	3,87	[1,79; 9,62]	0,0003*
Zweimal täglich	69	14 (20,3)	NE [NE; NE]	79	3 (3,8)	NE [NE; NE]	6,09	[1,99; 26,41]	0,0009*
Interaktions p-Wert									0,5451
Bestes Ansprechen auf cCRT - DEU									
CR	31	3 (9,7)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	1,63	[0,27; 12,36]	0,5894
PR	189	30 (15,9)	NE [NE; NE]	199	7 (3,5)	NE [NE; NE]	4,82	[2,25; 11,95]	<0,0001*
SD	42	9 (21,4)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	6,65	[1,25;122,56]	0,0230*
Interaktions p-Wert									0,5237
Geschlecht - DEU									
Männer	178	23 (12,9)	NE [NE; NE]	187	4 (2,1)	NE [NE; NE]	6,11	[2,35; 20,85]	<0,0001*
Frauen	84	19 (22,6)	NE [NE; NE]	78	6 (7,7)	NE [NE; NE]	3,28	[1,38; 9,00]	0,0060*
Interaktions p-Wert									0,3790
Altersgruppe - DEU									
<65 Jahre	159	29 (18,2)	NE [NE; NE]	161	5 (3,1)	NE [NE; NE]	6,17	[2,61; 18,15]	<0,0001*
>=65 Jahre	103	13 (12,6)	NE [NE; NE]	104	5 (4,8)	NE [NE; NE]	2,70	[1,02; 8,42]	0,0456*
Interaktions p-Wert									0,2499

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.4 ADRIATIC: Summary of subgroup analysis of time to first PT: Hypothyreose
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	13 (16,7)	NE [NE; NE]	72	2 (2,8)	NE [NE; NE]	6,31	[1,74; 40,36]	0,0032*
TC or IC >=1%	84	13 (15,5)	NE [NE; NE]	98	4 (4,1)	NE [NE; NE]	3,85	[1,36; 13,68]	0,0098*
Interaktions p-Wert									0,5976
Raucherstatus - DEU									
Raucher	239	35 (14,6)	NE [NE; NE]	239	9 (3,8)	NE [NE; NE]	3,99	[2,00; 8,83]	<0,0001*
Nichtraucher	23	7 (30,4)	NE [NE; NE]	26	1 (3,8)	NE [NE; NE]	9,86	[1,75;184,25]	0,0067*
Interaktions p-Wert									0,3854
Abstammung - DEU									
Weiß	128	21 (16,4)	NE [NE; NE]	137	6 (4,4)	NE [NE; NE]	3,93	[1,68; 10,71]	0,0011*
Schwarz/Afroamerikanisch	1	1 (100)	2,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	20 (15,3)	NE [NE; NE]	121	4 (3,3)	NE [NE; NE]	4,88	[1,85; 16,77]	0,0008*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7623
Geographische Region - DEU									
Asien	129	20 (15,5)	NE [NE; NE]	120	3 (2,5)	NE [NE; NE]	6,52	[2,24; 27,69]	0,0002*
Europa	94	15 (16,0)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	5,97	[1,97; 25,79]	0,0009*
Nordamerika	39	7 (17,9)	NE [NE; NE]	33	4 (12,1)	NE [NE; NE]	1,65	[0,50; 6,29]	0,4184
Interaktions p-Wert									0,2375
ECOG-Status zu Baseline - DEU									
0	131	18 (13,7)	NE [NE; NE]	131	4 (3,1)	NE [NE; NE]	4,50	[1,68; 15,57]	0,0019*
1	131	24 (18,3)	NE [NE; NE]	134	6 (4,5)	NE [NE; NE]	4,45	[1,94; 12,01]	0,0002*
Interaktions p-Wert									0,9876

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Nutzenbewertung nach AMNOG

Table 5.1.5 ADRIATIC: Summary of subgroup analysis of time to first SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	15 (41,7)	12,0 [4,1; NE]	37	14 (37,8)	23,5 [13,6; NE]	1,27	[0,61; 2,66]	0,5242
Stadium III	226	107 (47,3)	12,8 [8,3;24,5]	228	73 (32,0)	NE [NE; NE]	1,49	[1,11; 2,01]	0,0084*
Interaktions p-Wert									0,6908
TNM Status (eCRF) - DEU									
Stadium I/II	33	13 (39,4)	NE [NE; NE]	34	12 (35,3)	NE [NE; NE]	1,21	[0,55; 2,69]	0,6349
Stadium III	229	109 (47,6)	12,8 [8,1;22,7]	231	75 (32,5)	NE [NE; NE]	1,49	[1,11; 2,01]	0,0074*
Interaktions p-Wert									0,6268
Erhalt einer PCI (IVRS) - DEU									
Ja	141	67 (47,5)	12,0 [8,1; NE]	143	46 (32,2)	NE [NE; NE]	1,51	[1,04; 2,22]	0,0286*
Nein	121	55 (45,5)	14,7 [5,7; NE]	122	41 (33,6)	21,0 [11,1; NE]	1,39	[0,93; 2,09]	0,1120
Interaktions p-Wert									0,7514
Erhalt einer PCI (eCRF) - DEU									
Ja	141	67 (47,5)	12,0 [8,1; NE]	142	46 (32,4)	NE [NE; NE]	1,50	[1,03; 2,19]	0,0329*
Nein	121	55 (45,5)	14,7 [5,7; NE]	123	41 (33,3)	21,0 [11,1; NE]	1,40	[0,94; 2,12]	0,0980
Interaktions p-Wert									0,8166
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	14 (45,2)	14,7 [4,5; NE]	32	12 (37,5)	NE [NE; NE]	1,20	[0,55; 2,63]	0,6487
>=14 bis <28 Tage	79	44 (55,7)	5,7 [3,3;16,4]	80	25 (31,3)	NE [NE; NE]	2,15	[1,32; 3,56]	0,0018*
>=28 Tage	152	64 (42,1)	21,2 [9,6; NE]	153	50 (32,7)	NE [NE; NE]	1,23	[0,85; 1,79]	0,2684
Interaktions p-Wert									0,1754
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	11 (68,8)	4,7 [1,8;14,7]	24	10 (41,7)	21,0 [3,6; NE]	1,89	[0,79; 4,52]	0,1486

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.5 ADRIATIC: Summary of subgroup analysis of time to first SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=28 bis <56 Tage	103	48 (46,6)	12,0 [5,7; NE]	103	35 (34,0)	22,1 [11,1; NE]	1,43	[0,93; 2,22]	0,1056
>=56 bis <84 Tage	98	45 (45,9)	12,0 [8,1; NE]	76	27 (35,5)	25,2 [9,8; NE]	1,16	[0,72; 1,89]	0,5483
>=84 Tage	45	18 (40,0)	NE [NE; NE]	62	15 (24,2)	NE [NE; NE]	1,89	[0,95; 3,81]	0,0681
Interaktions p-Wert									0,6196
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	49 (55,1)	8,4 [5,0;20,0]	88	28 (31,8)	NE [NE; NE]	1,81	[1,15; 2,92]	0,0104*
Cisplatin	173	73 (42,2)	21,2 [9,6; NE]	177	59 (33,3)	NE [NE; NE]	1,28	[0,91; 1,81]	0,1530
Interaktions p-Wert									0,2383
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	90 (46,6)	12,0 [8,1;24,5]	186	66 (35,5)	23,5 [15,7; NE]	1,32	[0,96; 1,82]	0,0854
Zweimal täglich	69	32 (46,4)	14,7 [7,2; NE]	79	21 (26,6)	NE [NE; NE]	1,84	[1,07; 3,24]	0,0272*
Interaktions p-Wert									0,2995
Bestes Ansprechen auf cCRT - DEU									
CR	31	10 (32,3)	NE [NE; NE]	34	9 (26,5)	NE [NE; NE]	1,26	[0,51; 3,17]	0,6133
PR	189	91 (48,1)	12,0 [7,1;24,5]	199	70 (35,2)	25,2 [14,8; NE]	1,46	[1,07; 1,99]	0,0175*
SD	42	21 (50,0)	16,4 [8,3; NE]	32	8 (25,0)	NE [NE; NE]	1,80	[0,83; 4,32]	0,1428
Interaktions p-Wert									0,8377
Geschlecht - DEU									
Männer	178	80 (44,9)	14,7 [8,1; NE]	187	57 (30,5)	NE [NE; NE]	1,56	[1,11; 2,20]	0,0100*
Frauen	84	42 (50,0)	12,8 [5,5; NE]	78	30 (38,5)	NE [NE; NE]	1,23	[0,77; 1,99]	0,3806
Interaktions p-Wert									0,4294
Altersgruppe - DEU									
<65 Jahre	159	76 (47,8)	12,0 [7,4;24,5]	161	56 (34,8)	NE [NE; NE]	1,33	[0,95; 1,89]	0,1015
>=65 Jahre	103	46 (44,7)	14,7 [8,1; NE]	104	31 (29,8)	NE [NE; NE]	1,67	[1,06; 2,65]	0,0260*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.5 ADRIATIC: Summary of subgroup analysis of time to first SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktions p-Wert									0,4397
PD-L1-Status - DEU									
TC and IC <1%	78	36 (46,2)	20,0 [5,7; NE]	72	24 (33,3)	NE [NE; NE]	1,39	[0,83; 2,36]	0,2073
TC or IC >=1%	84	37 (44,0)	14,7 [7,4; NE]	98	29 (29,6)	NE [NE; NE]	1,52	[0,94; 2,50]	0,0877
Interaktions p-Wert									0,7999
Raucherstatus - DEU									
Raucher	239	112 (46,9)	12,8 [8,3;24,5]	239	81 (33,9)	NE [NE; NE]	1,42	[1,07; 1,89]	0,0158*
Nichtraucher	23	10 (43,5)	12,0 [4,1; NE]	26	6 (23,1)	NE [NE; NE]	1,92	[0,71; 5,63]	0,1994
Interaktions p-Wert									0,5716
Abstammung - DEU									
Weiß	128	61 (47,7)	14,7 [8,3; NE]	137	50 (36,5)	NE [NE; NE]	1,29	[0,89; 1,88]	0,1862
Schwarz/Afroamerikanisch	1	1 (100)	12,8 [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	60 (45,8)	11,1 [5,7; NE]	121	34 (28,1)	NE [NE; NE]	1,81	[1,20; 2,78]	0,0048*
Andere	2	0	NE [NE; NE]	4	2 (50,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2327
Geographische Region - DEU									
Asien	129	58 (45,0)	12,0 [6,4; NE]	120	33 (27,5)	NE [NE; NE]	1,79	[1,18; 2,77]	0,0065*
Europa	94	39 (41,5)	22,6 [9,4; NE]	112	36 (32,1)	NE [NE; NE]	1,18	[0,75; 1,87]	0,4651
Nordamerika	39	25 (64,1)	3,3 [1,6;16,4]	33	18 (54,5)	7,8 [1,9;14,8]	1,25	[0,69; 2,33]	0,4641
Interaktions p-Wert									0,3818
ECOG-Status zu Baseline - DEU									
0	131	55 (42,0)	22,7 [8,1; NE]	131	36 (27,5)	NE [NE; NE]	1,53	[1,01; 2,35]	0,0448*
1	131	67 (51,1)	10,9 [5,5;20,0]	134	51 (38,1)	22,1 [11,1; NE]	1,41	[0,98; 2,04]	0,0613
Interaktions p-Wert									0,7791

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.6 ADRIATIC: Summary of subgroup analysis of time to first PT: Pruritus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	5 (13,9)	NE [NE; NE]	37	5 (13,5)	NE [NE; NE]	1,11	[0,31; 4,00]	0,8657
Stadium III	226	29 (12,8)	NE [NE; NE]	228	14 (6,1)	NE [NE; NE]	2,05	[1,10; 4,00]	0,0228*
Interaktions p-Wert									0,3920
TNM Status (eCRF) - DEU									
Stadium I/II	33	5 (15,2)	NE [NE; NE]	34	3 (8,8)	NE [NE; NE]	1,85	[0,45; 9,03]	0,3901
Stadium III	229	29 (12,7)	NE [NE; NE]	231	16 (6,9)	NE [NE; NE]	1,80	[0,99; 3,38]	0,0550
Interaktions p-Wert									0,9686
Erhalt einer PCI (IVRS) - DEU									
Ja	141	16 (11,3)	NE [NE; NE]	143	15 (10,5)	NE [NE; NE]	1,05	[0,52; 2,14]	0,8959
Nein	121	18 (14,9)	NE [NE; NE]	122	4 (3,3)	NE [NE; NE]	4,66	[1,74; 16,12]	0,0015*
Interaktions p-Wert									0,0163*
Erhalt einer PCI (eCRF) - DEU									
Ja	141	16 (11,3)	NE [NE; NE]	142	15 (10,6)	NE [NE; NE]	1,04	[0,51; 2,12]	0,9168
Nein	121	18 (14,9)	NE [NE; NE]	123	4 (3,3)	NE [NE; NE]	4,71	[1,76; 16,30]	0,0013*
Interaktions p-Wert									0,0148*
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	11 (13,9)	NE [NE; NE]	80	7 (8,8)	NE [NE; NE]	1,64	[0,64; 4,45]	0,3015
>=28 Tage	152	20 (13,2)	NE [NE; NE]	153	12 (7,8)	NE [NE; NE]	1,67	[0,83; 3,51]	0,1544
Interaktions p-Wert									0,9753
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	3 (18,8)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	14 (13,6)	NE [NE; NE]	103	6 (5,8)	NE [NE; NE]	2,37	[0,95; 6,69]	0,0644

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.6 ADRIATIC: Summary of subgroup analysis of time to first PT: Pruritus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	13 (13,3)	NE [NE; NE]	76	6 (7,9)	NE [NE; NE]	1,60	[0,63; 4,56]	0,3279
>=84 Tage	45	4 (8,9)	NE [NE; NE]	62	7 (11,3)	NE [NE; NE]	0,85	[0,22; 2,82]	0,7981
Interaktions p-Wert									0,4209
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	13 (14,6)	NE [NE; NE]	88	4 (4,5)	NE [NE; NE]	3,11	[1,10; 11,05]	0,0315*
Cisplatin	173	21 (12,1)	NE [NE; NE]	177	15 (8,5)	NE [NE; NE]	1,45	[0,75; 2,86]	0,2724
Interaktions p-Wert									0,2342
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	25 (13,0)	NE [NE; NE]	186	10 (5,4)	NE [NE; NE]	2,39	[1,18; 5,22]	0,0144*
Zweimal täglich	69	9 (13,0)	NE [NE; NE]	79	9 (11,4)	NE [NE; NE]	1,14	[0,45; 2,92]	0,7805
Interaktions p-Wert									0,2169
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	4 (11,8)	NE [NE; NE]	0,26	[0,01; 1,77]	0,1814
PR	189	28 (14,8)	NE [NE; NE]	199	12 (6,0)	NE [NE; NE]	2,52	[1,31; 5,14]	0,0051*
SD	42	5 (11,9)	NE [NE; NE]	32	3 (9,4)	NE [NE; NE]	1,15	[0,28; 5,59]	0,8521
Interaktions p-Wert									0,0723
Geschlecht - DEU									
Männer	178	20 (11,2)	NE [NE; NE]	187	13 (7,0)	NE [NE; NE]	1,59	[0,80; 3,27]	0,1888
Frauen	84	14 (16,7)	NE [NE; NE]	78	6 (7,7)	NE [NE; NE]	2,21	[0,89; 6,24]	0,0907
Interaktions p-Wert									0,5831
Altersgruppe - DEU									
<65 Jahre	159	21 (13,2)	NE [NE; NE]	161	12 (7,5)	NE [NE; NE]	1,75	[0,87; 3,67]	0,1156
>=65 Jahre	103	13 (12,6)	NE [NE; NE]	104	7 (6,7)	NE [NE; NE]	1,89	[0,77; 5,02]	0,1655
Interaktions p-Wert									0,8979

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.6 ADRIATIC: Summary of subgroup analysis of time to first PT: Pruritus
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	8 (10,3)	NE [NE; NE]	72	3 (4,2)	NE [NE; NE]	2,38	[0,69; 10,88]	0,1764
TC or IC >=1%	84	11 (13,1)	NE [NE; NE]	98	7 (7,1)	NE [NE; NE]	1,79	[0,70; 4,86]	0,2221
Interaktions p-Wert									0,7289
Raucherstatus - DEU									
Raucher	239	31 (13,0)	NE [NE; NE]	239	18 (7,5)	NE [NE; NE]	1,71	[0,97; 3,12]	0,0653
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	1 (3,8)	NE [NE; NE]	3,41	[0,44; 68,89]	0,2509
Interaktions p-Wert									0,5452
Abstammung - DEU									
Weiß	128	14 (10,9)	NE [NE; NE]	137	10 (7,3)	NE [NE; NE]	1,51	[0,68; 3,51]	0,3143
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	20 (15,3)	NE [NE; NE]	121	9 (7,4)	NE [NE; NE]	2,05	[0,96; 4,74]	0,0636
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5964
Geographische Region - DEU									
Asien	129	20 (15,5)	NE [NE; NE]	120	9 (7,5)	NE [NE; NE]	2,05	[0,96; 4,74]	0,0633
Europa	94	8 (8,5)	NE [NE; NE]	112	7 (6,3)	NE [NE; NE]	1,28	[0,46; 3,64]	0,6357
Nordamerika	39	6 (15,4)	NE [NE; NE]	33	3 (9,1)	NE [NE; NE]	1,98	[0,52; 9,37]	0,3219
Interaktions p-Wert									0,7577
ECOG-Status zu Baseline - DEU									
0	131	21 (16,0)	NE [NE; NE]	131	11 (8,4)	NE [NE; NE]	1,89	[0,93; 4,06]	0,0800
1	131	13 (9,9)	NE [NE; NE]	134	8 (6,0)	NE [NE; NE]	1,66	[0,70; 4,20]	0,2516
Interaktions p-Wert									0,8269

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.7 ADRIATIC: Summary of subgroup analysis of time to first SOC: Herzerkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	1 (2,8)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	1,10	[0,04; 27,77]	0,9468
Stadium III	226	31 (13,7)	NE [NE; NE]	228	13 (5,7)	NE [NE; NE]	2,28	[1,22; 4,51]	0,0092*
Interaktions p-Wert									0,6186
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	32 (14,0)	NE [NE; NE]	231	13 (5,6)	NE [NE; NE]	2,37	[1,27; 4,68]	0,0060*
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	20 (14,2)	NE [NE; NE]	143	7 (4,9)	NE [NE; NE]	2,78	[1,23; 7,09]	0,0129*
Nein	121	12 (9,9)	NE [NE; NE]	122	7 (5,7)	NE [NE; NE]	1,68	[0,68; 4,52]	0,2666
Interaktions p-Wert									0,4363
Erhalt einer PCI (eCRF) - DEU									
Ja	141	20 (14,2)	NE [NE; NE]	142	7 (4,9)	NE [NE; NE]	2,76	[1,22; 7,04]	0,0137*
Nein	121	12 (9,9)	NE [NE; NE]	123	7 (5,7)	NE [NE; NE]	1,70	[0,68; 4,56]	0,2571
Interaktions p-Wert									0,4531
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	5 (16,1)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	4,50	[0,72; 86,16]	0,1140
>=14 bis <28 Tage	79	9 (11,4)	NE [NE; NE]	80	2 (2,5)	NE [NE; NE]	4,54	[1,17; 29,75]	0,0273*
>=28 Tage	152	18 (11,8)	NE [NE; NE]	153	11 (7,2)	NE [NE; NE]	1,60	[0,77; 3,49]	0,2142
Interaktions p-Wert									0,3394
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	3 (18,8)	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	3,59	[0,46; 72,57]	0,2309
>=28 bis <56 Tage	103	13 (12,6)	NE [NE; NE]	103	2 (1,9)	NE [NE; NE]	6,56	[1,81; 41,97]	0,0025*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.7 ADRIATIC: Summary of subgroup analysis of time to first SOC: Herzerkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	14 (14,3)	NE [NE; NE]	76	7 (9,2)	NE [NE; NE]	1,38	[0,57; 3,64]	0,4812
>=84 Tage	45	2 (4,4)	NE [NE; NE]	62	4 (6,5)	NE [NE; NE]	0,75	[0,10; 3,83]	0,7324
Interaktions p-Wert									0,1401
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	14 (15,7)	NE [NE; NE]	88	7 (8,0)	NE [NE; NE]	1,77	[0,73; 4,66]	0,2080
Cisplatin	173	18 (10,4)	NE [NE; NE]	177	7 (4,0)	NE [NE; NE]	2,64	[1,15; 6,80]	0,0212*
Interaktions p-Wert									0,5310
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	25 (13,0)	NE [NE; NE]	186	10 (5,4)	NE [NE; NE]	2,32	[1,15; 5,06]	0,0185*
Zweimal täglich	69	7 (10,1)	NE [NE; NE]	79	4 (5,1)	NE [NE; NE]	1,92	[0,58; 7,33]	0,2881
Interaktions p-Wert									0,7971
Bestes Ansprechen auf cCRT - DEU									
CR	31	4 (12,9)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	2,22	[0,43; 16,03]	0,3407
PR	189	24 (12,7)	NE [NE; NE]	199	12 (6,0)	NE [NE; NE]	2,09	[1,06; 4,32]	0,0318*
SD	42	4 (9,5)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9464
Geschlecht - DEU									
Männer	178	19 (10,7)	NE [NE; NE]	187	11 (5,9)	NE [NE; NE]	1,73	[0,84; 3,76]	0,1400
Frauen	84	13 (15,5)	NE [NE; NE]	78	3 (3,8)	NE [NE; NE]	4,00	[1,29; 17,44]	0,0148*
Interaktions p-Wert									0,2427
Altersgruppe - DEU									
<65 Jahre	159	20 (12,6)	NE [NE; NE]	161	7 (4,3)	NE [NE; NE]	2,70	[1,20; 6,89]	0,0158*
>=65 Jahre	103	12 (11,7)	NE [NE; NE]	104	7 (6,7)	NE [NE; NE]	1,76	[0,71; 4,72]	0,2274
Interaktions p-Wert									0,5055

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.1.7 ADRIATIC: Summary of subgroup analysis of time to first SOC: Herzerkrankungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	9 (11,5)	NE [NE; NE]	72	4 (5,6)	NE [NE; NE]	1,94	[0,63; 7,15]	0,2547
TC or IC >=1%	84	9 (10,7)	NE [NE; NE]	98	5 (5,1)	NE [NE; NE]	1,91	[0,66; 6,21]	0,2365
Interaktions p-Wert									0,9848
Raucherstatus - DEU									
Raucher	239	28 (11,7)	NE [NE; NE]	239	12 (5,0)	NE [NE; NE]	2,25	[1,17; 4,60]	0,0140*
Nichtraucher	23	4 (17,4)	NE [NE; NE]	26	2 (7,7)	NE [NE; NE]	2,16	[0,42; 15,61]	0,3586
Interaktions p-Wert									0,9645
Abstammung - DEU									
Weiß	128	17 (13,3)	NE [NE; NE]	137	6 (4,4)	NE [NE; NE]	3,09	[1,29; 8,57]	0,0108*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	15 (11,5)	NE [NE; NE]	121	6 (5,0)	NE [NE; NE]	2,16	[0,88; 6,06]	0,0956
Andere	2	0	NE [NE; NE]	4	2 (50,0)	3,5 [0,1; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5968
Geographische Region - DEU									
Asien	129	14 (10,9)	NE [NE; NE]	120	6 (5,0)	NE [NE; NE]	2,01	[0,81; 5,69]	0,1368
Europa	94	12 (12,8)	NE [NE; NE]	112	6 (5,4)	NE [NE; NE]	2,17	[0,84; 6,24]	0,1099
Nordamerika	39	6 (15,4)	NE [NE; NE]	33	2 (6,1)	NE [NE; NE]	3,39	[0,78; 23,19]	0,1072
Interaktions p-Wert									0,8513
ECOG-Status zu Baseline - DEU									
0	131	13 (9,9)	NE [NE; NE]	131	6 (4,6)	NE [NE; NE]	1,96	[0,78; 5,59]	0,1579
1	131	19 (14,5)	NE [NE; NE]	134	8 (6,0)	NE [NE; NE]	2,50	[1,13; 6,06]	0,0226*
Interaktions p-Wert									0,7101

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Nutzenbewertung nach AMNOG

Table 5.1.8 ADRIATIC: Summary of subgroup analysis of time to first SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	13 (36,1)	NE [NE; NE]	37	10 (27,0)	NE [NE; NE]	1,55	[0,68; 3,64]	0,2919
Stadium III	226	75 (33,2)	NE [NE; NE]	228	56 (24,6)	NE [NE; NE]	1,38	[0,98; 1,95]	0,0687
Interaktions p-Wert									0,7900
TNM Status (eCRF) - DEU									
Stadium I/II	33	13 (39,4)	19,2 [8,0; NE]	34	9 (26,5)	NE [NE; NE]	1,71	[0,74; 4,15]	0,2096
Stadium III	229	75 (32,8)	NE [NE; NE]	231	57 (24,7)	NE [NE; NE]	1,36	[0,96; 1,92]	0,0813
Interaktions p-Wert									0,6159
Erhalt einer PCI (IVRS) - DEU									
Ja	141	57 (40,4)	NE [NE; NE]	143	51 (35,7)	NE [NE; NE]	1,21	[0,83; 1,76]	0,3301
Nein	121	31 (25,6)	NE [NE; NE]	122	15 (12,3)	NE [NE; NE]	2,11	[1,16; 4,02]	0,0141*
Interaktions p-Wert									0,1242
Erhalt einer PCI (eCRF) - DEU									
Ja	141	57 (40,4)	NE [NE; NE]	142	51 (35,9)	NE [NE; NE]	1,19	[0,82; 1,75]	0,3557
Nein	121	31 (25,6)	NE [NE; NE]	123	15 (12,2)	NE [NE; NE]	2,13	[1,17; 4,06]	0,0128*
Interaktions p-Wert									0,1110
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	8 (25,8)	NE [NE; NE]	32	5 (15,6)	NE [NE; NE]	1,60	[0,53; 5,30]	0,4029
>=14 bis <28 Tage	79	27 (34,2)	NE [NE; NE]	80	15 (18,8)	NE [NE; NE]	1,88	[1,02; 3,63]	0,0445*
>=28 Tage	152	53 (34,9)	NE [NE; NE]	153	46 (30,1)	NE [NE; NE]	1,23	[0,83; 1,83]	0,3108
Interaktions p-Wert									0,5083
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	2 (8,3)	NE [NE; NE]	1,31	[0,16; 10,89]	0,7891
>=28 bis <56 Tage	103	34 (33,0)	NE [NE; NE]	103	25 (24,3)	NE [NE; NE]	1,41	[0,84; 2,38]	0,1907

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.1.8 ADRIATIC: Summary of subgroup analysis of time to first SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	40 (40,8)	NE [NE; NE]	76	25 (32,9)	NE [NE; NE]	1,19	[0,73; 1,98]	0,4958
>=84 Tage	45	12 (26,7)	NE [NE; NE]	62	14 (22,6)	NE [NE; NE]	1,44	[0,65; 3,12]	0,3598
Interaktions p-Wert									0,9647
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	35 (39,3)	23,0 [9,2; NE]	88	24 (27,3)	NE [NE; NE]	1,37	[0,82; 2,34]	0,2265
Cisplatin	173	53 (30,6)	NE [NE; NE]	177	42 (23,7)	NE [NE; NE]	1,40	[0,94; 2,11]	0,1016
Interaktions p-Wert									0,9555
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	59 (30,6)	NE [NE; NE]	186	45 (24,2)	NE [NE; NE]	1,27	[0,87; 1,89]	0,2182
Zweimal täglich	69	29 (42,0)	NE [NE; NE]	79	21 (26,6)	NE [NE; NE]	1,76	[1,01; 3,13]	0,0464*
Interaktions p-Wert									0,3522
Bestes Ansprechen auf cCRT - DEU									
CR	31	14 (45,2)	8,0 [3,1; NE]	34	12 (35,3)	NE [NE; NE]	1,37	[0,63; 3,01]	0,4261
PR	189	67 (35,4)	NE [NE; NE]	199	46 (23,1)	NE [NE; NE]	1,67	[1,15; 2,44]	0,0070*
SD	42	7 (16,7)	NE [NE; NE]	32	8 (25,0)	NE [NE; NE]	0,56	[0,20; 1,56]	0,2626
Interaktions p-Wert									0,1433
Geschlecht - DEU									
Männer	178	58 (32,6)	NE [NE; NE]	187	41 (21,9)	NE [NE; NE]	1,58	[1,06; 2,37]	0,0244*
Frauen	84	30 (35,7)	NE [NE; NE]	78	25 (32,1)	NE [NE; NE]	1,10	[0,65; 1,88]	0,7258
Interaktions p-Wert									0,2888
Altersgruppe - DEU									
<65 Jahre	159	50 (31,4)	NE [NE; NE]	161	41 (25,5)	NE [NE; NE]	1,25	[0,83; 1,90]	0,2852
>=65 Jahre	103	38 (36,9)	NE [NE; NE]	104	25 (24,0)	NE [NE; NE]	1,66	[1,01; 2,78]	0,0474*
Interaktions p-Wert									0,3994

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.1.8 ADRIATIC: Summary of subgroup analysis of time to first SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	30 (38,5)	NE [NE; NE]	72	21 (29,2)	NE [NE; NE]	1,33	[0,76; 2,35]	0,3169
TC or IC >=1%	84	27 (32,1)	NE [NE; NE]	98	24 (24,5)	NE [NE; NE]	1,29	[0,74; 2,24]	0,3692
Interaktions p-Wert									0,9376
Raucherstatus - DEU									
Raucher	239	76 (31,8)	NE [NE; NE]	239	56 (23,4)	NE [NE; NE]	1,40	[0,99; 1,98]	0,0551
Nichtraucher	23	12 (52,2)	9,2 [1,8; NE]	26	10 (38,5)	NE [NE; NE]	1,54	[0,66; 3,65]	0,3110
Interaktions p-Wert									0,8339
Abstammung - DEU									
Weiß	128	36 (28,1)	NE [NE; NE]	137	31 (22,6)	NE [NE; NE]	1,29	[0,80; 2,09]	0,3035
Schwarz/Afroamerikanisch	1	1 (100)	1,9 [NE; NE]	3	1 (33,3)	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	51 (38,9)	NE [NE; NE]	121	34 (28,1)	NE [NE; NE]	1,46	[0,95; 2,27]	0,0839
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,6998
Geographische Region - DEU									
Asien	129	50 (38,8)	NE [NE; NE]	120	34 (28,3)	NE [NE; NE]	1,43	[0,93; 2,22]	0,1062
Europa	94	24 (25,5)	NE [NE; NE]	112	21 (18,8)	NE [NE; NE]	1,38	[0,77; 2,50]	0,2824
Nordamerika	39	14 (35,9)	NE [NE; NE]	33	11 (33,3)	NE [NE; NE]	1,13	[0,51; 2,55]	0,7589
Interaktions p-Wert									0,8797
ECOG-Status zu Baseline - DEU									
0	131	38 (29,0)	NE [NE; NE]	131	29 (22,1)	NE [NE; NE]	1,34	[0,83; 2,18]	0,2372
1	131	50 (38,2)	NE [NE; NE]	134	37 (27,6)	NE [NE; NE]	1,46	[0,96; 2,25]	0,0777
Interaktions p-Wert									0,7840

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Anhang 4-G8.1.3: UE jeglichen Schweregrades - gesamt und nach SOC/PT - Subgruppenanalysen Kaplan-Meier-Plot

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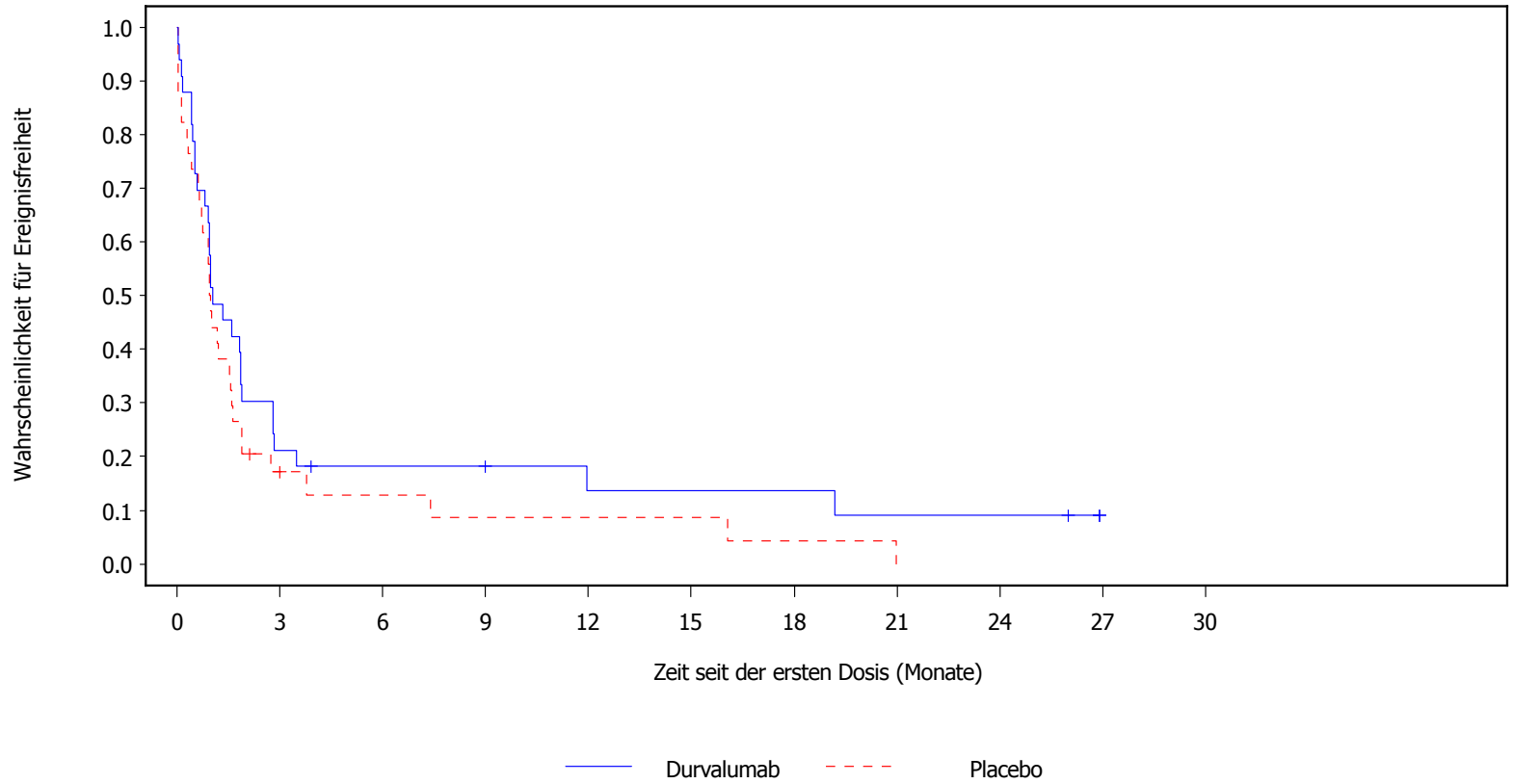
Figure 5.8.1 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for TNM Status (eCRF) - DEU=Stadium I/II
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

33	7	5	5	3	3	3	2	2	0	0	Durvalumab
34	4	3	2	2	2	1	0	0	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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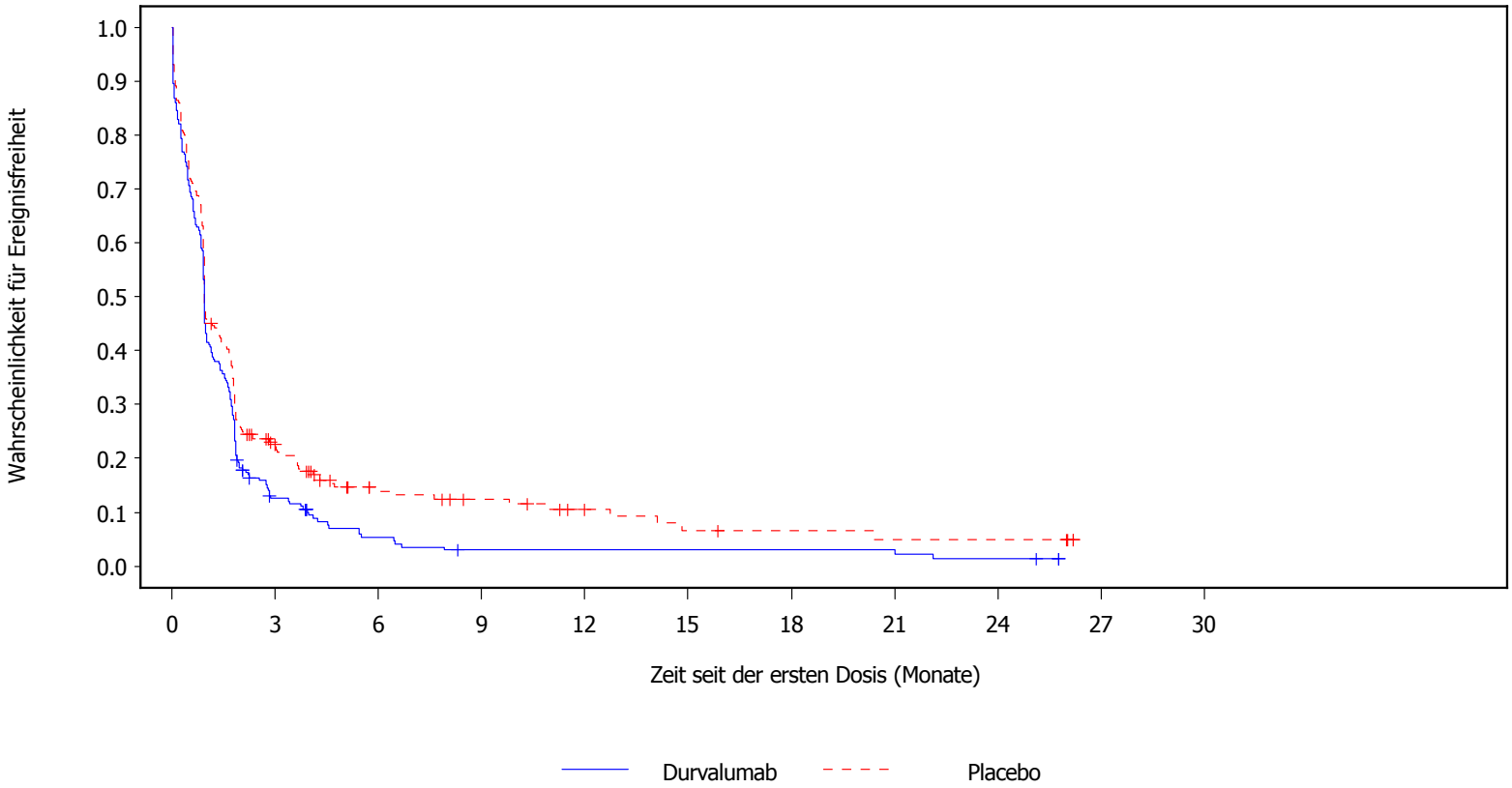
Figure 5.8.2 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for TNM Status (eCRF) - DEU=Stadium III
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

229	25	9	4	4	4	4	4	2	0	0	Durvalumab
231	45	20	14	8	5	4	3	3	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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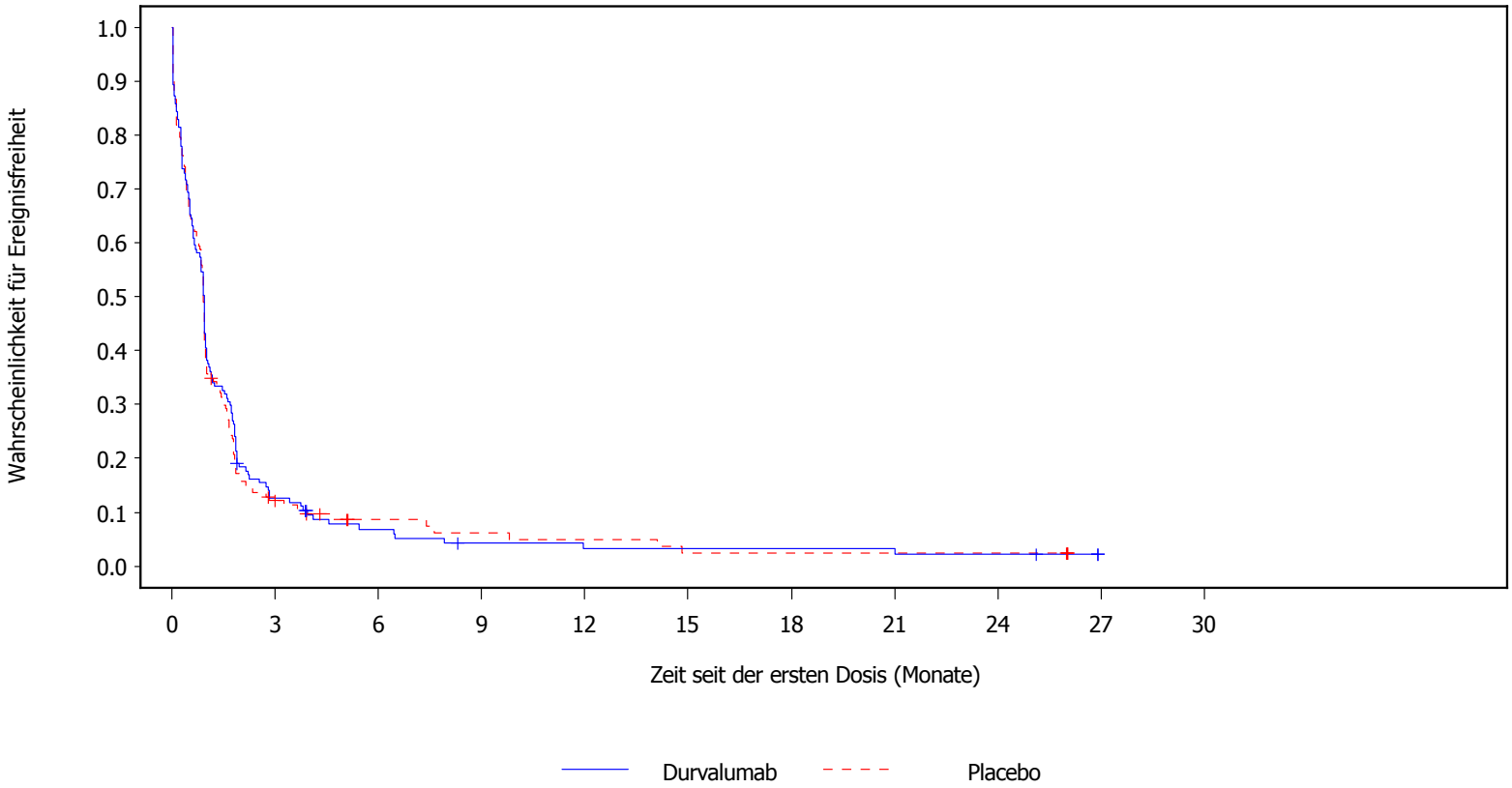
Figure 5.8.3 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for Erhalt einer PCI (IVRS) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	17	8	4	3	3	3	3	2	0	0	Durvalumab
143	15	7	5	4	2	2	2	2	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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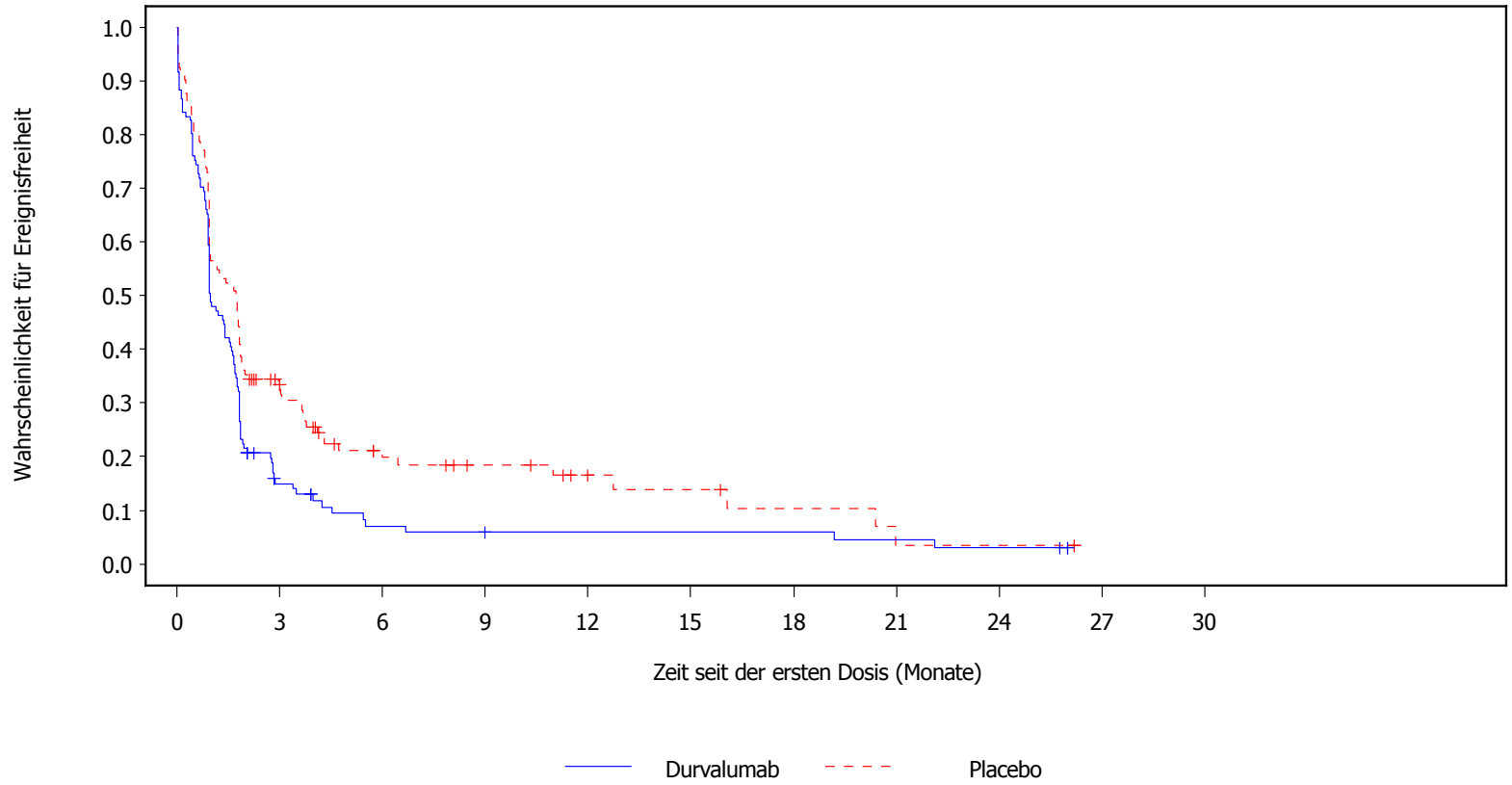
Figure 5.8.4 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for Erhalt einer PCI (IVRS) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	15	6	5	4	4	4	3	2	0	0	Durvalumab
122	34	16	11	6	5	3	1	1	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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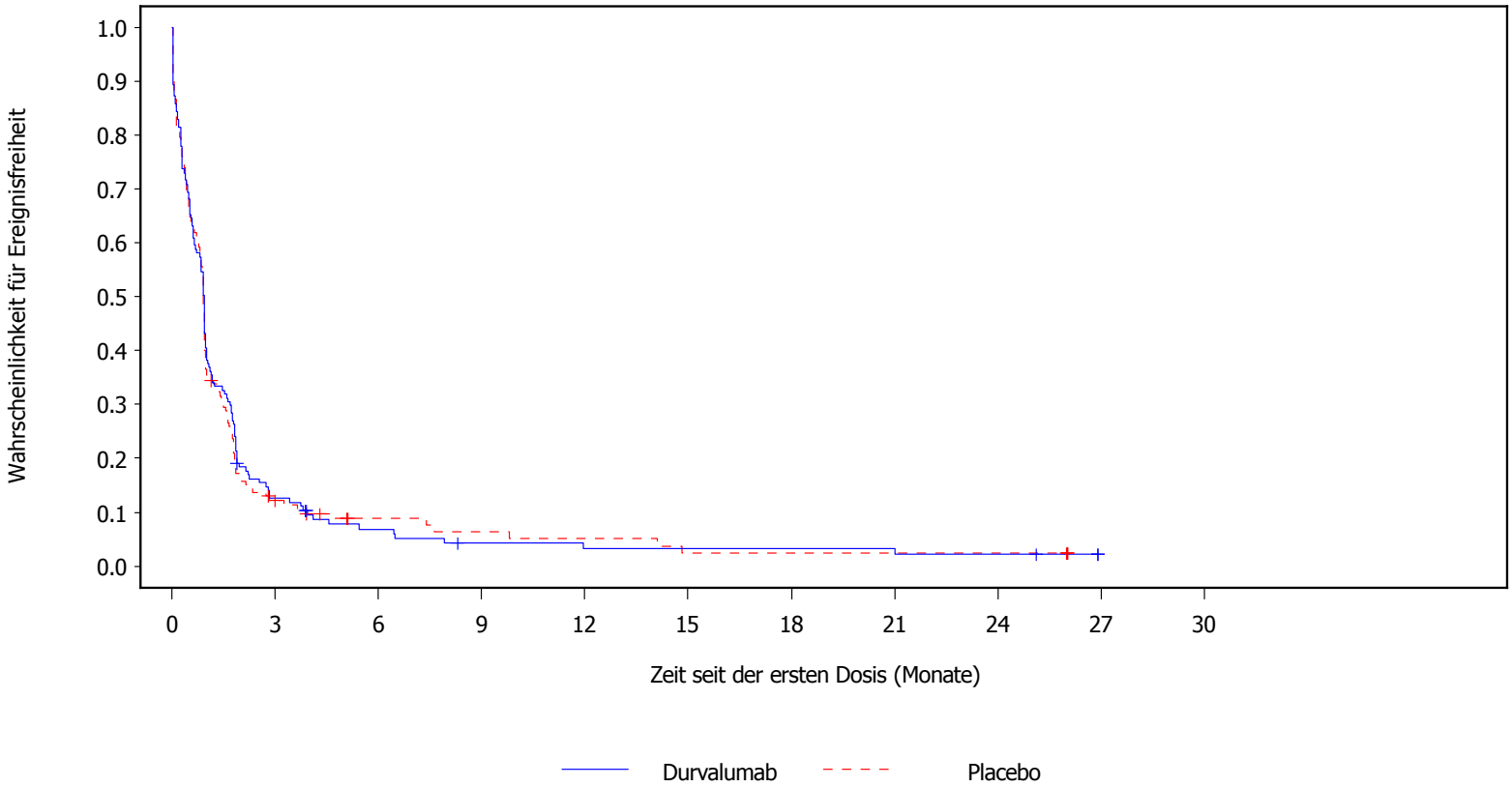
Figure 5.8.5 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for Erhalt einer PCI (eCRF) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	17	8	4	3	3	3	3	2	0	0	Durvalumab
142	15	7	5	4	2	2	2	2	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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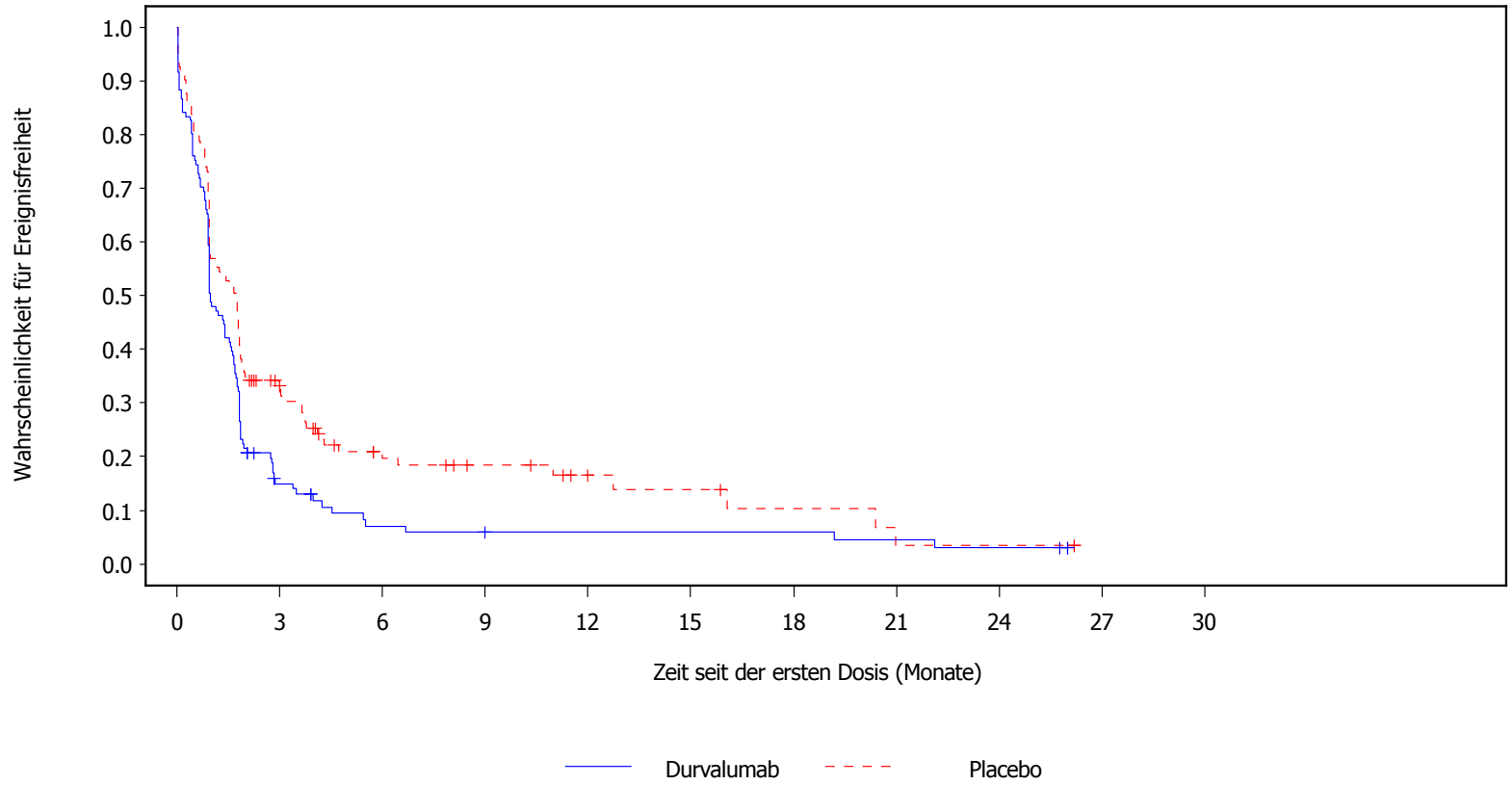
Figure 5.8.6 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UE for Erhalt einer PCI (eCRF) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	15	6	5	4	4	4	3	2	0	0	Durvalumab
123	34	16	11	6	5	3	1	1	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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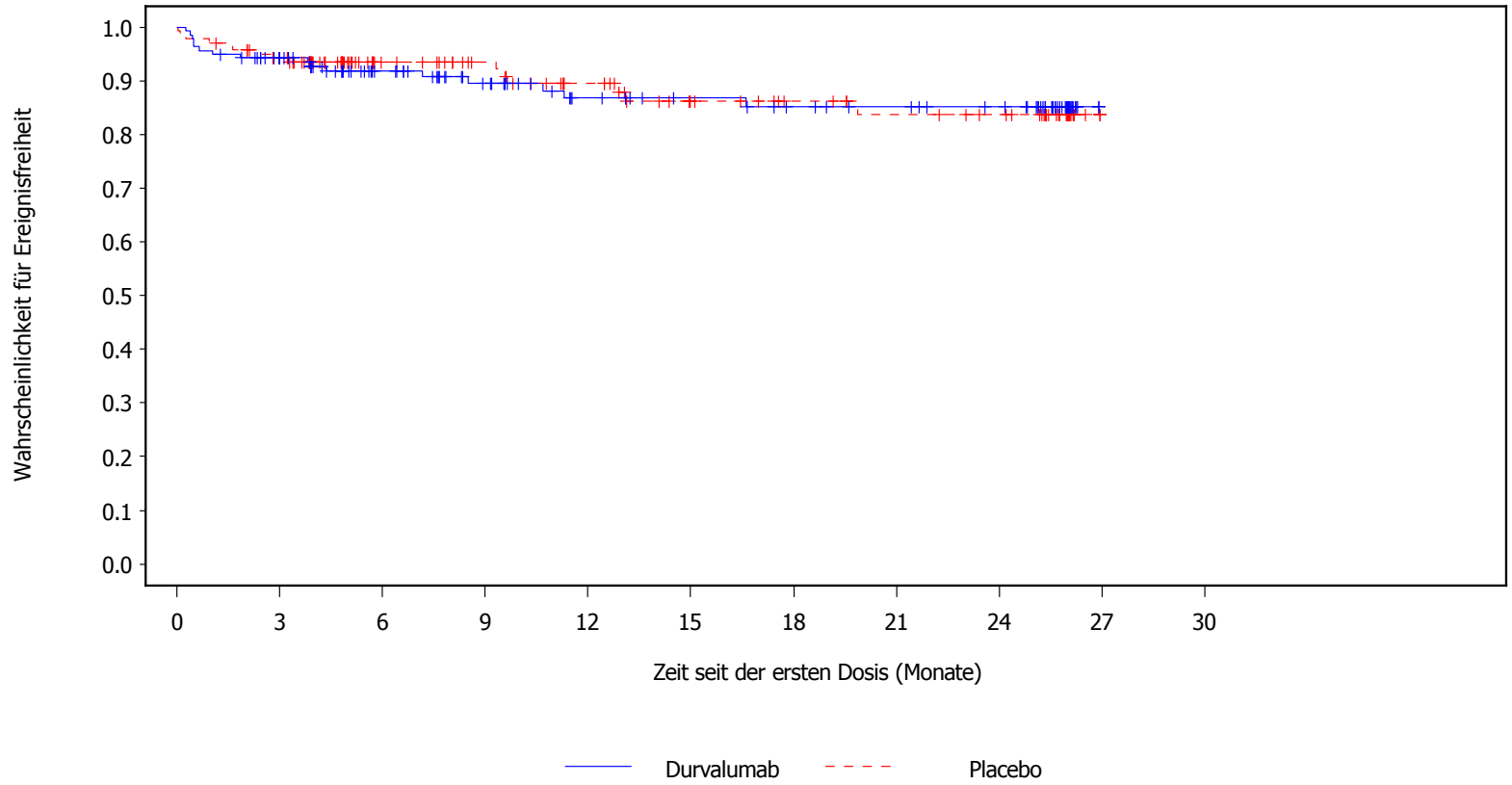
Figure 5.8.7 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of PT: Pruritus for Erhalt einer PCI (IVRS) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	121	91	74	60	54	50	47	43	0	0	Durvalumab
143	123	80	70	59	45	39	35	32	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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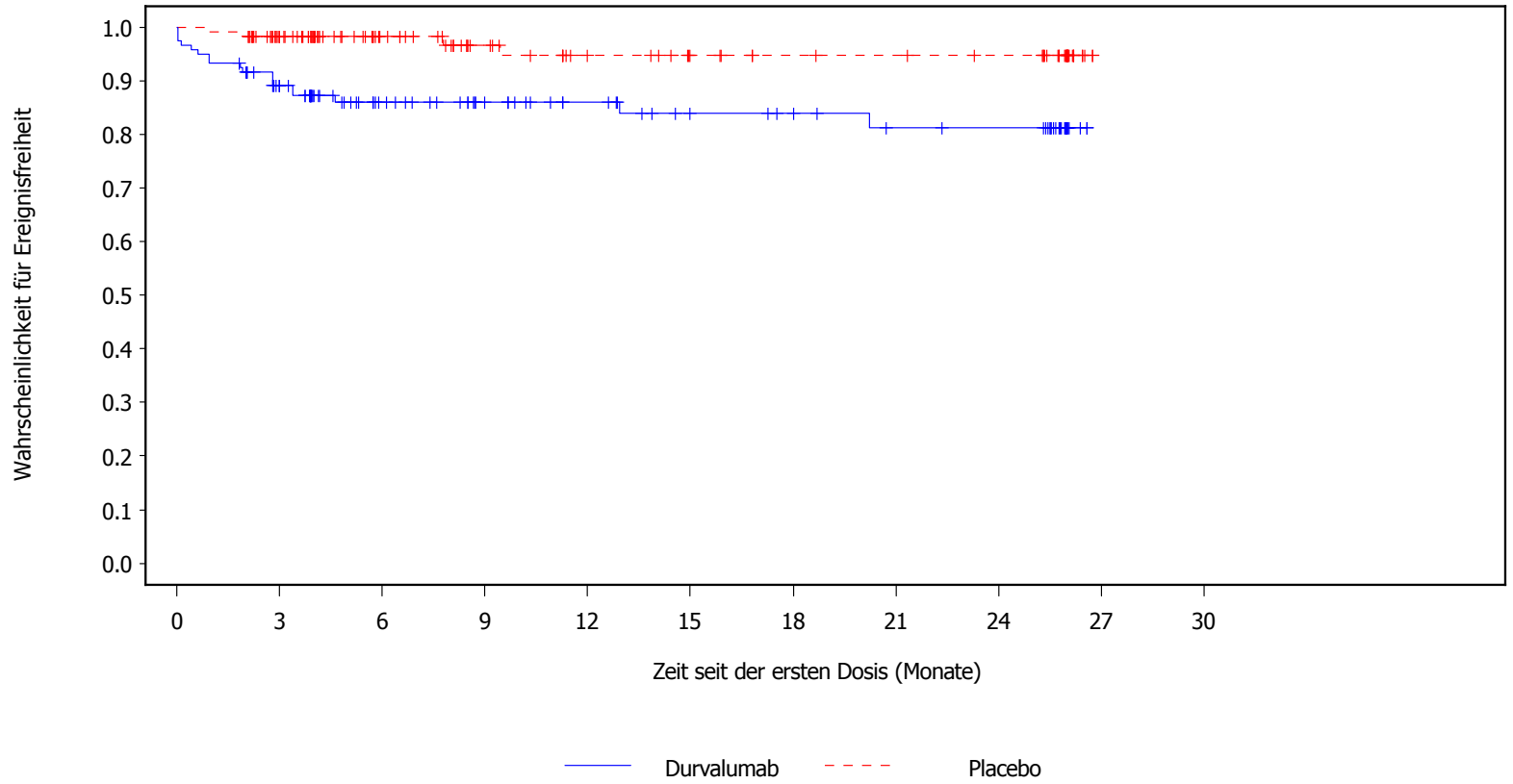
Figure 5.8.8 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of PT: Pruritus for Erhalt einer PCI (IVRS) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	97	64	52	43	35	33	29	28	0	0	Durvalumab
122	101	69	52	41	35	31	30	28	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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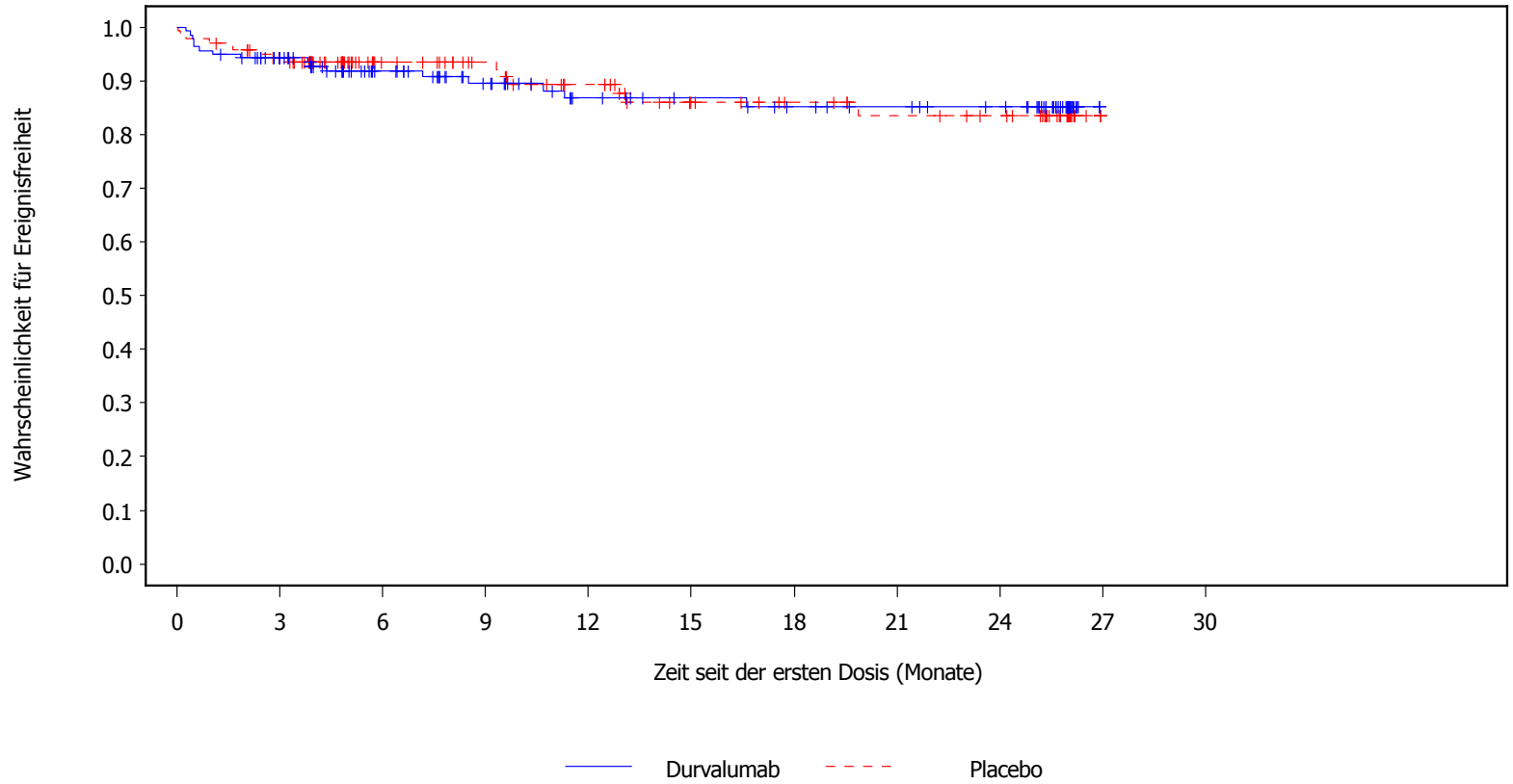
Figure 5.8.9 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of PT: Pruritus for Erhalt einer PCI (eCRF) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	121	91	74	60	54	50	47	43	0	0	Durvalumab
142	122	79	69	58	44	39	35	32	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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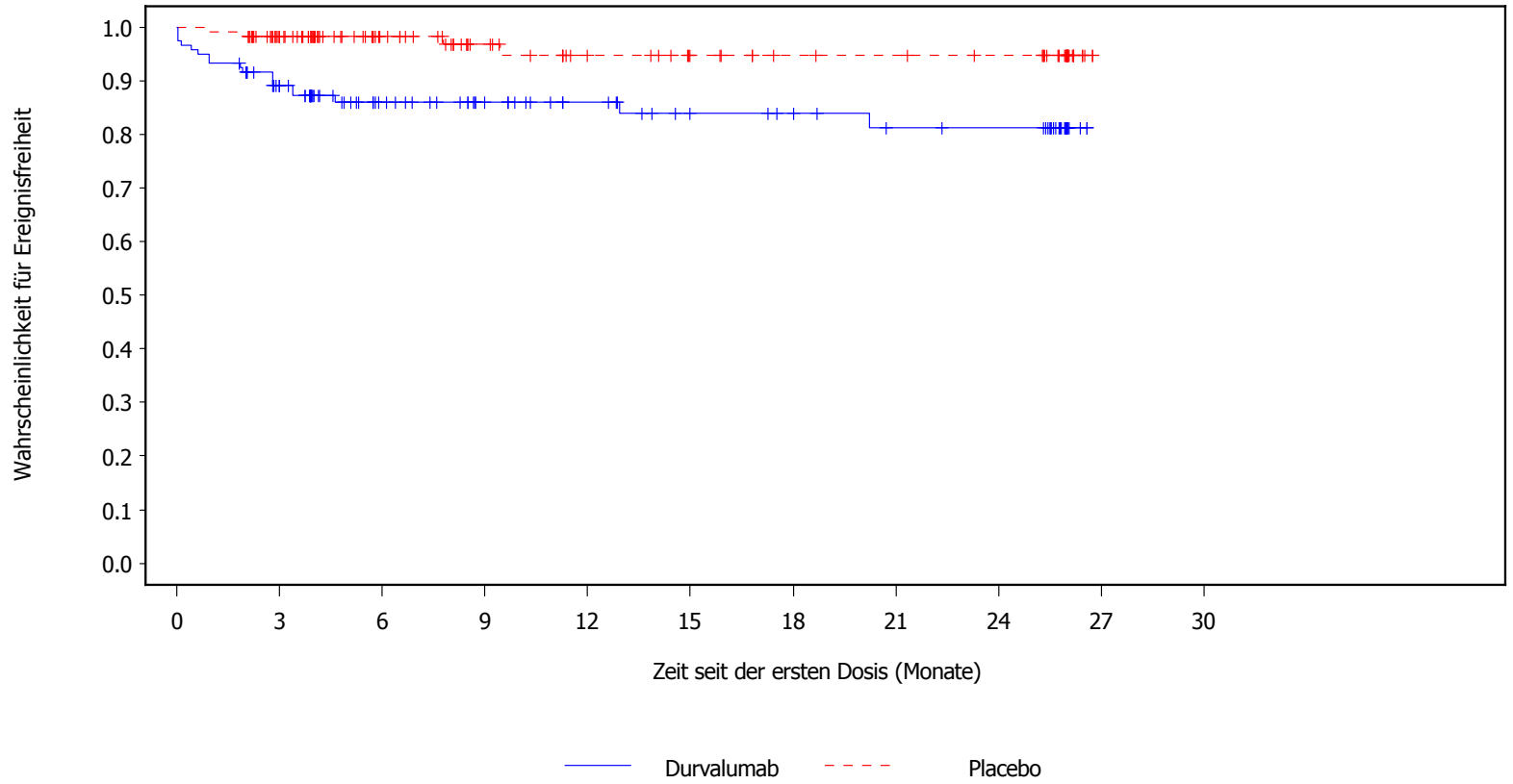
Figure 5.8.10 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of PT: Pruritus for Erhalt einer PCI (eCRF) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	97	64	52	43	35	33	29	28	0	0	Durvalumab
123	102	70	53	42	36	31	30	28	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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Anhang 4-G8.2: Schwere UE (CTCAE Grad >= 3) - gesamt und nach SOC/PT

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Table 2.2.4 ADRIATIC: Summary of analysis of time to first adverse event with max. CTCAE grade 3 or higher (total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UE mit CTCAE Grad >=3	262	69 (26,3)	NE [NE; NE]	265	68 (25,7)	NE [NE; NE]	0,97	[0,70; 1,36]	0,8786
G>=3 SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums	262	14 (5,3)	NE [NE; NE]	265	12 (4,5)	NE [NE; NE]	1,10	[0,51; 2,43]	0,8061
G>=3 SOC: Erkrankungen des Gastrointestinaltrakts	262	10 (3,8)	NE [NE; NE]	265	4 (1,5)	NE [NE; NE]	2,40	[0,80; 8,76]	0,1263
G>=3 SOC: Infektionen und parasitaere Erkrankungen	262	15 (5,7)	NE [NE; NE]	265	20 (7,5)	NE [NE; NE]	0,69	[0,35; 1,35]	0,2806
G>=3 PT: Pneumonie	262	9 (3,4)	NE [NE; NE]	265	11 (4,2)	NE [NE; NE]	0,74	[0,30; 1,79]	0,5042
G>=3 SOC: Untersuchungen	262	10 (3,8)	NE [NE; NE]	265	6 (2,3)	NE [NE; NE]	1,55	[0,57; 4,55]	0,3956

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G8.2.1: Schwere UE (CTCAE Grad >= 3) - gesamt und nach SOC/PT - Kaplan-Meier-Plot

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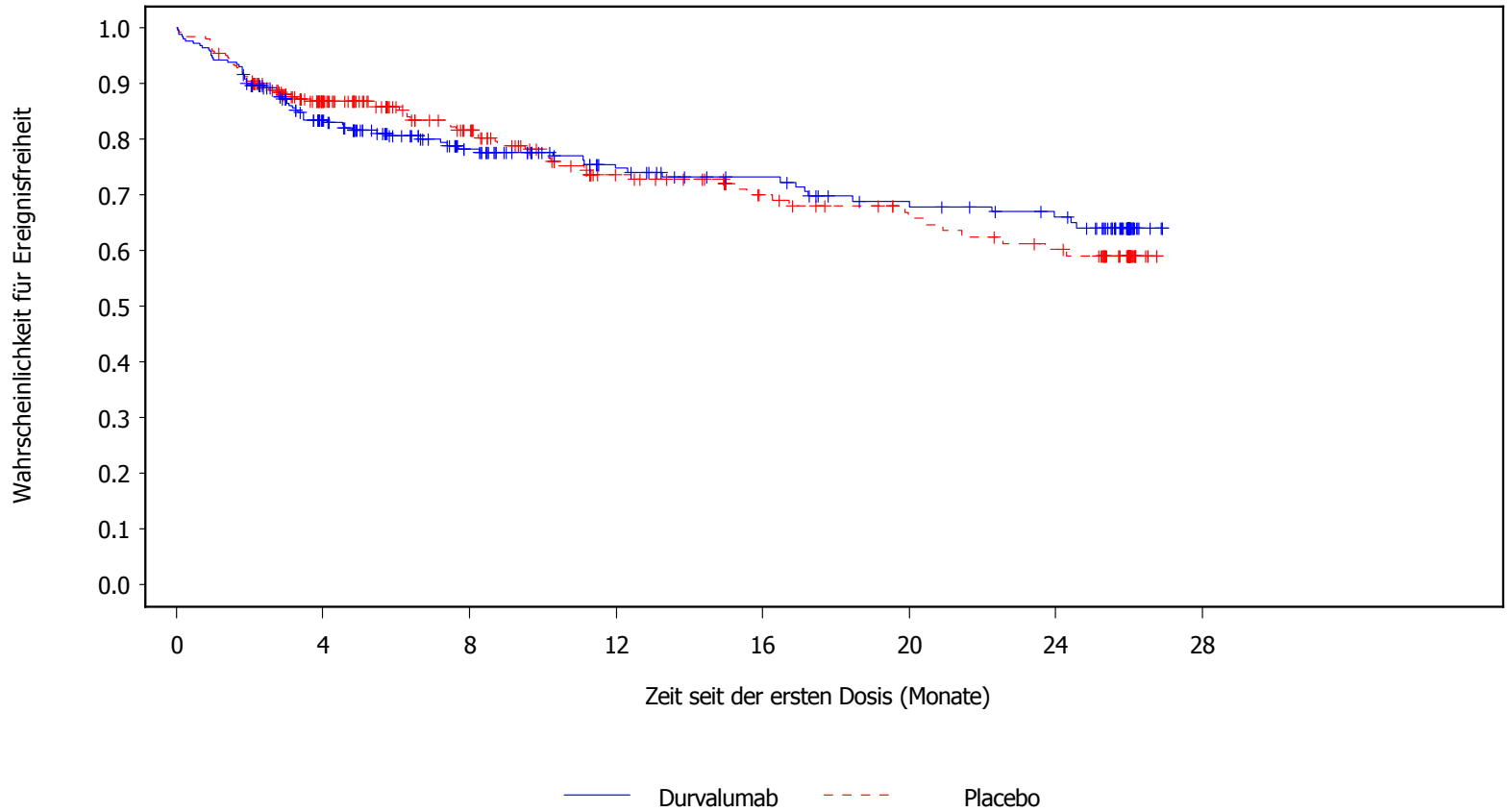
Figure 2.3.68 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	182	129	97	86	75	68	0	Durvalumab
265	182	129	89	70	59	52	0	Placebo

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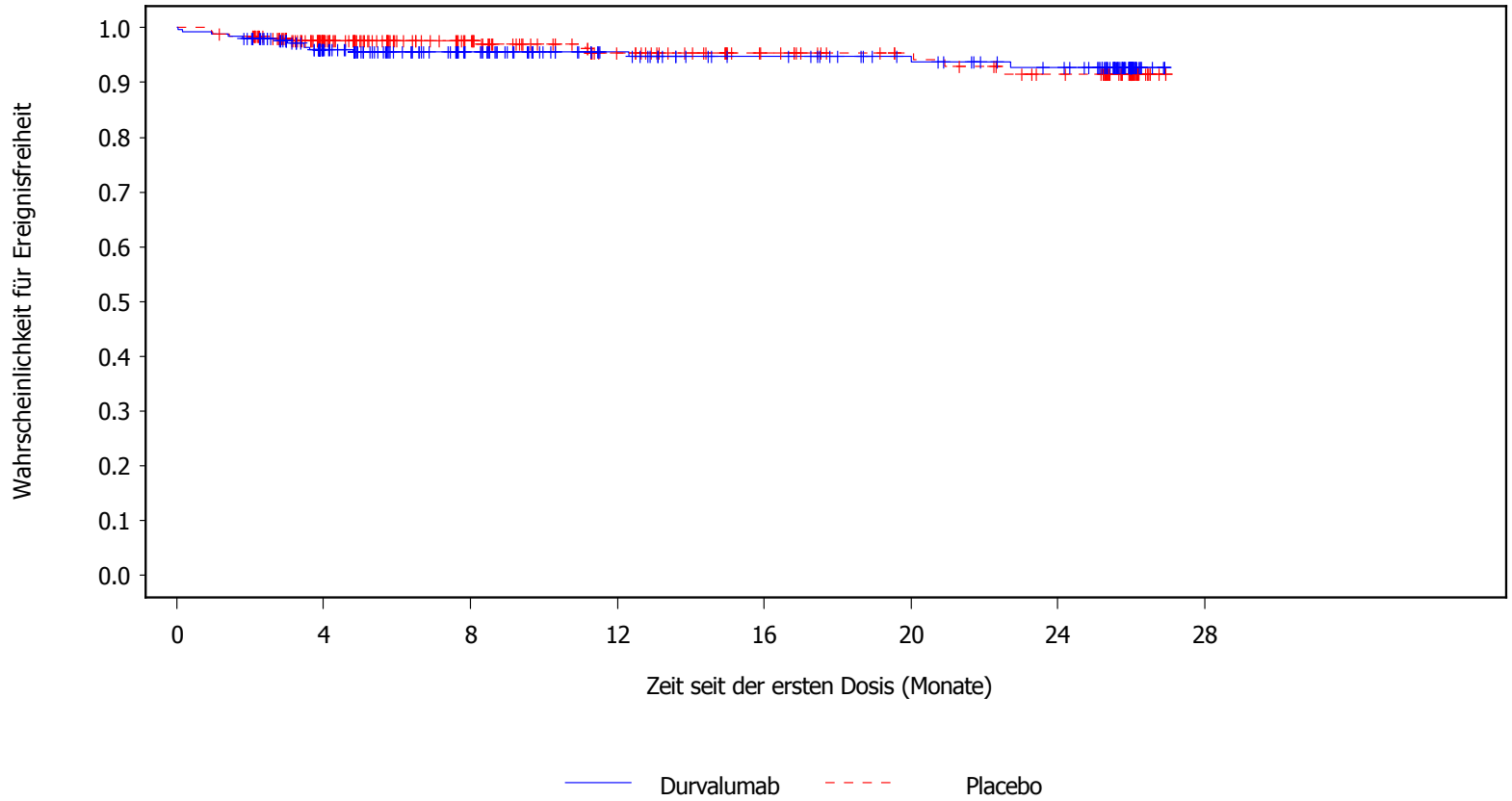
Figure 2.3.69 ADRIATIC: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	205	154	120	106	96	87	0	Durvalumab
265	200	146	108	87	76	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcq 05JUN2025:07:

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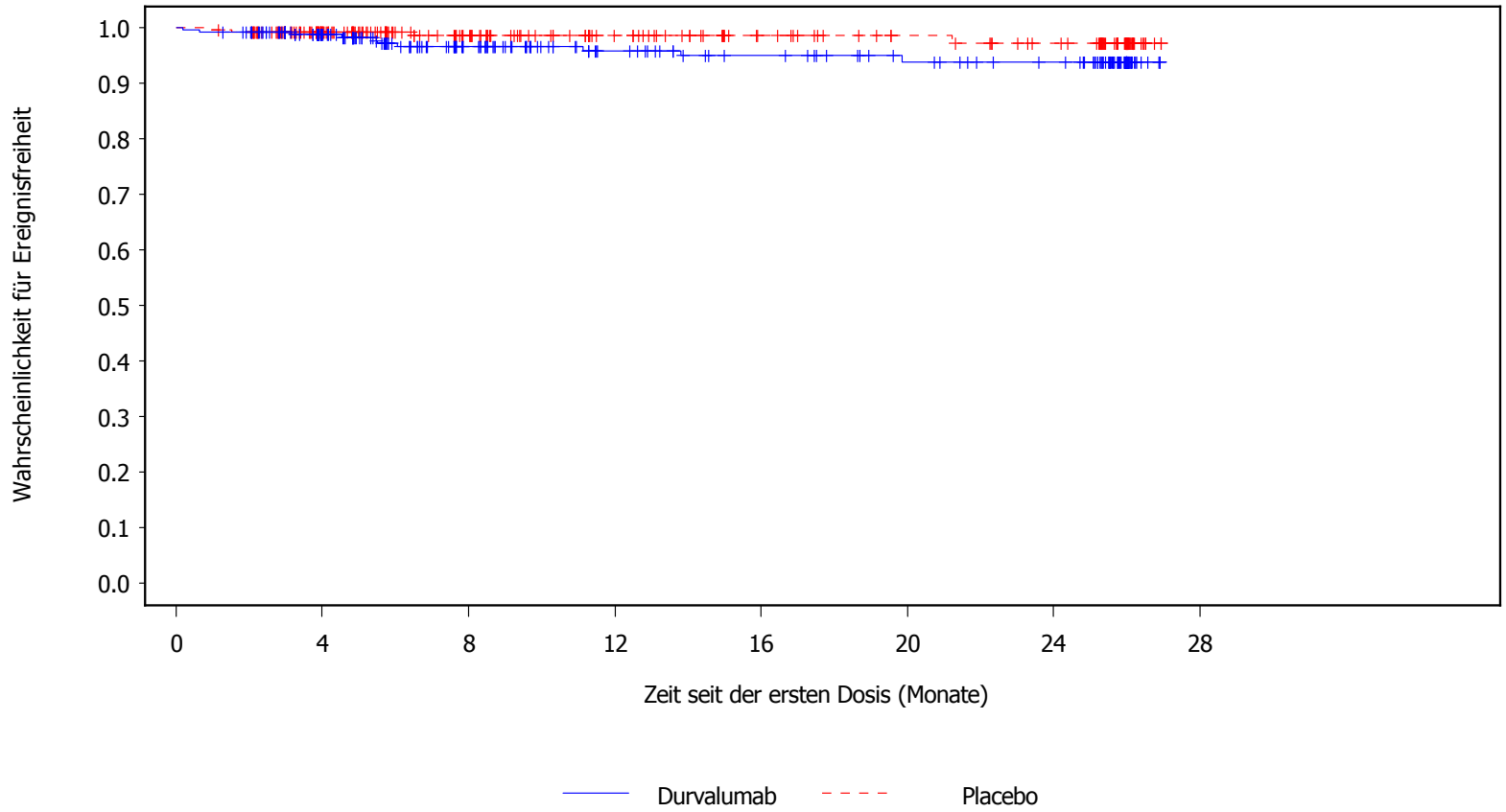
Figure 2.3.70 ADRIATIC: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	206	150	115	102	92	85	0	Durvalumab
265	204	146	111	89	78	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcr 05JUN2025:07:

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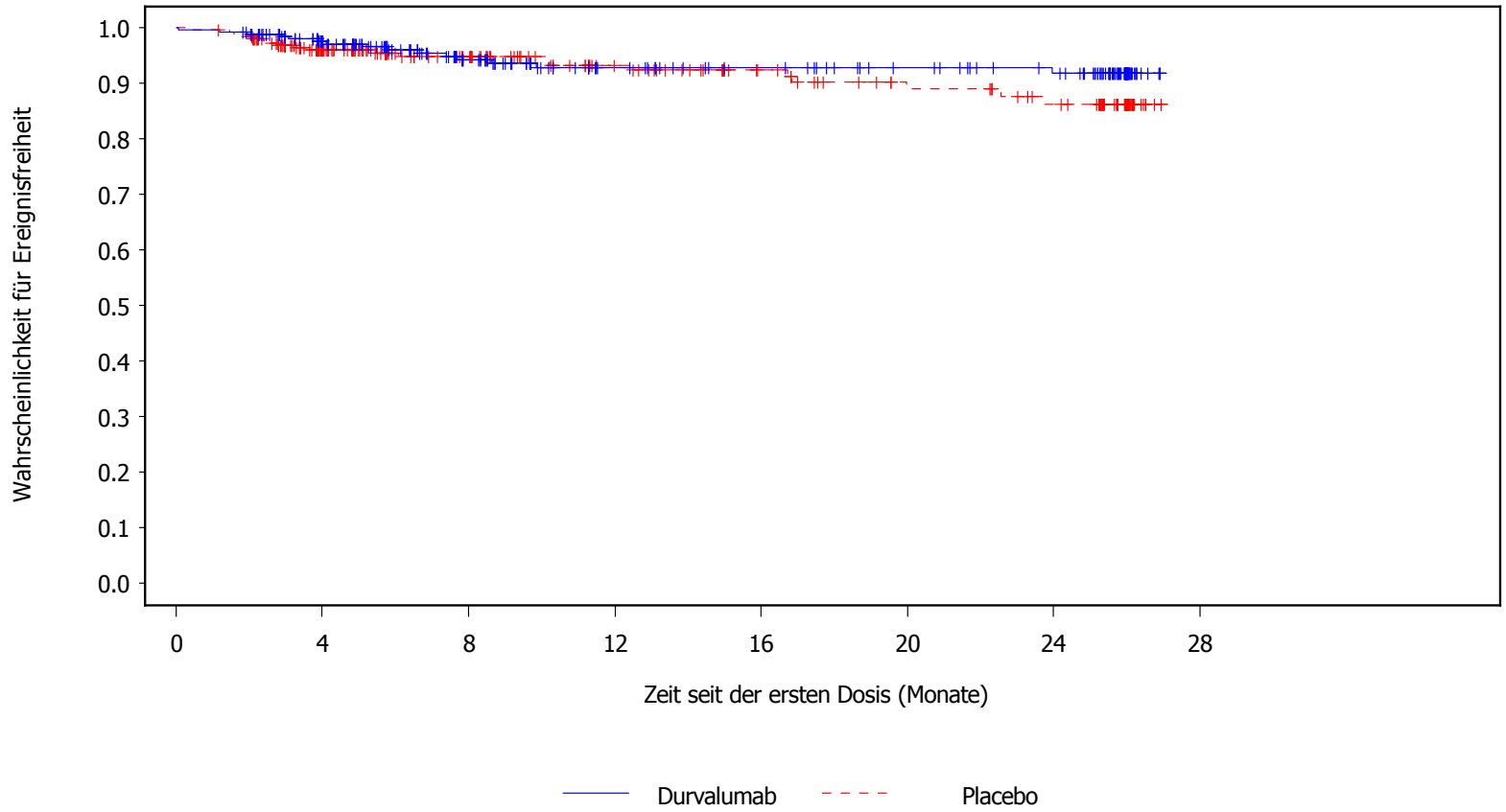
Figure 2.3.71 ADRIATIC: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	206	150	116	105	95	86	0	Durvalumab
265	198	142	106	86	72	64	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcs 05JUN2025:07:

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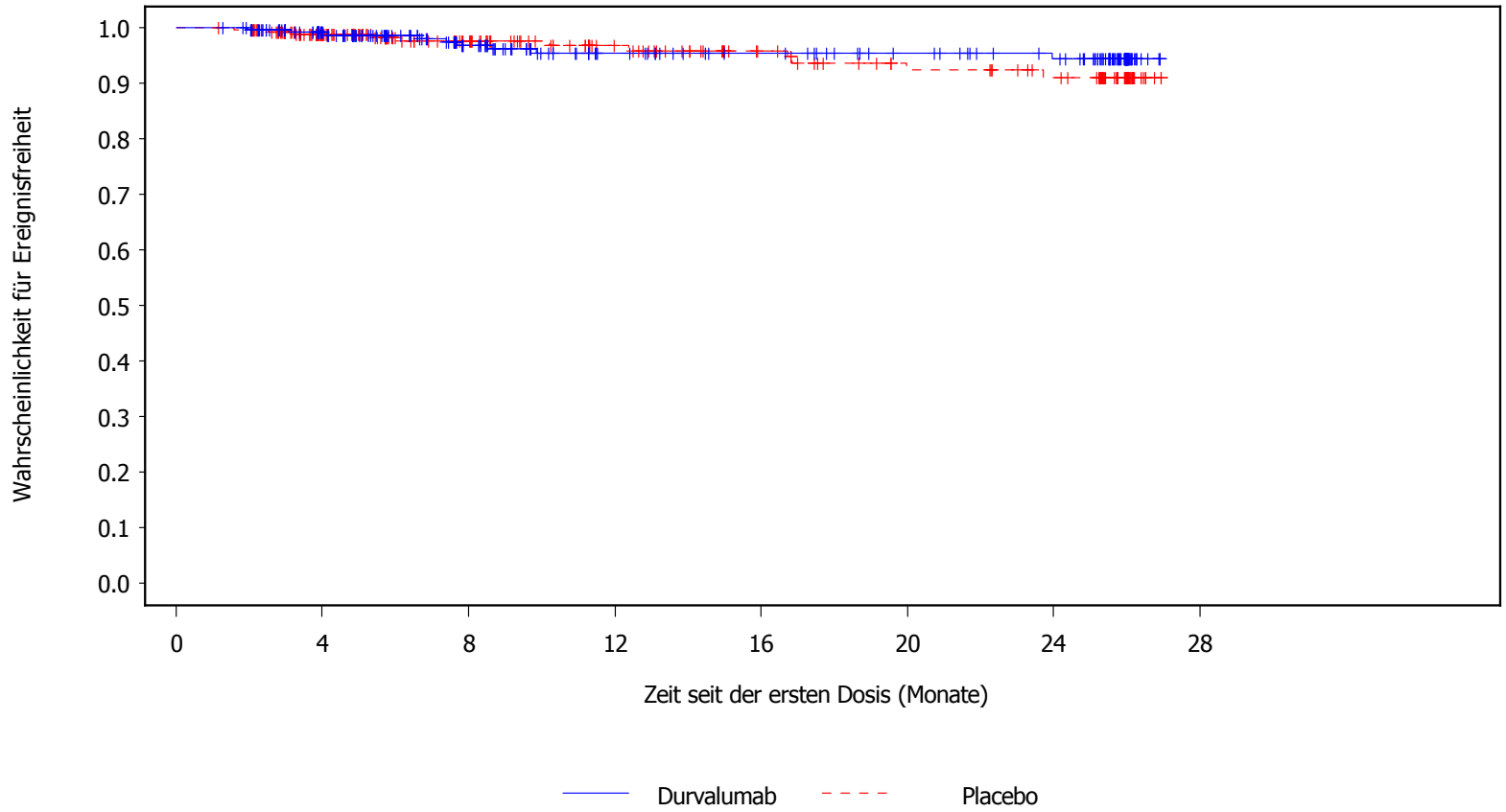
Figure 2.3.72 ADRIATIC: Kaplan-Meier plot of time to first occurrence of G>=3 PT: Pneumonie
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	153	118	107	97	88	0	Durvalumab
265	203	145	110	88	74	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bct 05JUN2025:07:

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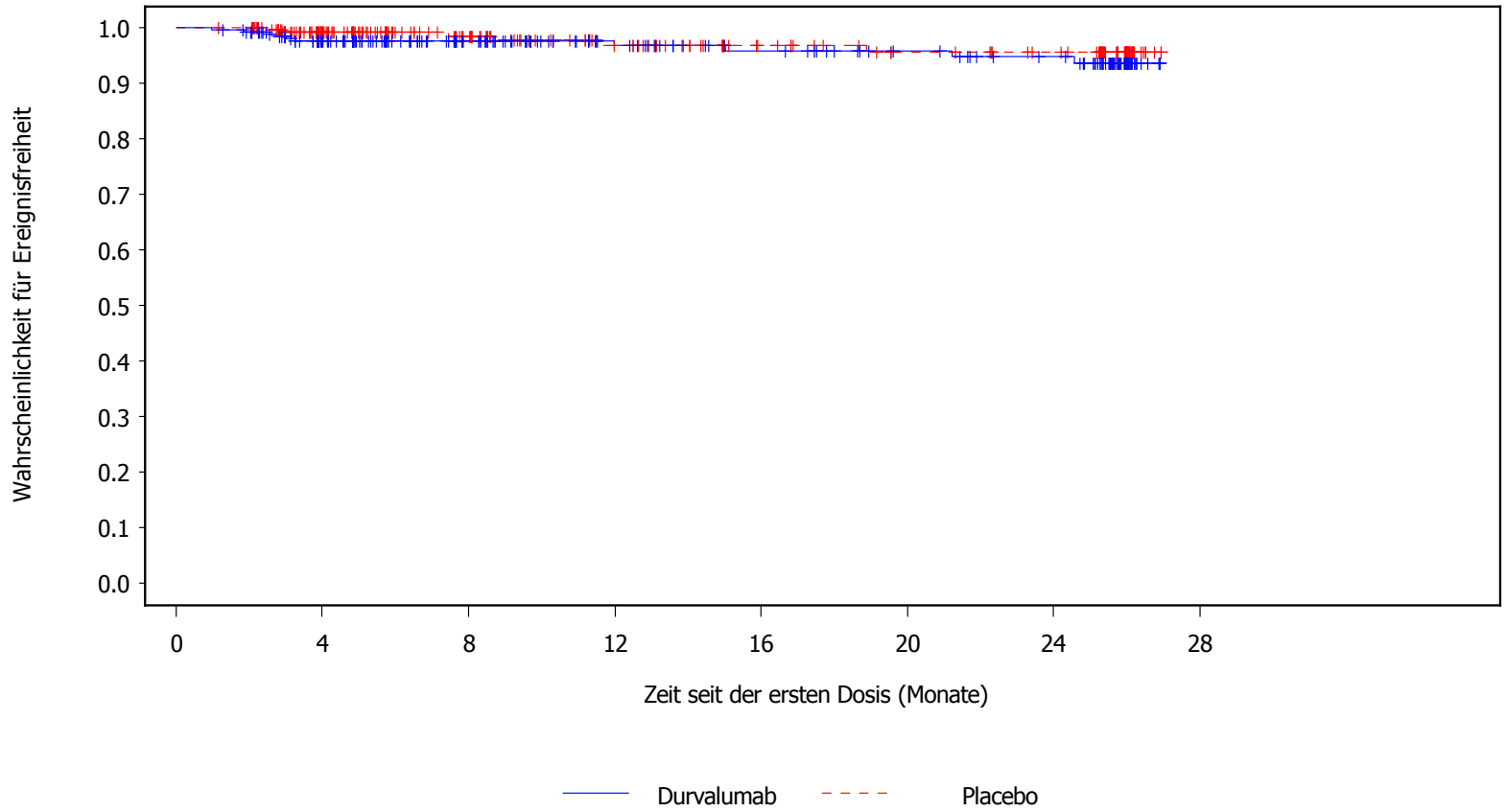
Figure 2.3.73 ADRIATIC: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Untersuchungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	207	154	120	106	96	88	0	Durvalumab
265	203	145	108	86	75	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcu 05JUN2025:07:

Anhang 4-G8.2.2: Schwere UE (CTCAE Grad >= 3) - gesamt und nach SOC/PT - Subgruppenanalysen

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Table 5.4.1 ADRIATIC: Summary of subgroup analysis of time to first UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	10 (27,8)	NE [NE; NE]	37	8 (21,6)	NE [NE; NE]	1,52	[0,60; 4,00]	0,3722
Stadium III	226	59 (26,1)	NE [NE; NE]	228	60 (26,3)	NE [NE; NE]	0,90	[0,63; 1,30]	0,5846
Interaktions p-Wert									0,3034
TNM Status (eCRF) - DEU									
Stadium I/II	33	9 (27,3)	NE [NE; NE]	34	8 (23,5)	NE [NE; NE]	1,32	[0,50; 3,52]	0,5676
Stadium III	229	60 (26,2)	NE [NE; NE]	231	60 (26,0)	NE [NE; NE]	0,93	[0,65; 1,33]	0,6835
Interaktions p-Wert									0,4976
Erhalt einer PCI (IVRS) - DEU									
Ja	141	44 (31,2)	NE [NE; NE]	143	44 (30,8)	NE [NE; NE]	0,98	[0,64; 1,49]	0,9163
Nein	121	25 (20,7)	NE [NE; NE]	122	24 (19,7)	NE [NE; NE]	0,98	[0,56; 1,72]	0,9430
Interaktions p-Wert									0,9956
Erhalt einer PCI (eCRF) - DEU									
Ja	141	44 (31,2)	NE [NE; NE]	142	44 (31,0)	NE [NE; NE]	0,97	[0,64; 1,47]	0,8795
Nein	121	25 (20,7)	NE [NE; NE]	123	24 (19,5)	NE [NE; NE]	0,99	[0,56; 1,75]	0,9775
Interaktions p-Wert									0,9457
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	10 (32,3)	NE [NE; NE]	32	7 (21,9)	NE [NE; NE]	1,30	[0,50; 3,59]	0,5887
>=14 bis <28 Tage	79	20 (25,3)	NE [NE; NE]	80	17 (21,3)	NE [NE; NE]	1,20	[0,63; 2,32]	0,5813
>=28 Tage	152	39 (25,7)	NE [NE; NE]	153	44 (28,8)	NE [NE; NE]	0,84	[0,54; 1,29]	0,4150
Interaktions p-Wert									0,5386
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	3 (12,5)	NE [NE; NE]	0,83	[0,11; 4,99]	0,8340
>=28 bis <56 Tage	103	26 (25,2)	NE [NE; NE]	103	29 (28,2)	NE [NE; NE]	0,83	[0,49; 1,41]	0,4977

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.4.1 ADRIATIC: Summary of subgroup analysis of time to first UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	32 (32,7)	NE [NE; NE]	76	19 (25,0)	NE [NE; NE]	1,20	[0,69; 2,16]	0,5218
>=84 Tage	45	9 (20,0)	NE [NE; NE]	62	17 (27,4)	NE [NE; NE]	0,78	[0,33; 1,72]	0,5527
Interaktions p-Wert									0,7648
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	29 (32,6)	NE [NE; NE]	88	29 (33,0)	NE [NE; NE]	0,89	[0,53; 1,50]	0,6611
Cisplatin	173	40 (23,1)	NE [NE; NE]	177	39 (22,0)	NE [NE; NE]	1,02	[0,66; 1,59]	0,9308
Interaktions p-Wert									0,6967
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	54 (28,0)	NE [NE; NE]	186	50 (26,9)	NE [NE; NE]	1,00	[0,68; 1,47]	0,9817
Zweimal täglich	69	15 (21,7)	NE [NE; NE]	79	18 (22,8)	NE [NE; NE]	0,88	[0,43; 1,74]	0,7016
Interaktions p-Wert									0,7469
Bestes Ansprechen auf cCRT - DEU									
CR	31	9 (29,0)	NE [NE; NE]	34	9 (26,5)	NE [NE; NE]	1,16	[0,45; 2,96]	0,7594
PR	189	47 (24,9)	NE [NE; NE]	199	50 (25,1)	NE [NE; NE]	0,95	[0,64; 1,42]	0,8081
SD	42	13 (31,0)	NE [NE; NE]	32	9 (28,1)	NE [NE; NE]	0,92	[0,40; 2,23]	0,8458
Interaktions p-Wert									0,9224
Geschlecht - DEU									
Männer	178	43 (24,2)	NE [NE; NE]	187	40 (21,4)	NE [NE; NE]	1,10	[0,72; 1,70]	0,6559
Frauen	84	26 (31,0)	NE [NE; NE]	78	28 (35,9)	20,5 [16,3; NE]	0,77	[0,45; 1,31]	0,3266
Interaktions p-Wert									0,2964
Altersgruppe - DEU									
<65 Jahre	159	37 (23,3)	NE [NE; NE]	161	36 (22,4)	NE [NE; NE]	0,95	[0,60; 1,51]	0,8332
>=65 Jahre	103	32 (31,1)	NE [NE; NE]	104	32 (30,8)	NE [NE; NE]	1,02	[0,62; 1,67]	0,9417
Interaktions p-Wert									0,8436

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.4.1 ADRIATIC: Summary of subgroup analysis of time to first UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	16 (20,5)	NE [NE; NE]	72	19 (26,4)	NE [NE; NE]	0,69	[0,35; 1,34]	0,2744
TC or IC >=1%	84	18 (21,4)	NE [NE; NE]	98	21 (21,4)	NE [NE; NE]	0,96	[0,51; 1,81]	0,9099
Interaktions p-Wert									0,4748
Raucherstatus - DEU									
Raucher	239	67 (28,0)	NE [NE; NE]	239	62 (25,9)	NE [NE; NE]	1,04	[0,73; 1,47]	0,8343
Nichtraucher	23	2 (8,7)	NE [NE; NE]	26	6 (23,1)	NE [NE; NE]	0,32	[0,05; 1,39]	0,1322
Interaktions p-Wert									0,1304
Abstammung - DEU									
Weiß	128	40 (31,3)	NE [NE; NE]	137	42 (30,7)	24,3 [19,9; NE]	0,99	[0,64; 1,52]	0,9560
Schwarz/Afroamerikanisch	1	1 (100)	11,1 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	28 (21,4)	NE [NE; NE]	121	25 (20,7)	NE [NE; NE]	0,99	[0,57; 1,70]	0,9575
Andere	2	0	NE [NE; NE]	4	1 (25,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9944
Geographische Region - DEU									
Asien	129	27 (20,9)	NE [NE; NE]	120	25 (20,8)	NE [NE; NE]	0,94	[0,55; 1,64]	0,8373
Europa	94	26 (27,7)	NE [NE; NE]	112	28 (25,0)	NE [NE; NE]	0,99	[0,58; 1,70]	0,9808
Nordamerika	39	16 (41,0)	11,1 [8,3; NE]	33	15 (45,5)	20,5 [10,2; NE]	1,04	[0,51; 2,12]	0,9202
Interaktions p-Wert									0,9783
ECOG-Status zu Baseline - DEU									
0	131	33 (25,2)	NE [NE; NE]	131	31 (23,7)	NE [NE; NE]	0,95	[0,58; 1,56]	0,8414
1	131	36 (27,5)	NE [NE; NE]	134	37 (27,6)	NE [NE; NE]	1,00	[0,63; 1,59]	0,9849
Interaktions p-Wert									0,8736

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Anhang 4-G8.3: SUE - gesamt und nach SOC/PT

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Table 2.2.2 ADRIATIC: Summary of analysis of time to first serious adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and 1% in either arm)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
SUE	262	78 (29,8)	NE [NE; NE]	265	64 (24,2)	NE [NE; NE]	1,20	[0,86; 1,67]	0,2864
SUE SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums	262	24 (9,2)	NE [NE; NE]	265	15 (5,7)	NE [NE; NE]	1,57	[0,83; 3,06]	0,1661
SUE SOC: Infektionen und parasitaere Erkrankungen	262	20 (7,6)	NE [NE; NE]	265	19 (7,2)	NE [NE; NE]	0,96	[0,51; 1,82]	0,9109
SUE PT: Pneumonie	262	12 (4,6)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	1,10	[0,48; 2,61]	0,8201
SUE SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	262	17 (6,5)	NE [NE; NE]	265	13 (4,9)	NE [NE; NE]	1,25	[0,61; 2,63]	0,5420
SUE PT: Strahlenbedingte Pneumonitis	262	13 (5,0)	NE [NE; NE]	265	7 (2,6)	NE [NE; NE]	1,86	[0,76; 4,95]	0,1783

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Anhang 4-G8.3.1: SUE - gesamt und nach SOC/PT - Kaplan-Meier-Plot

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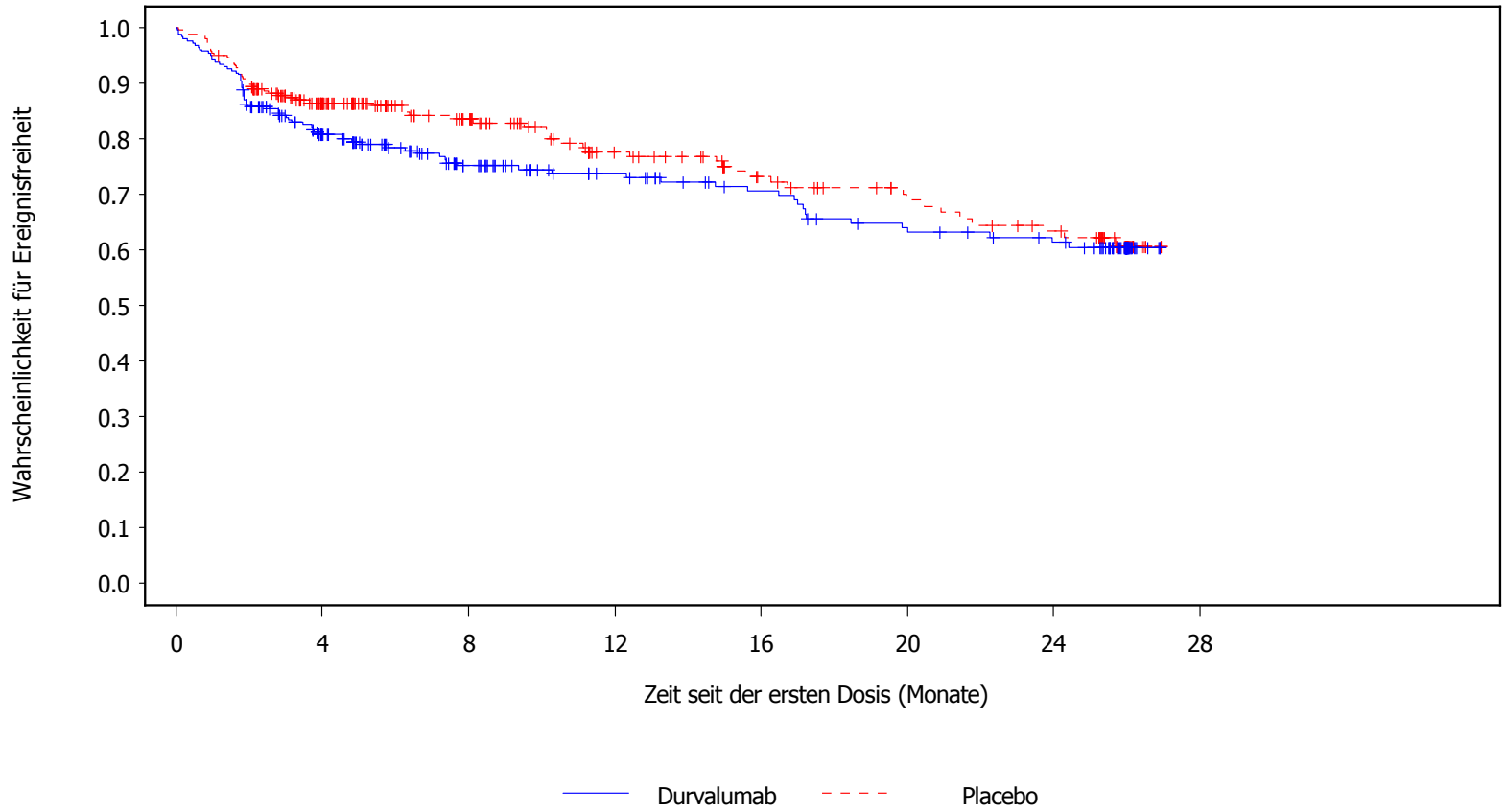
Figure 2.3.61 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	177	127	100	86	75	68	0	Durvalumab
265	183	132	94	74	62	54	0	Placebo

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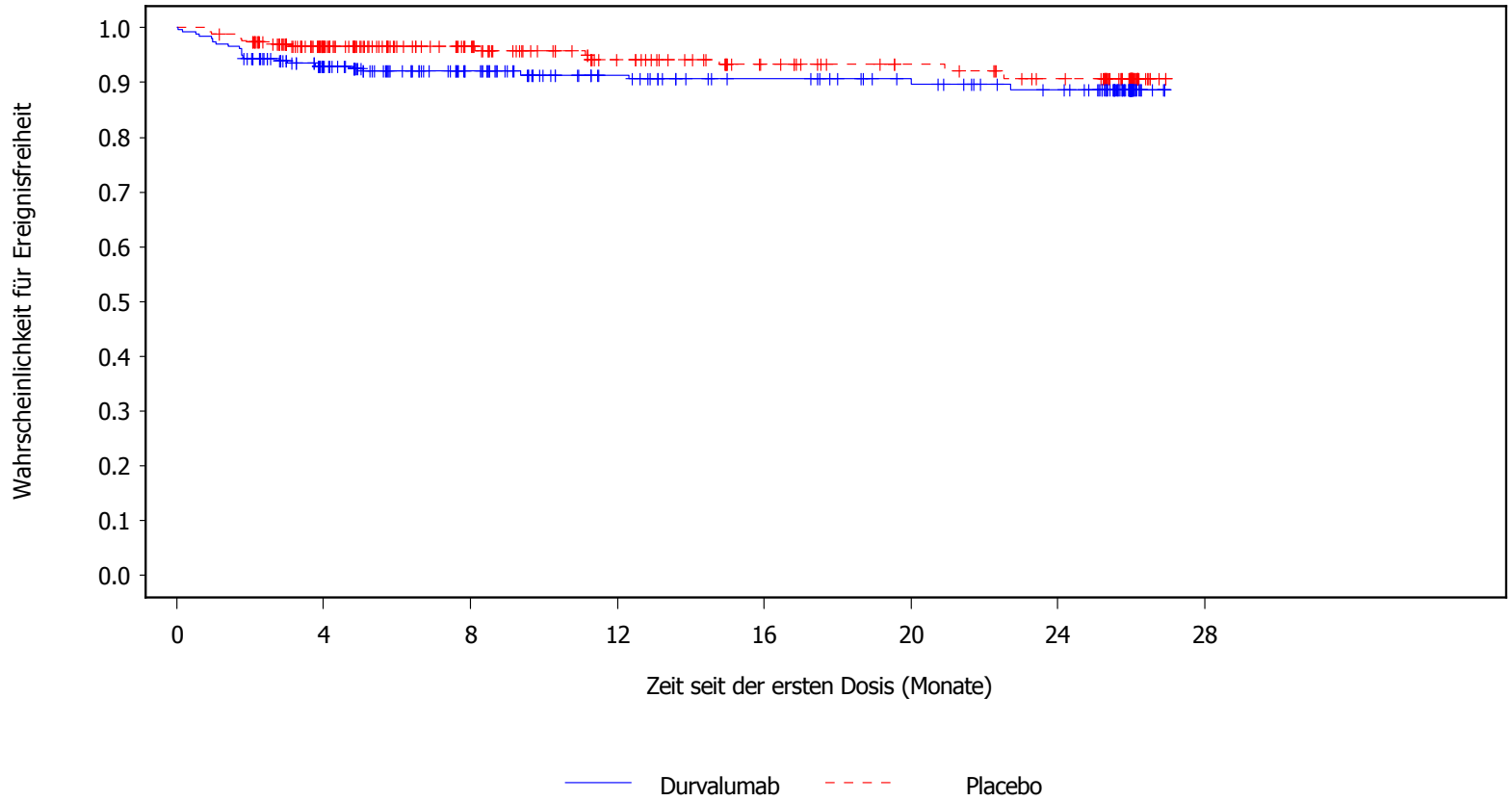
Figure 2.3.62 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	202	153	119	105	96	86	0	Durvalumab
265	200	146	109	87	76	67	0	Placebo

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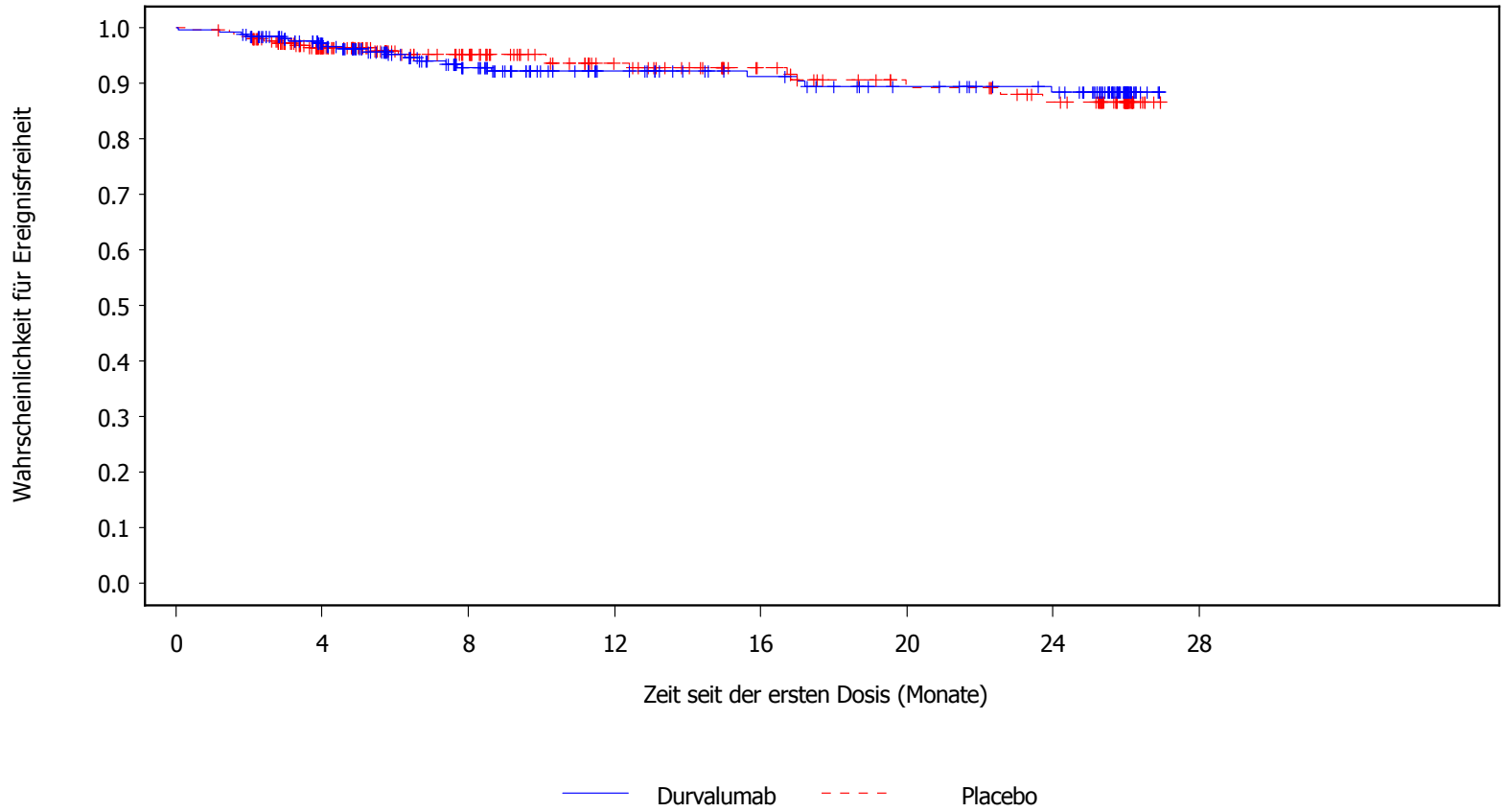
Figure 2.3.63 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	206	149	116	104	94	86	0	Durvalumab
265	199	142	106	86	72	64	0	Placebo

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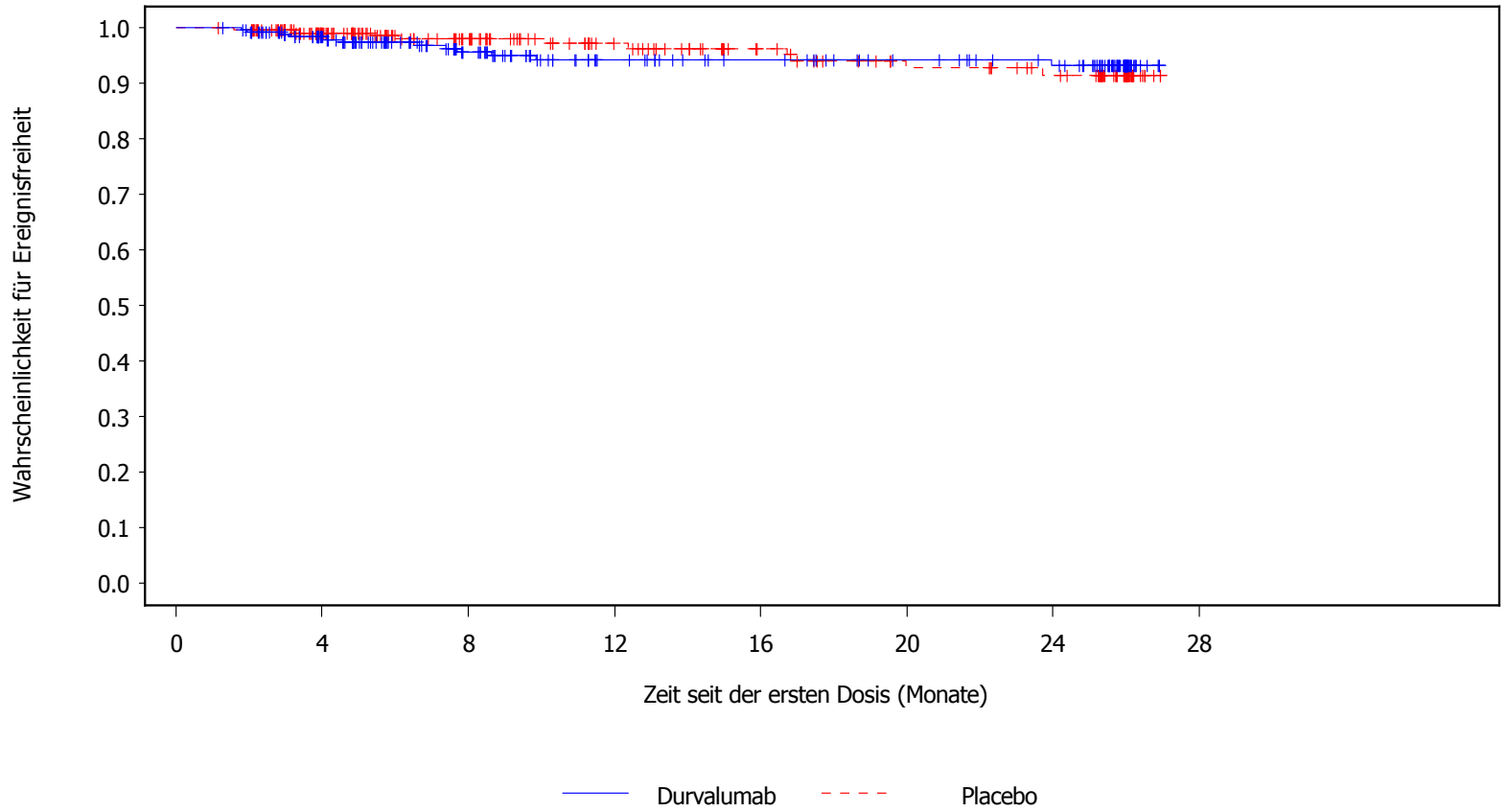
Figure 2.3.64 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE PT: Pneumonie
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	152	117	106	96	88	0	Durvalumab
265	204	145	110	88	74	67	0	Placebo

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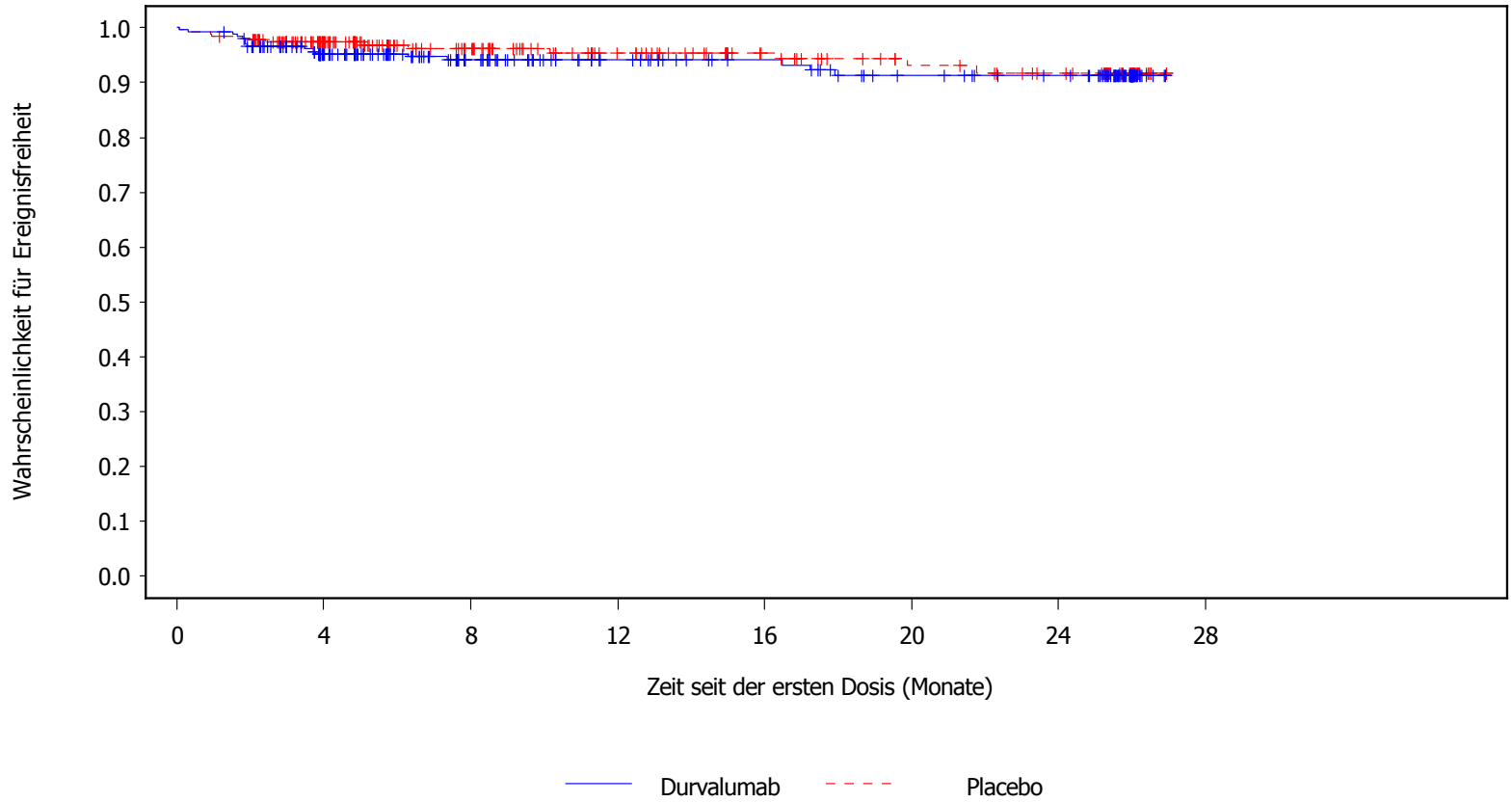
Figure 2.3.65 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	201	147	117	105	93	87	0	Durvalumab
265	202	144	110	89	75	68	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcm 05JUN2025:07:

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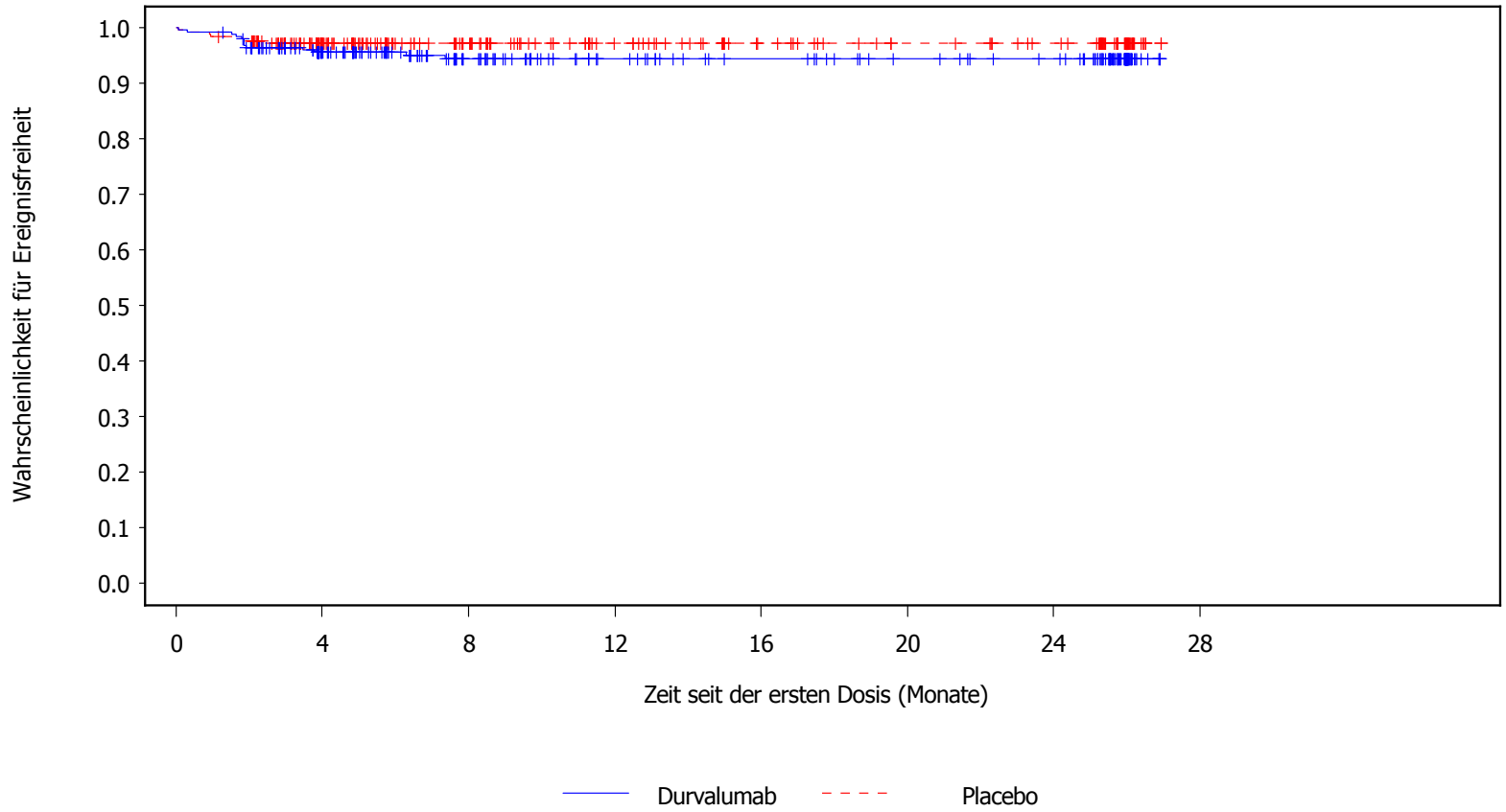
Figure 2.3.66 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUE PT: Strahlenbedingte Pneumonitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	201	147	117	105	96	90	0	Durvalumab
265	202	145	110	89	77	70	0	Placebo

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Anhang 4-G8.3.2: SUE - gesamt und nach SOC/PT - Subgruppenanalysen

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Table 5.2.1 ADRIATIC: Summary of subgroup analysis of time to first SUE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	8 (22,2)	NE [NE; NE]	37	10 (27,0)	NE [NE; NE]	0,89	[0,34; 2,26]	0,8079
Stadium III	226	70 (31,0)	NE [NE; NE]	228	54 (23,7)	NE [NE; NE]	1,25	[0,87; 1,78]	0,2240
Interaktions p-Wert									0,5085
TNM Status (eCRF) - DEU									
Stadium I/II	33	7 (21,2)	NE [NE; NE]	34	9 (26,5)	NE [NE; NE]	0,87	[0,31; 2,33]	0,7796
Stadium III	229	71 (31,0)	NE [NE; NE]	231	55 (23,8)	NE [NE; NE]	1,24	[0,87; 1,77]	0,2288
Interaktions p-Wert									0,5039
Erhalt einer PCI (IVRS) - DEU									
Ja	141	56 (39,7)	NE [NE; NE]	143	41 (28,7)	NE [NE; NE]	1,42	[0,95; 2,13]	0,0887
Nein	121	22 (18,2)	NE [NE; NE]	122	23 (18,9)	NE [NE; NE]	0,88	[0,49; 1,59]	0,6753
Interaktions p-Wert									0,1918
Erhalt einer PCI (eCRF) - DEU									
Ja	141	56 (39,7)	NE [NE; NE]	142	41 (28,9)	NE [NE; NE]	1,40	[0,94; 2,11]	0,0979
Nein	121	22 (18,2)	NE [NE; NE]	123	23 (18,7)	NE [NE; NE]	0,89	[0,50; 1,61]	0,7054
Interaktions p-Wert									0,2131
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	10 (32,3)	NE [NE; NE]	32	7 (21,9)	20,5 [11,2; NE]	1,27	[0,49; 3,50]	0,6267
>=14 bis <28 Tage	79	21 (26,6)	NE [NE; NE]	80	17 (21,3)	NE [NE; NE]	1,26	[0,67; 2,43]	0,4712
>=28 Tage	152	47 (30,9)	NE [NE; NE]	153	40 (26,1)	NE [NE; NE]	1,15	[0,76; 1,77]	0,5072
Interaktions p-Wert									0,9645
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	5 (31,3)	NE [NE; NE]	24	3 (12,5)	NE [NE; NE]	2,49	[0,61; 12,13]	0,2024
>=28 bis <56 Tage	103	28 (27,2)	NE [NE; NE]	103	25 (24,3)	NE [NE; NE]	1,08	[0,63; 1,87]	0,7676

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.2.1 ADRIATIC: Summary of subgroup analysis of time to first SUE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	34 (34,7)	NE [NE; NE]	76	20 (26,3)	NE [NE; NE]	1,18	[0,68; 2,08]	0,5647
>=84 Tage	45	11 (24,4)	NE [NE; NE]	62	16 (25,8)	NE [NE; NE]	1,04	[0,47; 2,23]	0,9125
Interaktions p-Wert									0,7361
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	32 (36,0)	NE [NE; NE]	88	25 (28,4)	NE [NE; NE]	1,16	[0,69; 1,97]	0,5848
Cisplatin	173	46 (26,6)	NE [NE; NE]	177	39 (22,0)	NE [NE; NE]	1,21	[0,79; 1,86]	0,3870
Interaktions p-Wert									0,9021
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	59 (30,6)	NE [NE; NE]	186	45 (24,2)	NE [NE; NE]	1,24	[0,84; 1,83]	0,2803
Zweimal täglich	69	19 (27,5)	NE [NE; NE]	79	19 (24,1)	NE [NE; NE]	1,08	[0,57; 2,04]	0,8226
Interaktions p-Wert									0,7122
Bestes Ansprechen auf cCRT - DEU									
CR	31	12 (38,7)	NE [NE; NE]	34	6 (17,6)	NE [NE; NE]	2,46	[0,95; 7,05]	0,0629
PR	189	54 (28,6)	NE [NE; NE]	199	49 (24,6)	NE [NE; NE]	1,14	[0,78; 1,69]	0,4959
SD	42	12 (28,6)	NE [NE; NE]	32	9 (28,1)	NE [NE; NE]	0,83	[0,35; 2,03]	0,6733
Interaktions p-Wert									0,2321
Geschlecht - DEU									
Männer	178	52 (29,2)	NE [NE; NE]	187	45 (24,1)	NE [NE; NE]	1,18	[0,79; 1,77]	0,4130
Frauen	84	26 (31,0)	NE [NE; NE]	78	19 (24,4)	NE [NE; NE]	1,23	[0,69; 2,26]	0,4839
Interaktions p-Wert									0,9038
Altersgruppe - DEU									
<65 Jahre	159	43 (27,0)	NE [NE; NE]	161	33 (20,5)	NE [NE; NE]	1,26	[0,80; 1,99]	0,3188
>=65 Jahre	103	35 (34,0)	NE [NE; NE]	104	31 (29,8)	NE [NE; NE]	1,14	[0,70; 1,86]	0,5952
Interaktions p-Wert									0,7698

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.2.1 ADRIATIC: Summary of subgroup analysis of time to first SUE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	23 (29,5)	NE [NE; NE]	72	17 (23,6)	NE [NE; NE]	1,17	[0,63; 2,22]	0,6289
TC or IC >=1%	84	25 (29,8)	NE [NE; NE]	98	20 (20,4)	NE [NE; NE]	1,46	[0,81; 2,65]	0,2085
Interaktions p-Wert									0,6140
Raucherstatus - DEU									
Raucher	239	73 (30,5)	NE [NE; NE]	239	61 (25,5)	NE [NE; NE]	1,16	[0,83; 1,64]	0,3827
Nichtraucher	23	5 (21,7)	NE [NE; NE]	26	3 (11,5)	NE [NE; NE]	1,79	[0,44; 8,76]	0,4146
Interaktions p-Wert									0,5578
Abstammung - DEU									
Weiß	128	38 (29,7)	NE [NE; NE]	137	34 (24,8)	NE [NE; NE]	1,18	[0,74; 1,88]	0,4801
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	40 (30,5)	NE [NE; NE]	121	30 (24,8)	NE [NE; NE]	1,20	[0,75; 1,94]	0,4563
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9695
Geographische Region - DEU									
Asien	129	40 (31,0)	NE [NE; NE]	120	29 (24,2)	NE [NE; NE]	1,24	[0,77; 2,02]	0,3688
Europa	94	27 (28,7)	NE [NE; NE]	112	24 (21,4)	NE [NE; NE]	1,22	[0,71; 2,13]	0,4728
Nordamerika	39	11 (28,2)	19,8 [10,3; NE]	33	11 (33,3)	21,4 [16,7; NE]	0,99	[0,42; 2,31]	0,9755
Interaktions p-Wert									0,8896
ECOG-Status zu Baseline - DEU									
0	131	35 (26,7)	NE [NE; NE]	131	27 (20,6)	NE [NE; NE]	1,20	[0,73; 2,00]	0,4736
1	131	43 (32,8)	NE [NE; NE]	134	37 (27,6)	NE [NE; NE]	1,21	[0,78; 1,89]	0,3874
Interaktions p-Wert									0,9754

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Anhang 4-G8.4: Therapieabbrüche aufgrund von UE - gesamt und nach SOC/PT

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Table 2.2.3 ADRIATIC: Summary of analysis of time to first adverse event leading to discontinuation of study treatment
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
Therapieabbruch aufgrund von UE	262	43 (16,4)	NE [NE; NE]	265	28 (10,6)	NE [NE; NE]	1,49	[0,93; 2,43]	0,0982

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
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Table 2.4 ADRIATIC: Summary of adverse events leading to discontinuation of study treatment
Safety Analysis Set, DCO 15JAN2024

System organ class / MedDRA Preferred term	Number (%) of patients Durvalumab (N=262)	 Placebo (N=265)
Patienten mit Abbruch wegen UE	43 (16,4)	28 (10,6)
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	1 (0,4)	0
Ermuedung	1 (0,4)	0
Endokrine Erkrankungen	1 (0,4)	0
Hypothyreose	1 (0,4)	0
Erkrankungen der Atemwege, des Brustraums und Mediastinums	14 (5,3)	3 (1,1)
Akute respiratorische Insuffizienz	1 (0,4)	0
Immunvermittelte Lungenerkrankung	4 (1,5)	0
Interstitielle Lungenerkrankung	1 (0,4)	0
Pneumonitis	8 (3,1)	3 (1,1)
Erkrankungen der Nieren und Harnwege	0	1 (0,4)
Akute Nierenschaedigung	0	1 (0,4)
Erkrankungen des Blutes und des Lymphsystems	1 (0,4)	0
Anaemie	1 (0,4)	0
Erkrankungen des Gastrointestinaltrakts	2 (0,8)	3 (1,1)
Diarrhoe	2 (0,8)	0
Gastritis	0	1 (0,4)
Immunvermittelte Enterokolitis	0	1 (0,4)
Kolitis	0	1 (0,4)
Erkrankungen des Nervensystems	2 (0,8)	3 (1,1)
Enzephalitis autoimmun	1 (0,4)	0
Enzephalopathie	1 (0,4)	0
Erkrankung des Nervensystems	0	1 (0,4)

Includes adverse events with onset date after first dose of study treatment until 90 days following the date of last dose of study treatment.
All AEs are coded using MedDRA version 26.1.
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Table 2.4 ADRIATIC: Summary of adverse events leading to discontinuation of study treatment
Safety Analysis Set, DCO 15JAN2024

System organ class / MedDRA Preferred term	Number (%) of patients Durvalumab (N=262)	 Placebo (N=265)
Leukenzephalopathie	0	1 (0,4)
Metabolische Enzephalopathie	0	1 (0,4)
Gefaesserkrankungen	0	1 (0,4)
Hypotonie	0	1 (0,4)
Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	2 (0,8)	4 (1,5)
Akute promyelozytaere Leukaemie	0	1 (0,4)
Chronische myeloische Leukaemie	0	1 (0,4)
Paraneoplastisches Syndrom	1 (0,4)	0
Plattenepithelkarzinom der Lunge	0	1 (0,4)
Plattenepithelkarzinom des Hypopharynx	0	1 (0,4)
Prostatakarzinom	1 (0,4)	0
Herzerkrankungen	2 (0,8)	1 (0,4)
Akuter Myokardinfarkt	1 (0,4)	0
Herzinsuffizienz	1 (0,4)	0
Herzinsuffizienz akut	0	1 (0,4)
Infektionen und parasitaere Erkrankungen	4 (1,5)	4 (1,5)
COVID-19	0	1 (0,4)
Pneumocystis jirovecii-Pneumonie	0	1 (0,4)
Pneumonie	3 (1,1)	2 (0,8)
Pneumonie durch Bakterien	1 (0,4)	0
Leber- und Gallenerkrankungen	2 (0,8)	1 (0,4)
Cholestase	1 (0,4)	0
Hepatitis	0	1 (0,4)
Immunvermittelte Hepatitis	1 (0,4)	0

Includes adverse events with onset date after first dose of study treatment until 90 days following the date of last dose of study treatment.
All AEs are coded using MedDRA version 26.1.
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Table 2.4 ADRIATIC: Summary of adverse events leading to discontinuation of study treatment
Safety Analysis Set, DCO 15JAN2024

System organ class / MedDRA Preferred term	Number (%) of patients Durvalumab (N=262)	 Placebo (N=265)
Psychiatrische Erkrankungen	1 (0,4)	0
Delirium	1 (0,4)	0
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	2 (0,8)	1 (0,4)
Arthralgie	1 (0,4)	0
Myalgie	0	1 (0,4)
Schmerz in einer Extremitaet	1 (0,4)	0
Untersuchungen	1 (0,4)	1 (0,4)
Thrombozytenzahl vermindert	0	1 (0,4)
Transaminasen erhoeht	1 (0,4)	0
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	10 (3,8)	5 (1,9)
Strahlenbedingte Pneumonitis	10 (3,8)	5 (1,9)

Includes adverse events with onset date after first dose of study treatment until 90 days following the date of last dose of study treatment.
All AEs are coded using MedDRA version 26.1.
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Anhang 4-G8.4.1: Therapieabbrüche aufgrund von UE - gesamt und nach SOC/PT - Kaplan-Meier-Plot

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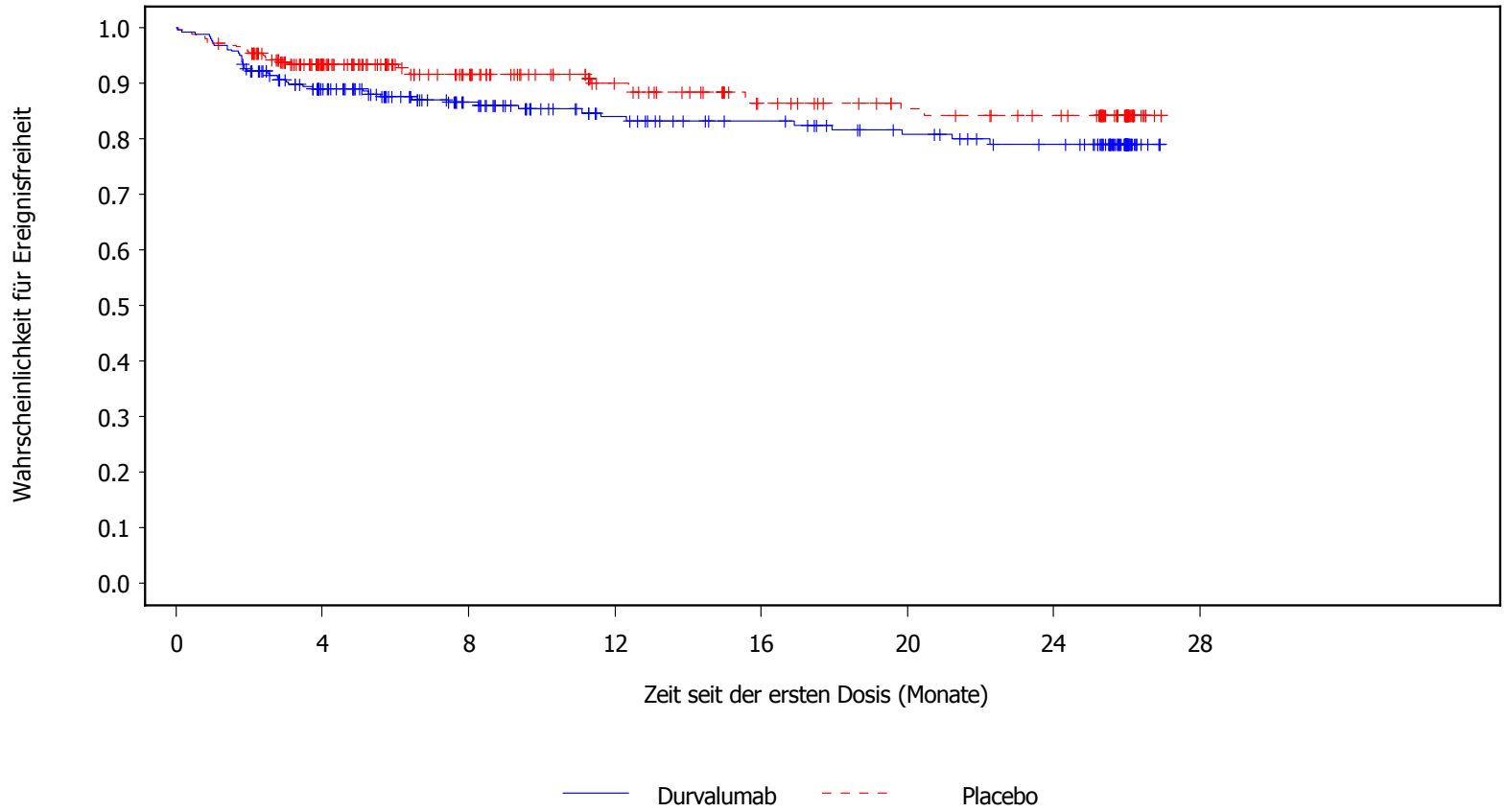
Figure 2.3.67 ADRIATIC: Kaplan-Meier plot of time to first occurrence of Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	199	151	120	108	97	88	0	Durvalumab
265	197	145	110	88	77	71	0	Placebo

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Anhang 4-G8.4.2: Therapieabbrüche aufgrund von UE - gesamt und nach SOC/PT - Subgruppenanalysen

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Table 5.3.1 ADRIATIC: Summary of subgroup analysis of time to first Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	11 (30,6)	NE [NE; NE]	37	6 (16,2)	NE [NE; NE]	2,13	[0,81; 6,18]	0,1265
Stadium III	226	32 (14,2)	NE [NE; NE]	228	22 (9,6)	NE [NE; NE]	1,37	[0,80; 2,39]	0,2508
Interaktions p-Wert									0,4424
TNM Status (eCRF) - DEU									
Stadium I/II	33	10 (30,3)	NE [NE; NE]	34	6 (17,6)	NE [NE; NE]	1,88	[0,70; 5,53]	0,2123
Stadium III	229	33 (14,4)	NE [NE; NE]	231	22 (9,5)	NE [NE; NE]	1,42	[0,83; 2,47]	0,1961
Interaktions p-Wert									0,6310
Erhalt einer PCI (IVRS) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	143	22 (15,4)	NE [NE; NE]	1,04	[0,58; 1,87]	0,8931
Nein	121	19 (15,7)	NE [NE; NE]	122	6 (4,9)	NE [NE; NE]	3,15	[1,33; 8,65]	0,0080*
Interaktions p-Wert									0,0376*
Erhalt einer PCI (eCRF) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	142	22 (15,5)	NE [NE; NE]	1,03	[0,58; 1,85]	0,9164
Nein	121	19 (15,7)	NE [NE; NE]	123	6 (4,9)	NE [NE; NE]	3,18	[1,34; 8,74]	0,0074*
Interaktions p-Wert									0,0343*
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	5 (16,1)	NE [NE; NE]	32	3 (9,4)	NE [NE; NE]	1,51	[0,37; 7,37]	0,5679
>=14 bis <28 Tage	79	11 (13,9)	NE [NE; NE]	80	5 (6,3)	NE [NE; NE]	2,20	[0,80; 6,98]	0,1289
>=28 Tage	152	27 (17,8)	NE [NE; NE]	153	20 (13,1)	NE [NE; NE]	1,31	[0,74; 2,37]	0,3574
Interaktions p-Wert									0,6927
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	18 (17,5)	NE [NE; NE]	103	11 (10,7)	NE [NE; NE]	1,60	[0,77; 3,50]	0,2116

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.3.1 ADRIATIC: Summary of subgroup analysis of time to first Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	14 (14,3)	NE [NE; NE]	76	12 (15,8)	NE [NE; NE]	0,80	[0,37; 1,77]	0,5810
>=84 Tage	45	9 (20,0)	NE [NE; NE]	62	5 (8,1)	NE [NE; NE]	2,78	[0,96; 9,05]	0,0595
Interaktions p-Wert									0,1622
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	15 (16,9)	NE [NE; NE]	88	9 (10,2)	NE [NE; NE]	1,50	[0,67; 3,58]	0,3280
Cisplatin	173	28 (16,2)	NE [NE; NE]	177	19 (10,7)	NE [NE; NE]	1,49	[0,84; 2,70]	0,1784
Interaktions p-Wert									0,9833
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	31 (16,1)	NE [NE; NE]	186	23 (12,4)	NE [NE; NE]	1,23	[0,72; 2,14]	0,4415
Zweimal täglich	69	12 (17,4)	NE [NE; NE]	79	5 (6,3)	NE [NE; NE]	2,67	[0,99; 8,41]	0,0519
Interaktions p-Wert									0,1853
Bestes Ansprechen auf cCRT - DEU									
CR	31	7 (22,6)	NE [NE; NE]	34	7 (20,6)	NE [NE; NE]	1,07	[0,37; 3,11]	0,9047
PR	189	29 (15,3)	NE [NE; NE]	199	18 (9,0)	NE [NE; NE]	1,68	[0,94; 3,08]	0,0803
SD	42	7 (16,7)	NE [NE; NE]	32	3 (9,4)	NE [NE; NE]	1,50	[0,42; 6,95]	0,5491
Interaktions p-Wert									0,7613
Geschlecht - DEU									
Männer	178	22 (12,4)	NE [NE; NE]	187	15 (8,0)	NE [NE; NE]	1,48	[0,77; 2,90]	0,2401
Frauen	84	21 (25,0)	NE [NE; NE]	78	13 (16,7)	NE [NE; NE]	1,44	[0,73; 2,96]	0,2928
Interaktions p-Wert									0,9633
Altersgruppe - DEU									
<65 Jahre	159	18 (11,3)	NE [NE; NE]	161	14 (8,7)	NE [NE; NE]	1,21	[0,61; 2,48]	0,5852
>=65 Jahre	103	25 (24,3)	NE [NE; NE]	104	14 (13,5)	NE [NE; NE]	1,81	[0,95; 3,58]	0,0692
Interaktions p-Wert									0,4124

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.3.1 ADRIATIC: Summary of subgroup analysis of time to first Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	12 (15,4)	NE [NE; NE]	72	11 (15,3)	NE [NE; NE]	0,93	[0,41; 2,15]	0,8685
TC or IC >=1%	84	11 (13,1)	NE [NE; NE]	98	11 (11,2)	NE [NE; NE]	1,10	[0,47; 2,58]	0,8151
Interaktions p-Wert									0,7772
Raucherstatus - DEU									
Raucher	239	40 (16,7)	NE [NE; NE]	239	23 (9,6)	NE [NE; NE]	1,68	[1,01; 2,85]	0,0437*
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	5 (19,2)	NE [NE; NE]	0,61	[0,13; 2,49]	0,4933
Interaktions p-Wert									0,1839
Abstammung - DEU									
Weiß	128	28 (21,9)	NE [NE; NE]	137	14 (10,2)	NE [NE; NE]	2,15	[1,15; 4,21]	0,0156*
Schwarz/Afroamerikanisch	1	1 (100)	11,1 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	14 (10,7)	NE [NE; NE]	121	13 (10,7)	NE [NE; NE]	0,93	[0,43; 2,00]	0,8439
Andere	2	0	NE [NE; NE]	4	1 (25,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,0947
Geographische Region - DEU									
Asien	129	13 (10,1)	NE [NE; NE]	120	14 (11,7)	NE [NE; NE]	0,79	[0,37; 1,70]	0,5456
Europa	94	14 (14,9)	NE [NE; NE]	112	9 (8,0)	NE [NE; NE]	1,71	[0,75; 4,10]	0,2056
Nordamerika	39	16 (41,0)	19,8 [3,7; NE]	33	5 (15,2)	NE [NE; NE]	3,41	[1,33; 10,44]	0,0093*
Interaktions p-Wert									0,0578
ECOG-Status zu Baseline - DEU									
0	131	18 (13,7)	NE [NE; NE]	131	13 (9,9)	NE [NE; NE]	1,31	[0,65; 2,73]	0,4545
1	131	25 (19,1)	NE [NE; NE]	134	15 (11,2)	NE [NE; NE]	1,66	[0,88; 3,22]	0,1154
Interaktions p-Wert									0,6304

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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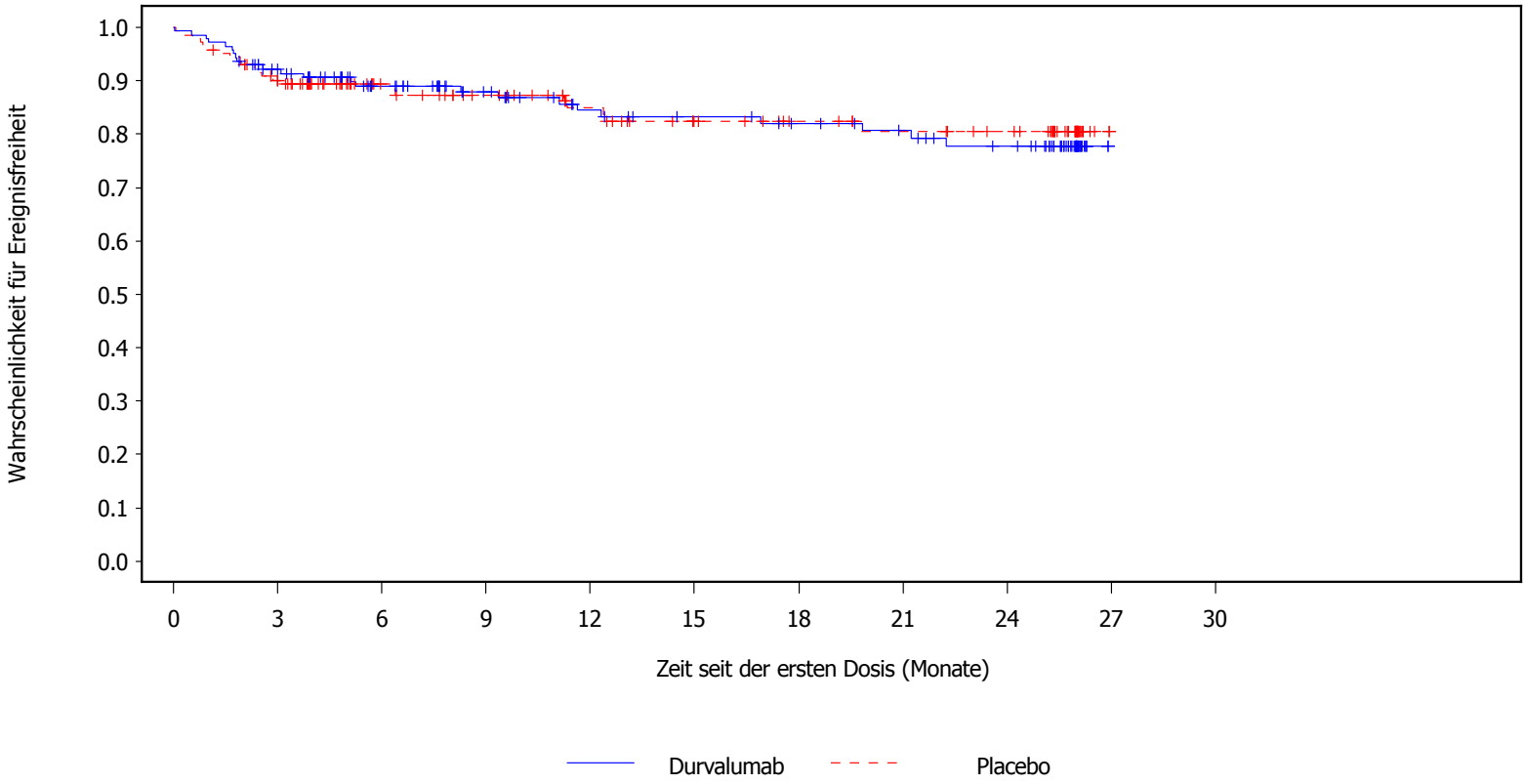
Anhang 4-G8.4.3: Therapieabbrüche aufgrund von UE - gesamt und nach SOC/PT - Subgruppenanalysen Kaplan-Meier-Plot

Figure 5.10.1 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for Erhalt einer PCI (IVRS) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	122	100	83	71	66	62	58	52	0	0	Durvalumab
143	121	89	79	67	56	50	46	42	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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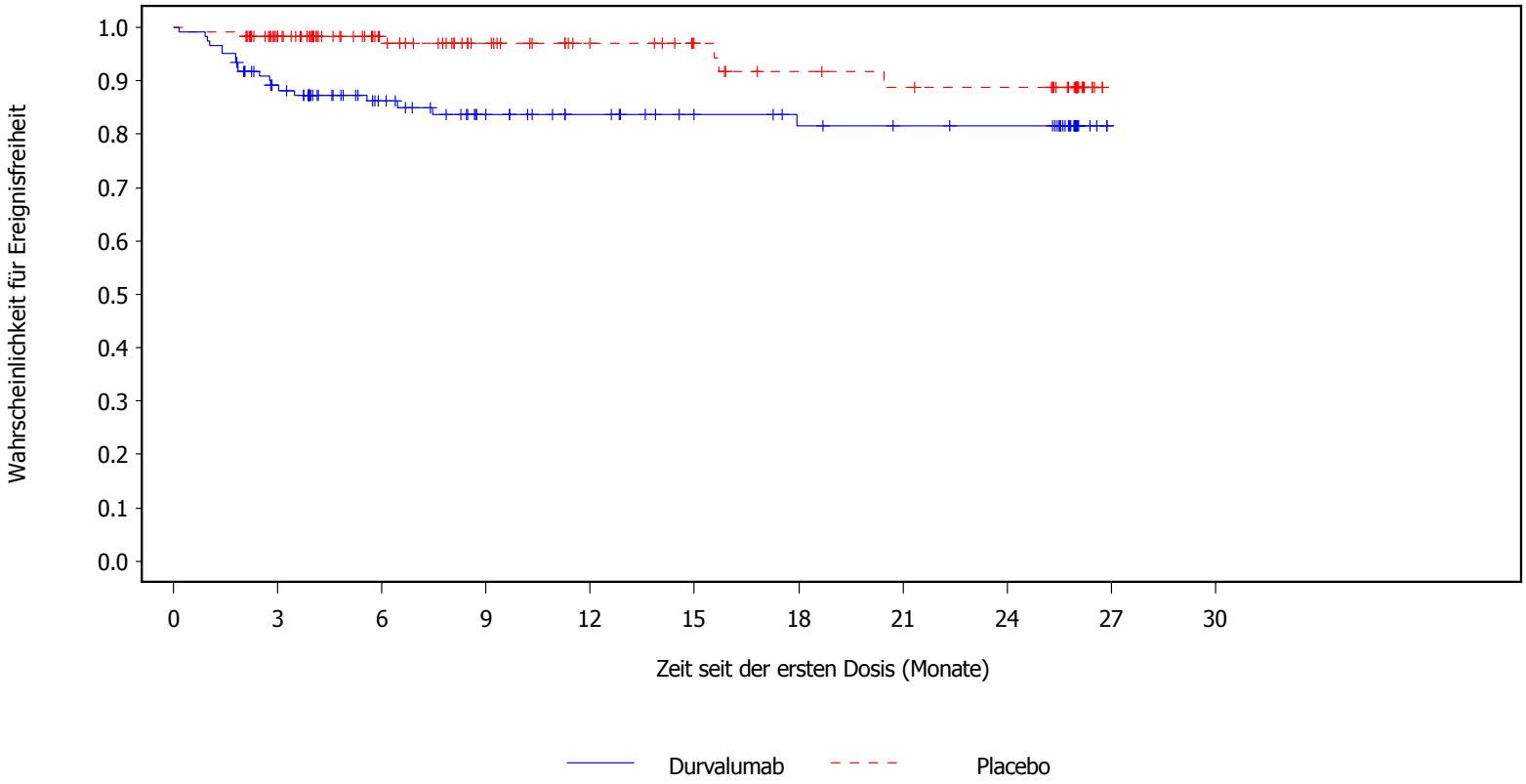
Figure 5.10.2 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for Erhalt einer PCI (IVRS) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	100	72	58	49	42	39	37	36	0	0	Durvalumab
122	102	71	55	43	37	32	30	29	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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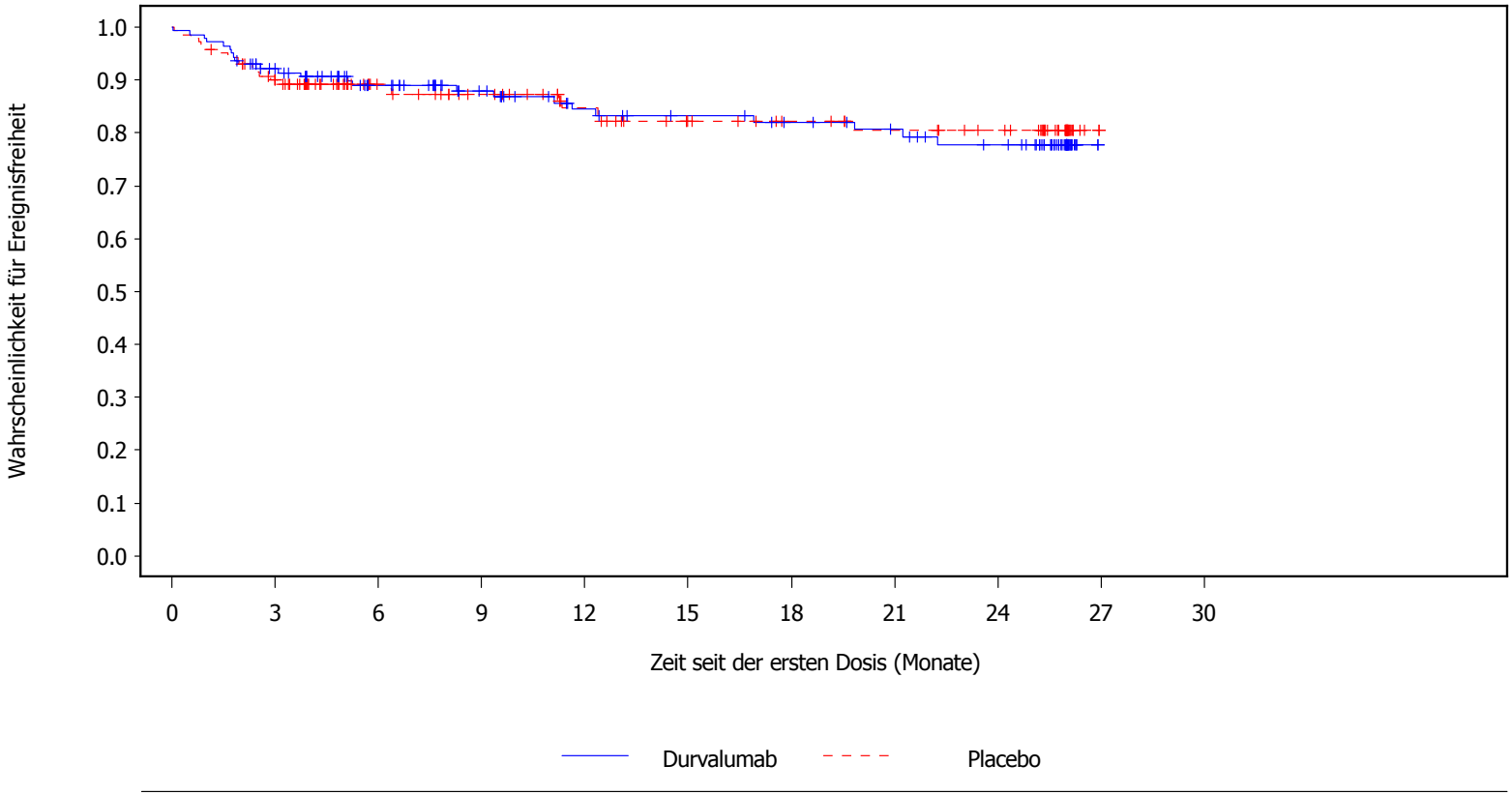
Figure 5.10.3 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for Erhalt einer PCI (eCRF) - DEU=Ja
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

141	122	100	83	71	66	62	58	52	0	0	Durvalumab
142	120	88	78	66	55	50	46	42	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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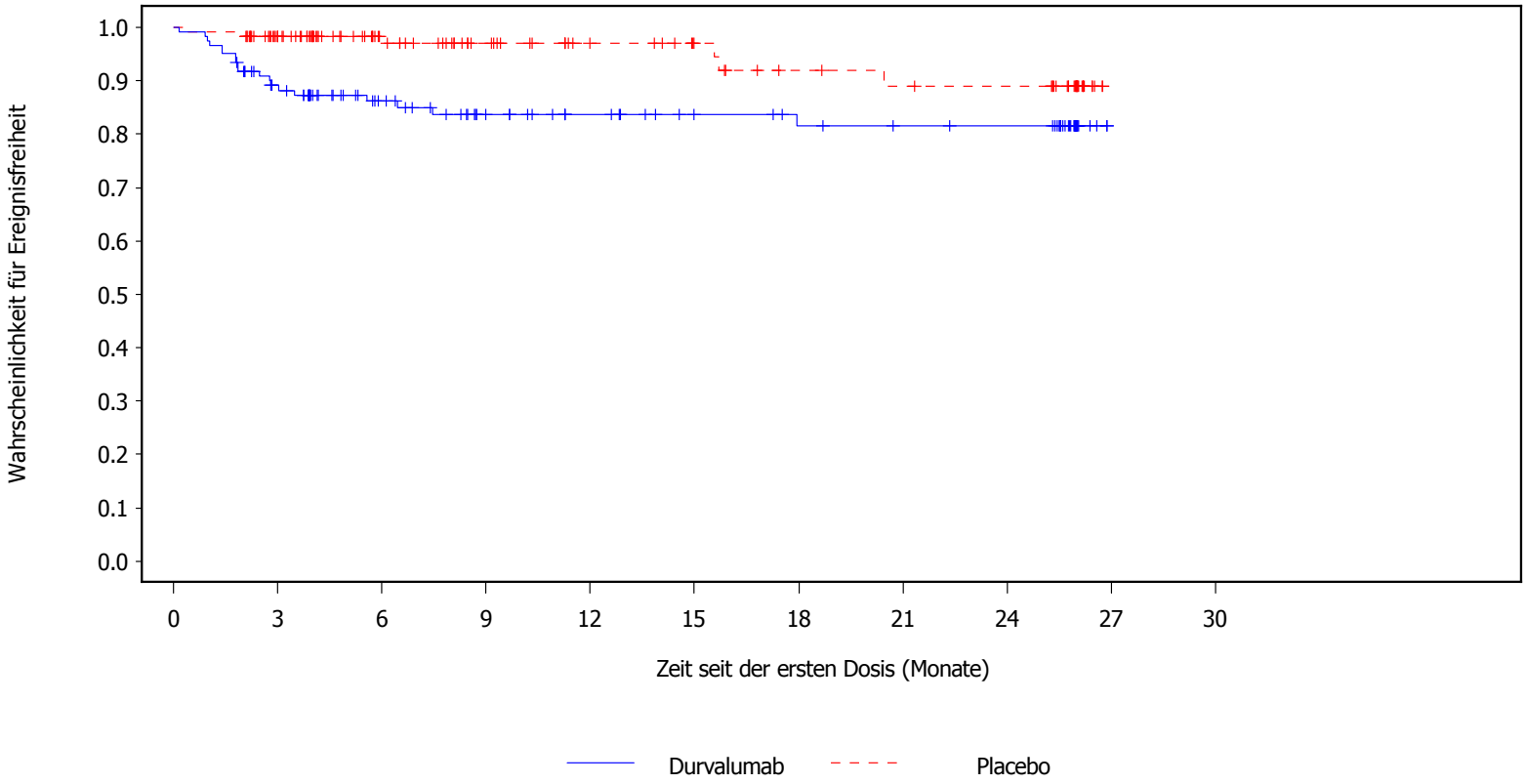
Figure 5.10.4 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for Erhalt einer PCI (eCRF) - DEU=Nein
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

121	100	72	58	49	42	39	37	36	0	0	Durvalumab
123	103	72	56	44	38	32	30	29	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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Anhang 4-G8.5: UESI jeglichen Schweregrades - gesamt und nach GT

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Table 2.2.5 ADRIATIC: Summary of analysis of time to first adverse event of special interest (total, and by grouped term)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UESI	262	134 (51,1)	9,0 [5,7;13,2]	265	73 (27,5)	NE [NE; NE]	2,13	[1,60; 2,84]	<0,0001*
UESI GT: Andere seltene/verschiedene	262	3 (1,1)	NE [NE; NE]	265	2 (0,8)	NE [NE; NE]	1,46	[0,24; 11,07]	0,6779
UESI GT: Dermatitis/Hautausschlag	262	42 (16,0)	NE [NE; NE]	265	29 (10,9)	NE [NE; NE]	1,42	[0,89; 2,29]	0,1480
UESI GT: Diabetes mellitus Typ 1	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3699
UESI GT: Durchfall/Colitis	262	29 (11,1)	NE [NE; NE]	265	24 (9,1)	NE [NE; NE]	1,17	[0,68; 2,02]	0,5727
UESI GT: Ereignisse der Bauchspeicheldrüse	262	1 (0,4)	NE [NE; NE]	265	1 (0,4)	NE [NE; NE]	0,98	[0,04; 24,78]	0,9890
UESI GT: Ereignisse der Nieren	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3145
UESI GT: Hepatische Ereignisse	262	4 (1,5)	NE [NE; NE]	265	3 (1,1)	NE [NE; NE]	1,25	[0,28; 6,34]	0,7709
UESI GT: Hyperthyreose Ereignisse	262	27 (10,3)	NE [NE; NE]	265	4 (1,5)	NE [NE; NE]	7,07	[2,76; 23,92]	<0,0001*

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1ae
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Table 2.2.5 ADRIATIC: Summary of analysis of time to first adverse event of special interest (total, and by grouped term)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UESI GT: Hypophysitis	262	2 (0,8)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,1614
UESI GT: Hypothyreose Ereignisse	262	42 (16,0)	NE [NE; NE]	265	10 (3,8)	NE [NE; NE]	4,43	[2,32; 9,34]	<0,0001*
UESI GT: Myokarditis	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3145
UESI GT: Nebenniereninsuffizienz	262	3 (1,1)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,0869
UESI GT: Pneumonitis	262	43 (16,4)	NE [NE; NE]	265	17 (6,4)	NE [NE; NE]	2,59	[1,50; 4,66]	0,0006*
UESI GT: Thyroiditis	262	3 (1,1)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,0813

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1ae
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Anhang 4-G8.5.1: UESI jeglichen Schweregrades - gesamt und nach GT - Kaplan-Meier-Plot

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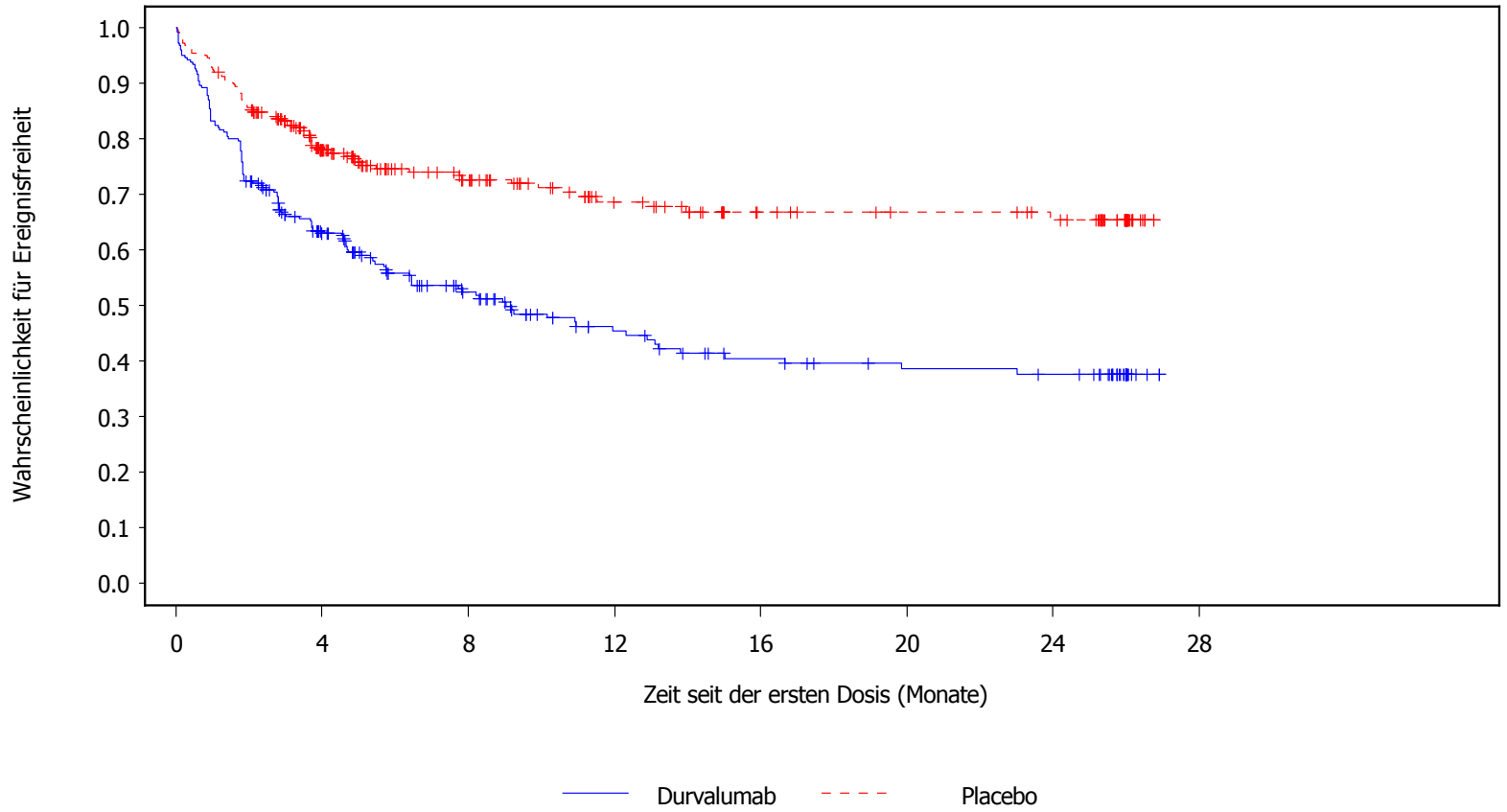
Figure 2.3.74 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	132	85	57	45	39	37	0	Durvalumab
265	160	107	75	56	51	47	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcv 05JUN2025:07:

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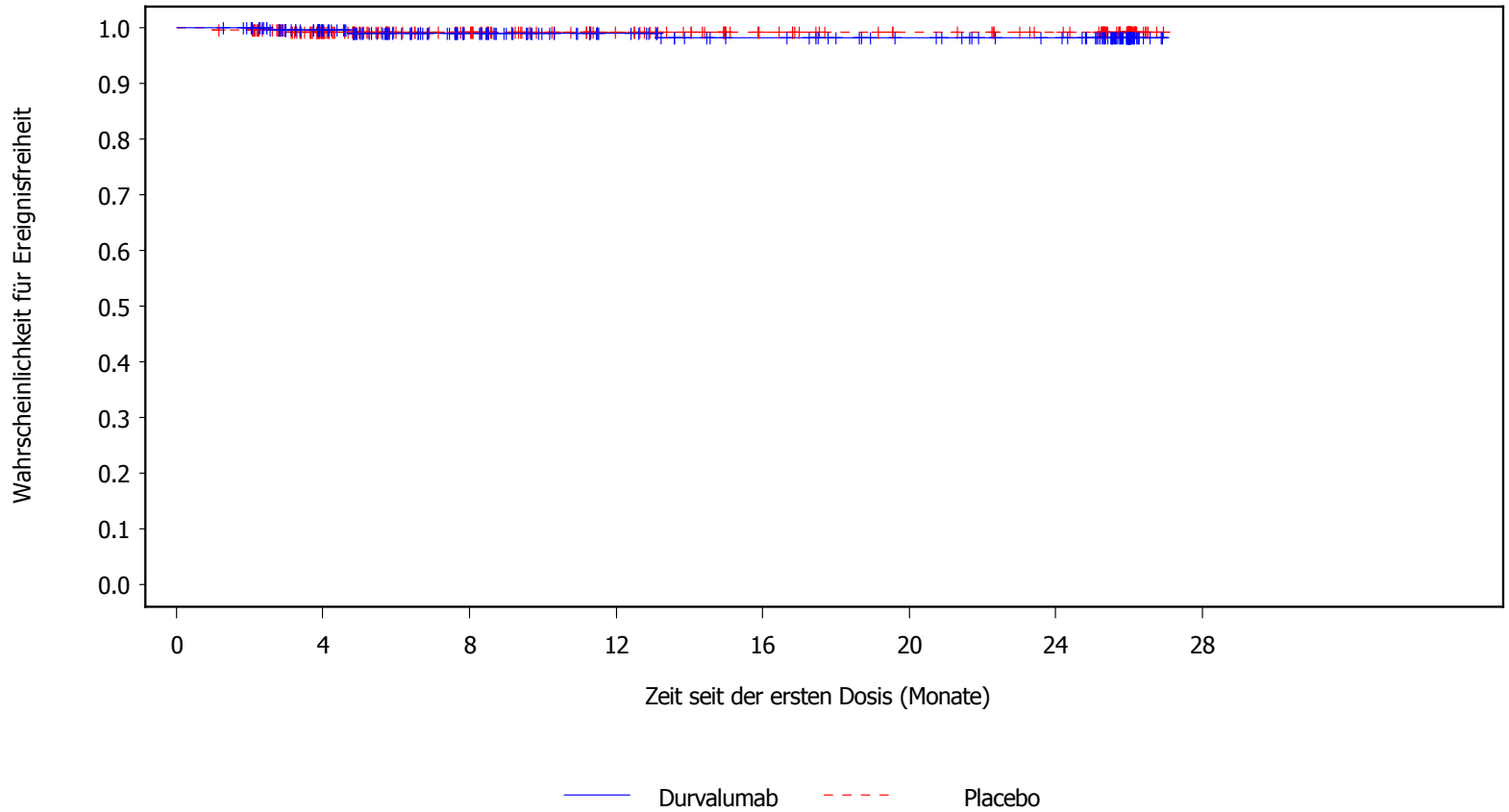
Figure 2.3.75 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024



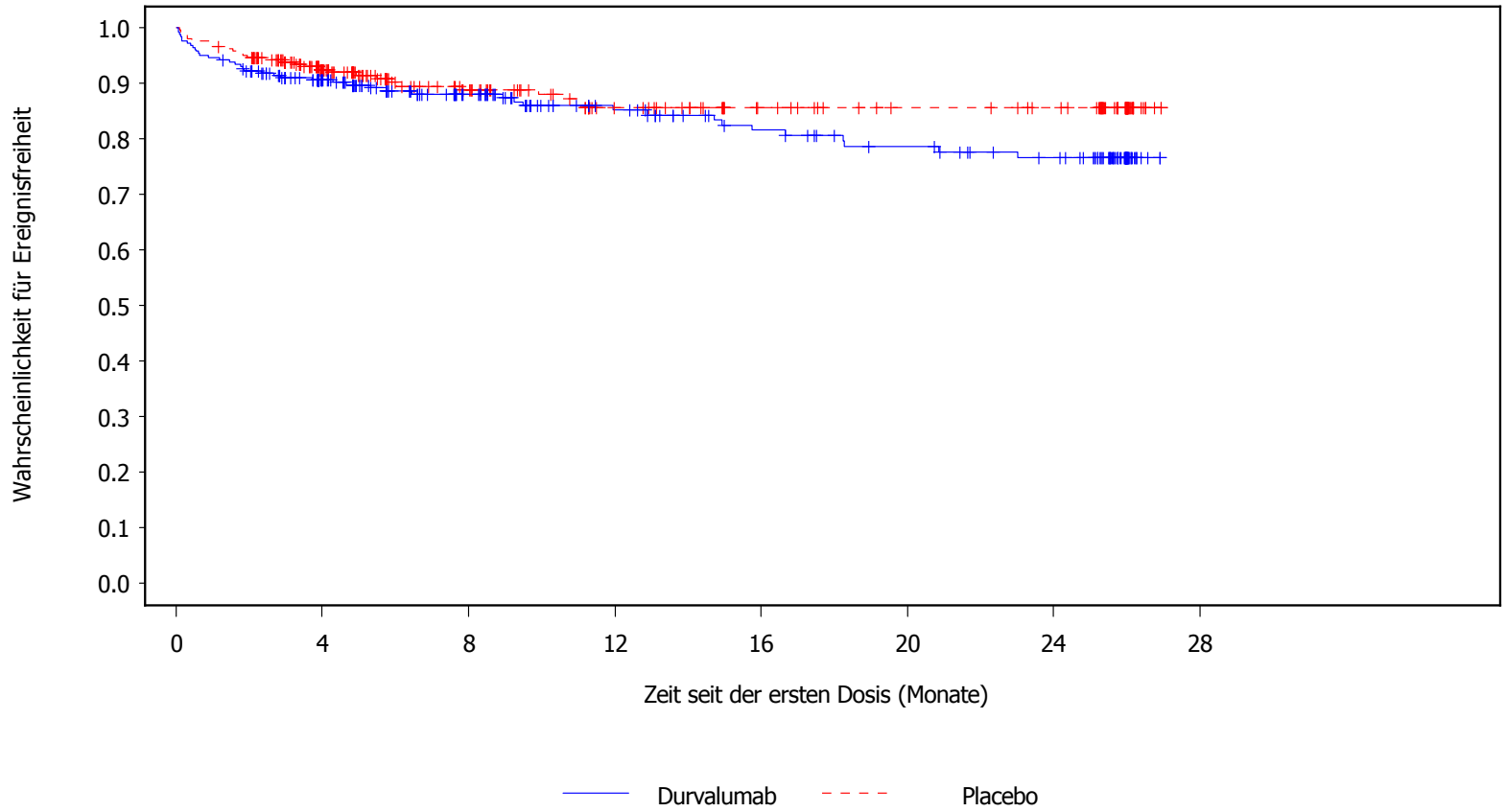
Anzahl an Patienten unter Risiko:

262	208	156	122	108	98	90	0	Durvalumab
265	203	146	111	89	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcw 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.76 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024



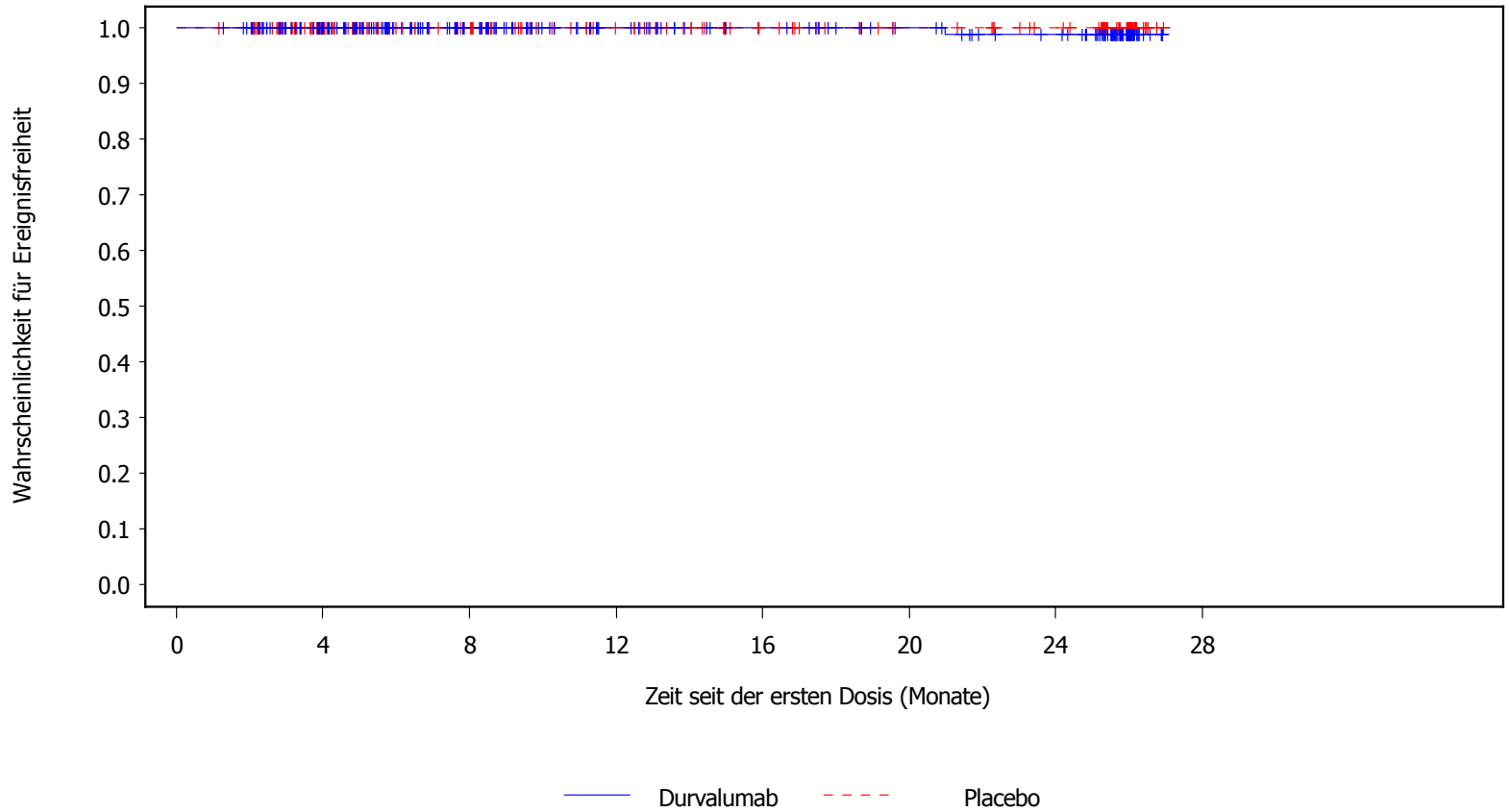
Anzahl an Patienten unter Risiko:

262	190	140	105	88	79	70	0	Durvalumab
265	187	126	93	75	66	62	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcx 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.77 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024



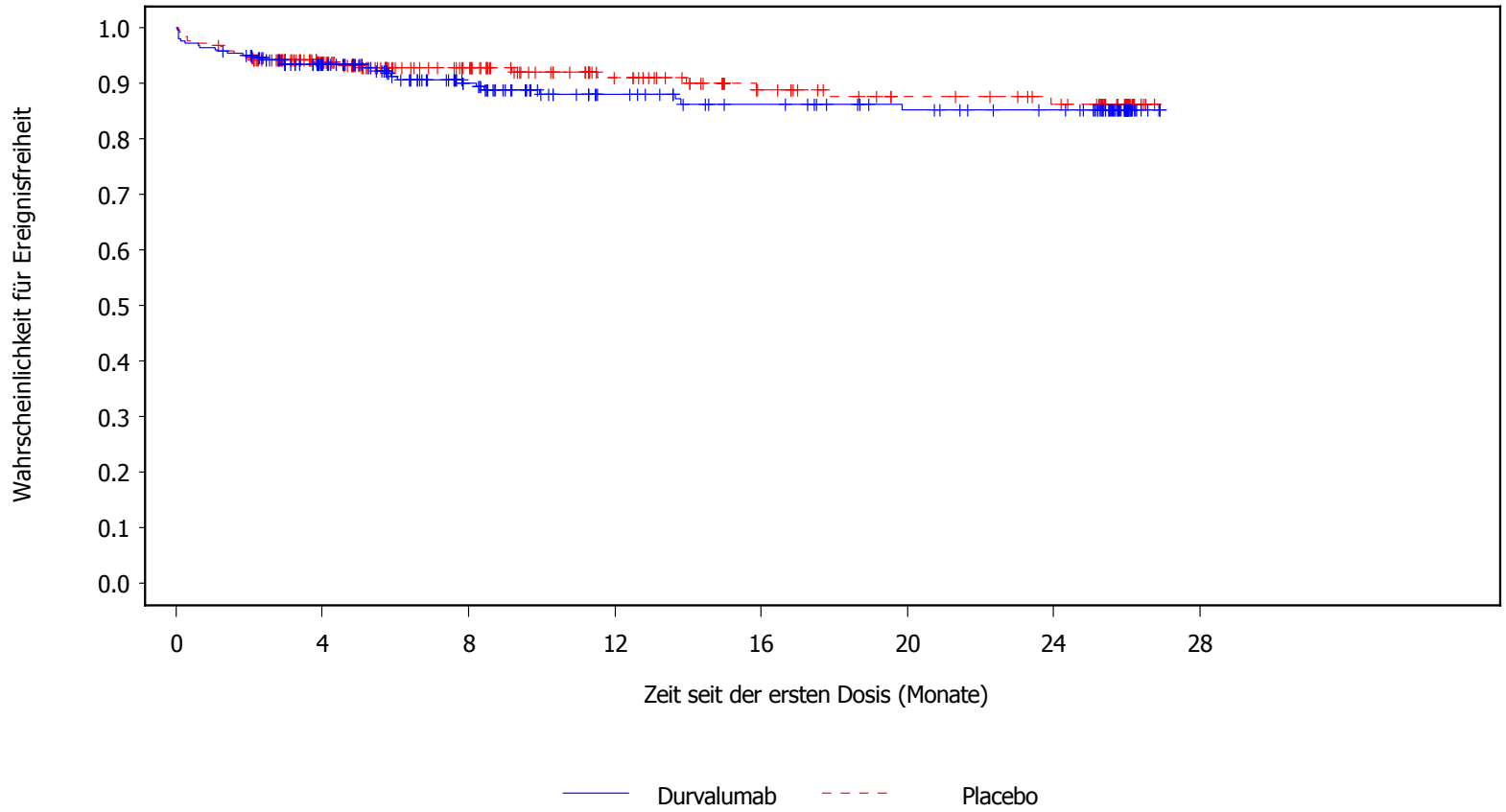
Anzahl an Patienten unter Risiko:

262	209	156	122	109	99	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcy 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.78 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	195	142	107	95	86	80	0	Durvalumab
265	194	136	99	76	64	58	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bcz 05JUN2025:07:

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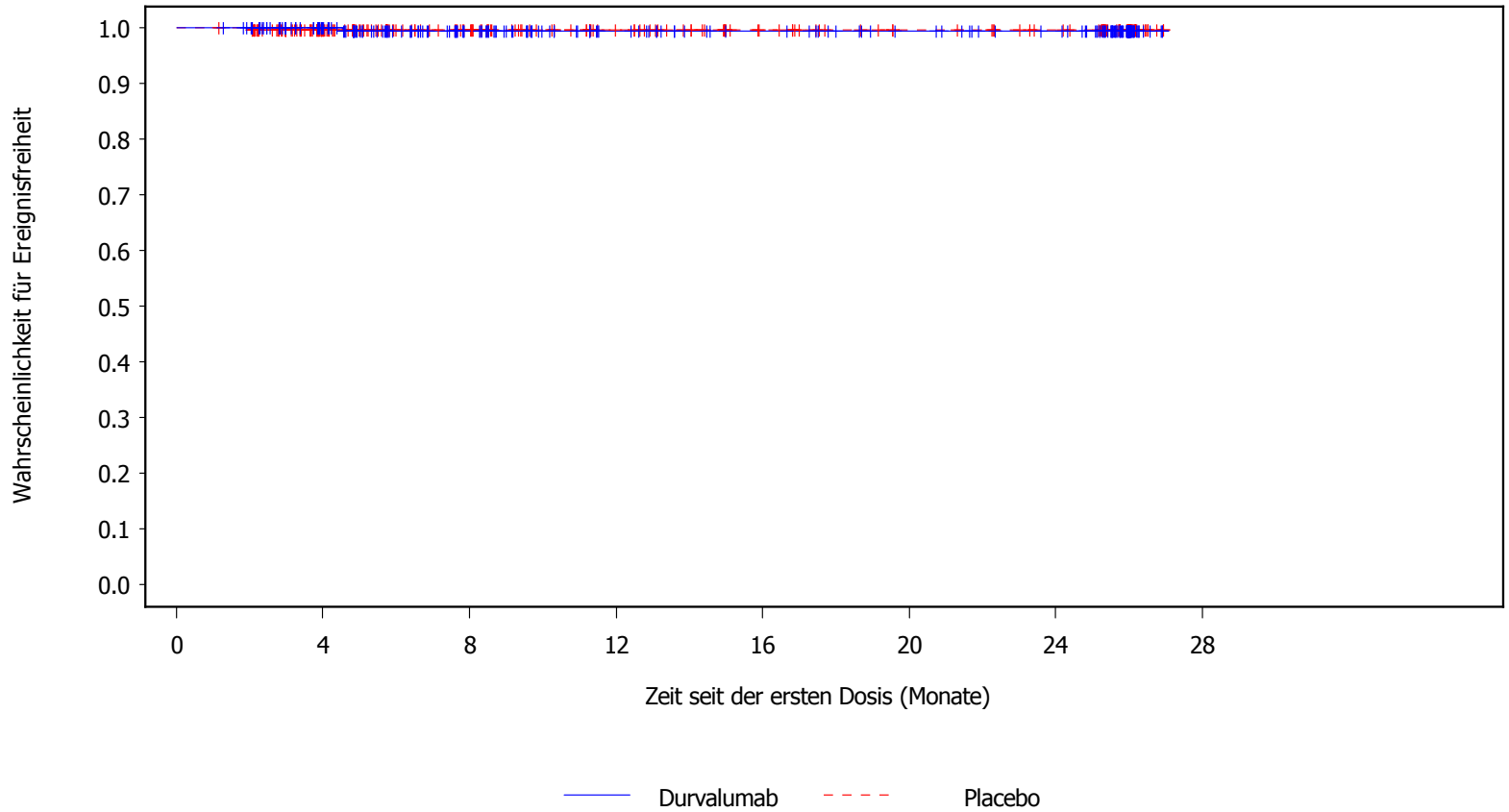
Figure 2.3.79 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bda 05JUN2025:07:

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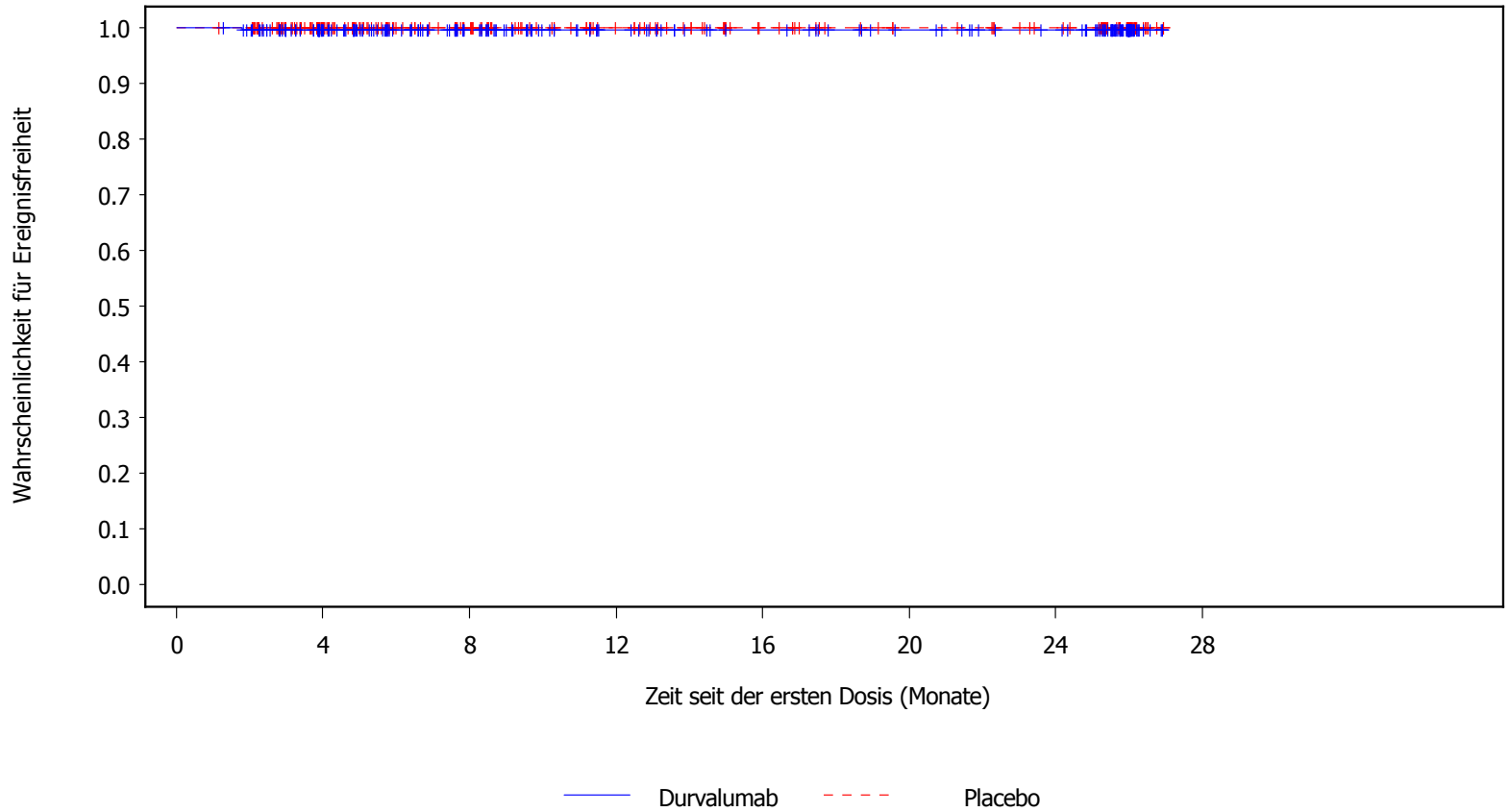
Figure 2.3.80 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Ereignisse der Nieren
Safety Analysis Set, DCO 15JAN2024

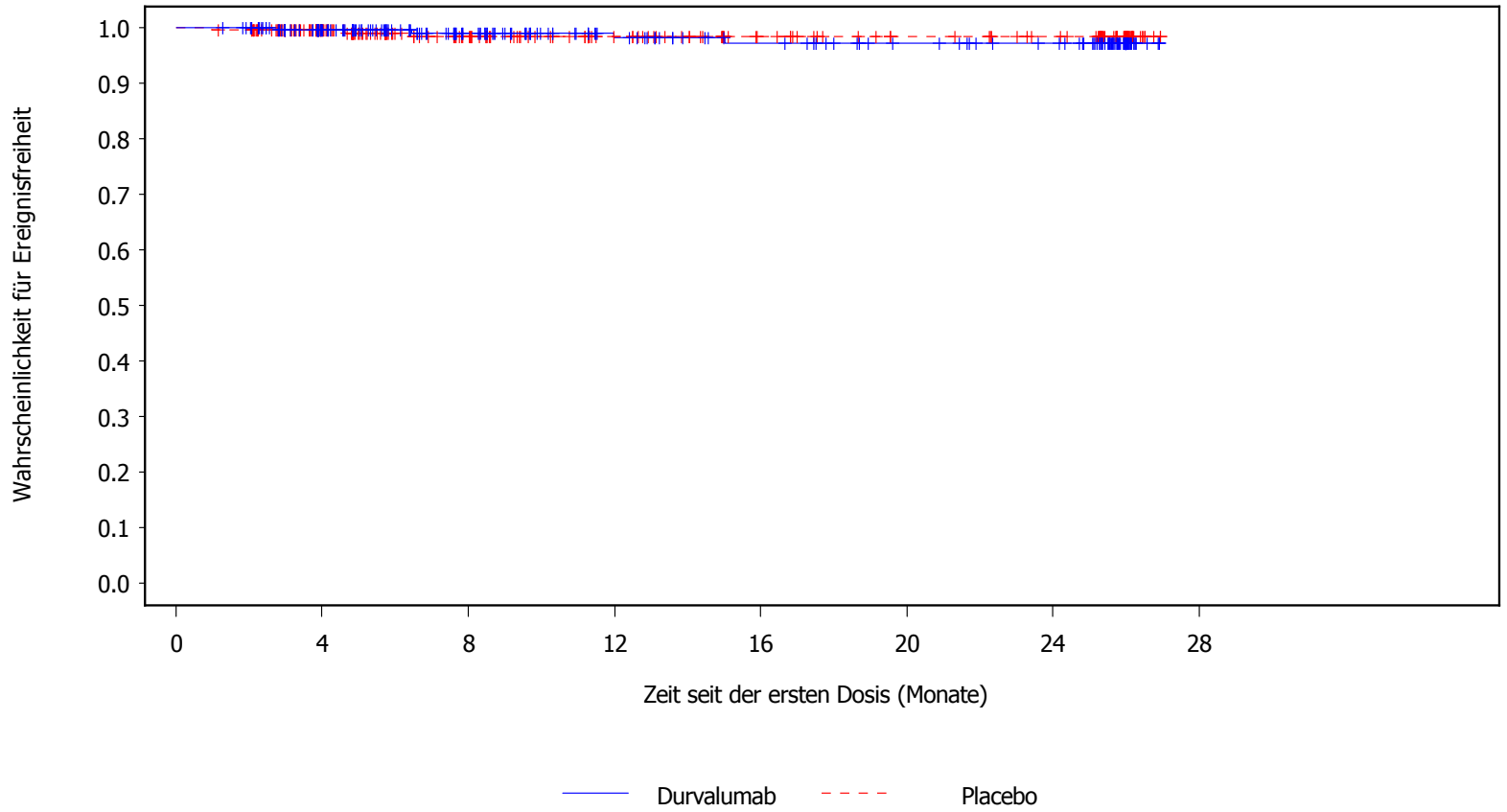


Anzahl an Patienten unter Risiko:

262	208	155	121	108	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdb 05JUN2025:07:

Figure 2.3.81 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	155	120	106	96	89	0	Durvalumab
265	204	145	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdc 05JUN2025:07:

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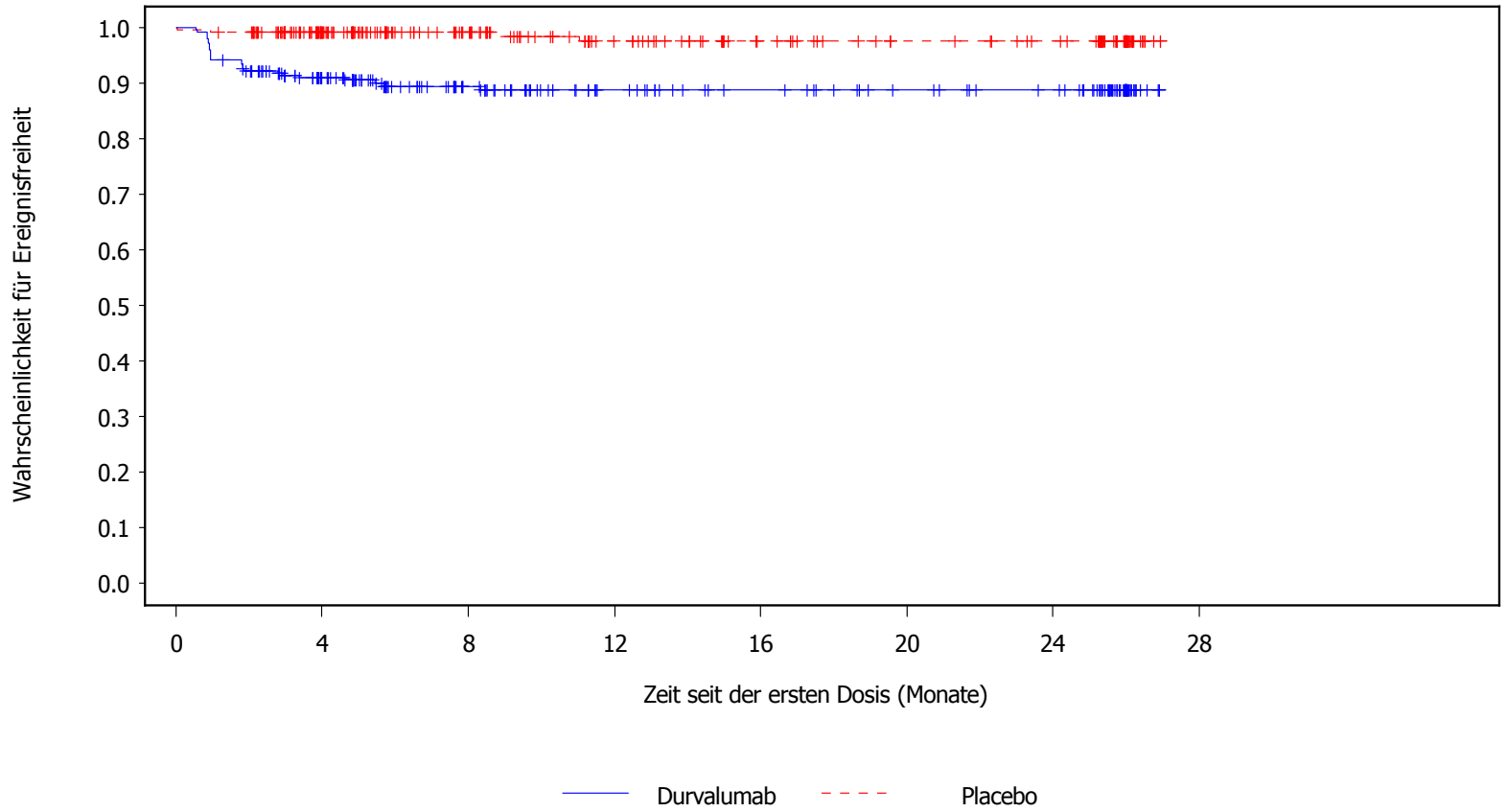
Figure 2.3.82 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Hyperthyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024



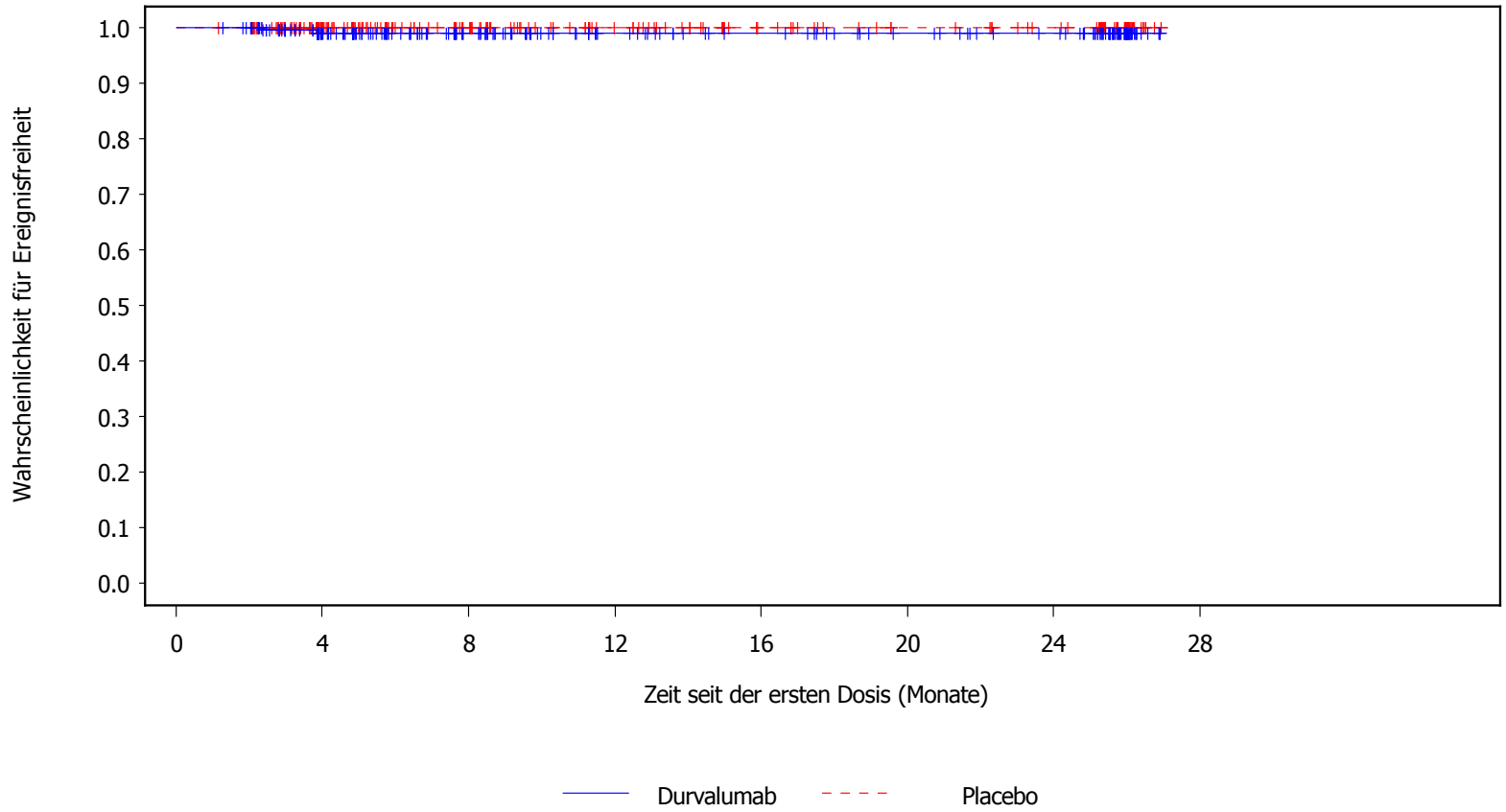
Anzahl an Patienten unter Risiko:

262	189	138	108	96	87	81	0	Durvalumab
265	204	146	109	87	75	69	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdd 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.83 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024



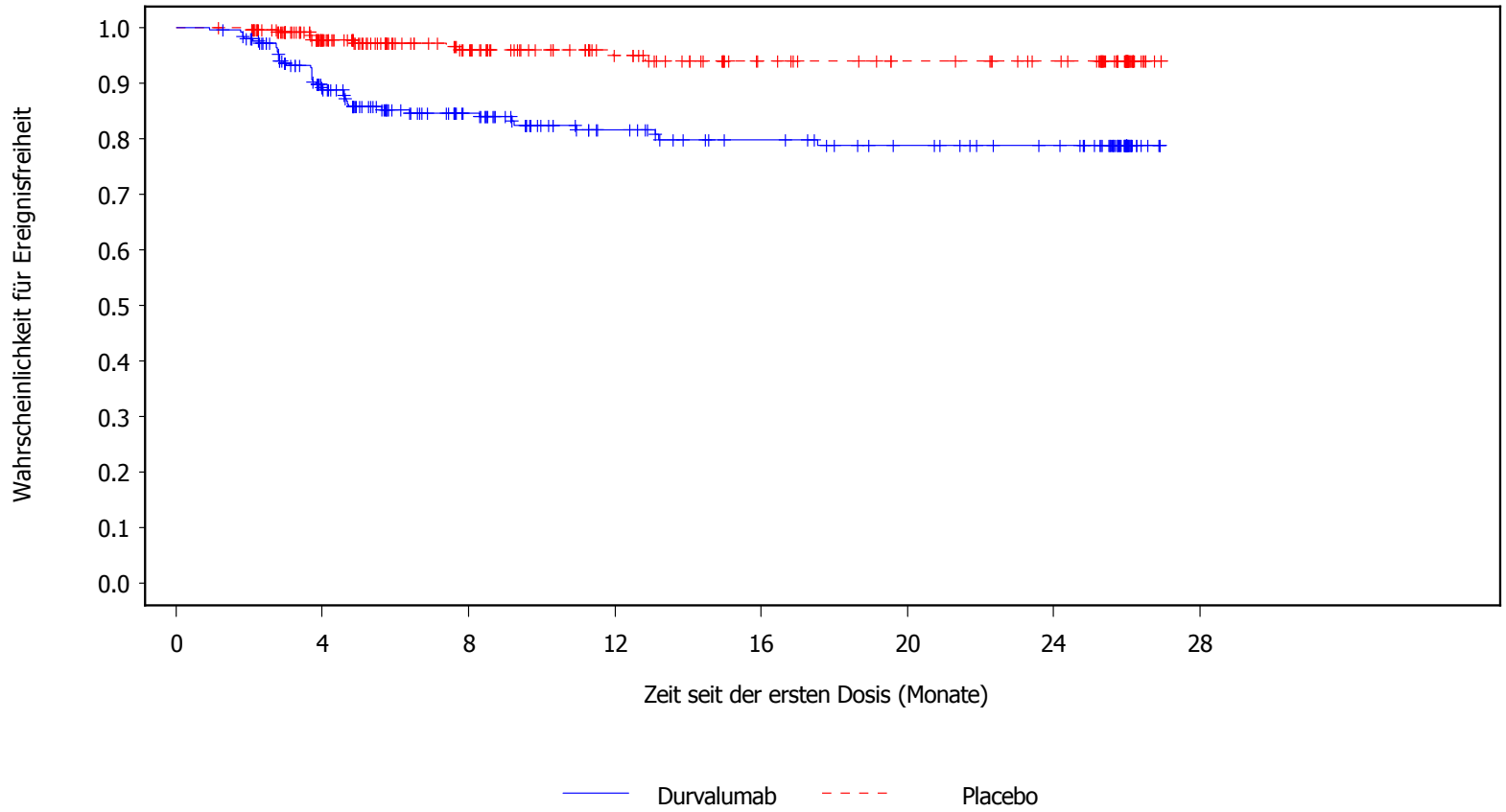
Anzahl an Patienten unter Risiko:

262	207	154	120	108	98	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bde 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.84 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Hypothyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024



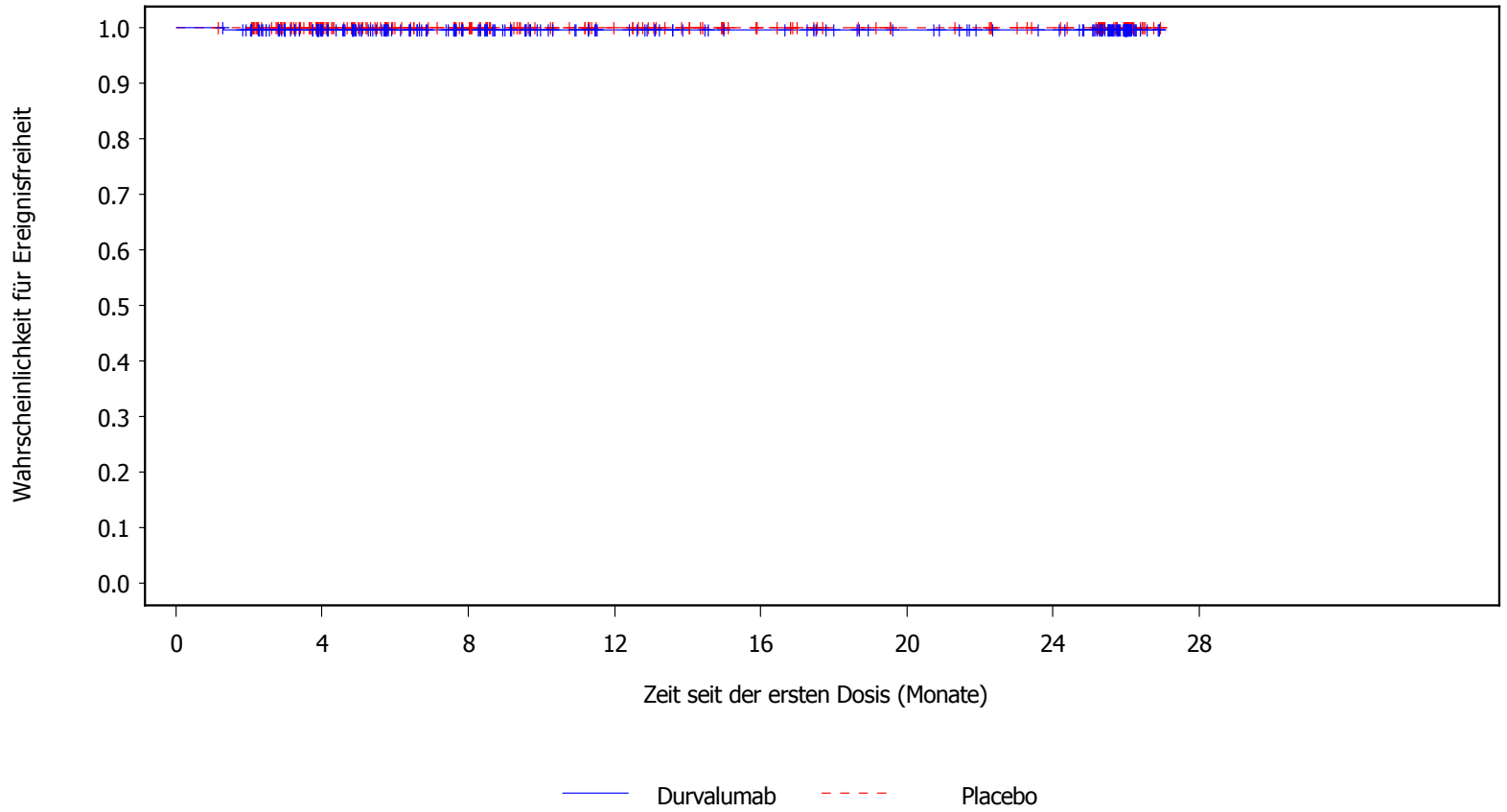
Anzahl an Patienten unter Risiko:

262	184	129	95	82	73	66	0	Durvalumab
265	200	141	105	82	74	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdf 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.85 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024



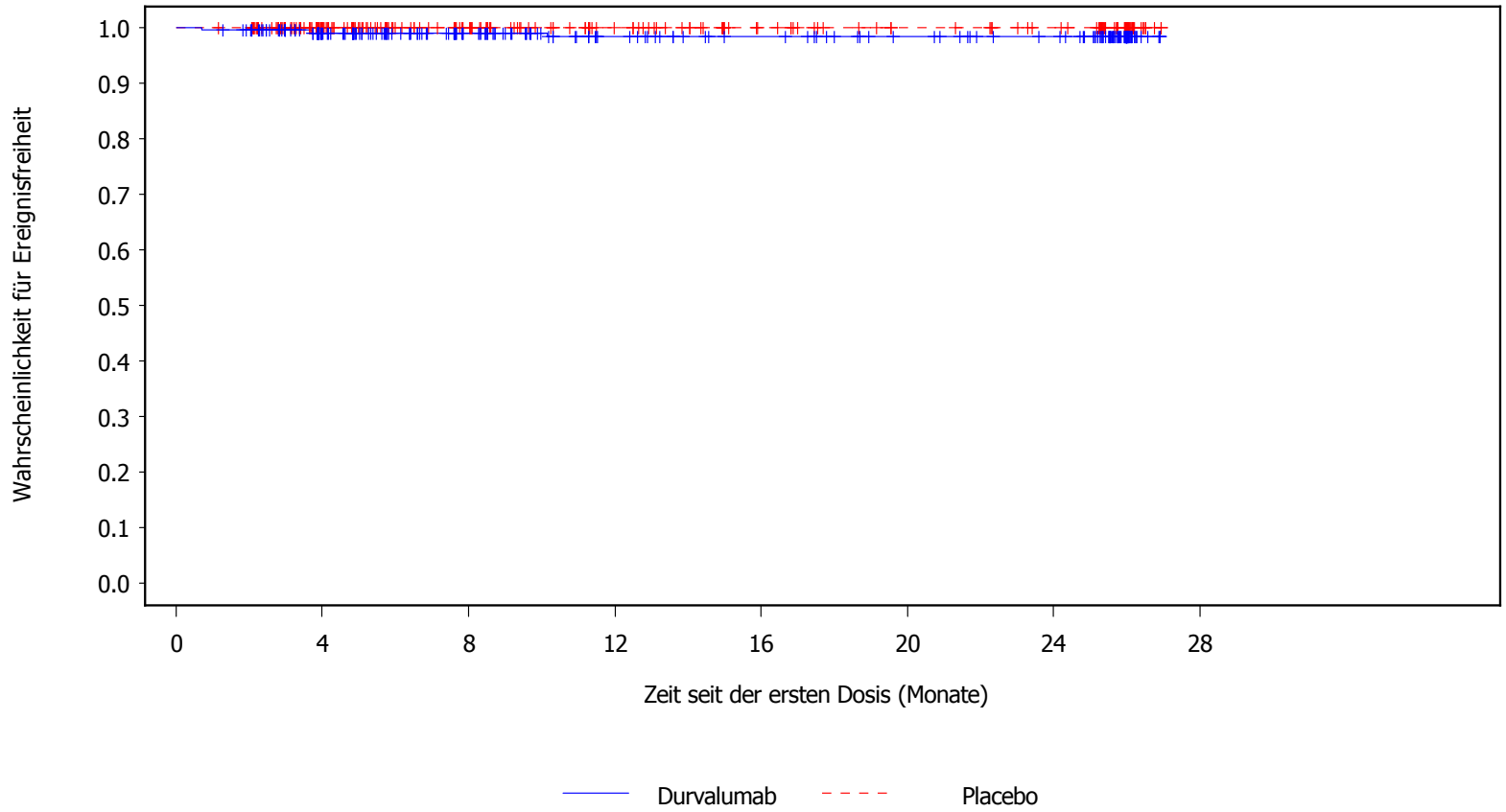
Anzahl an Patienten unter Risiko:

262	208	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdg 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.86 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024



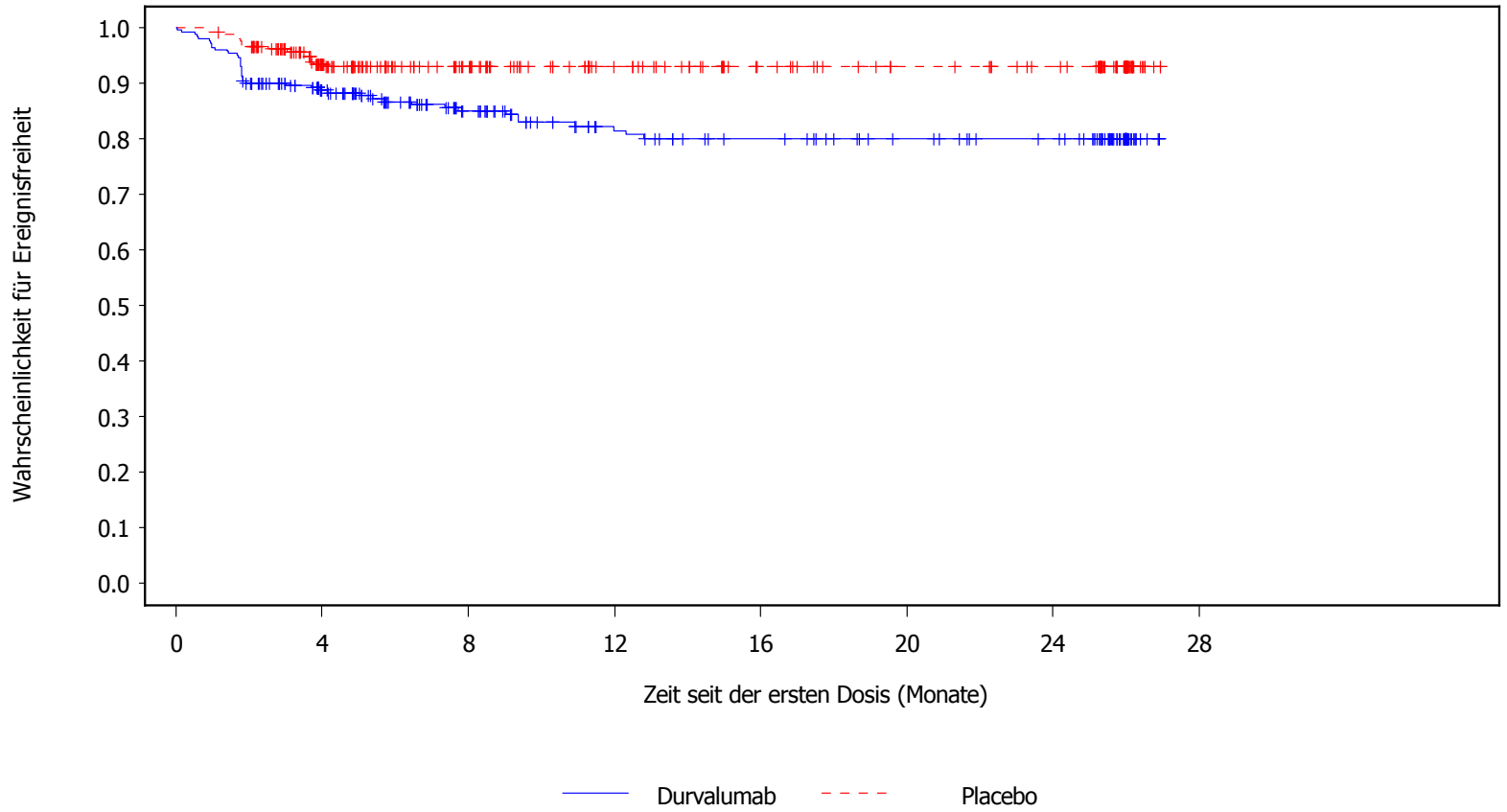
Anzahl an Patienten unter Risiko:

262	207	155	120	108	98	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdh 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.87 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024



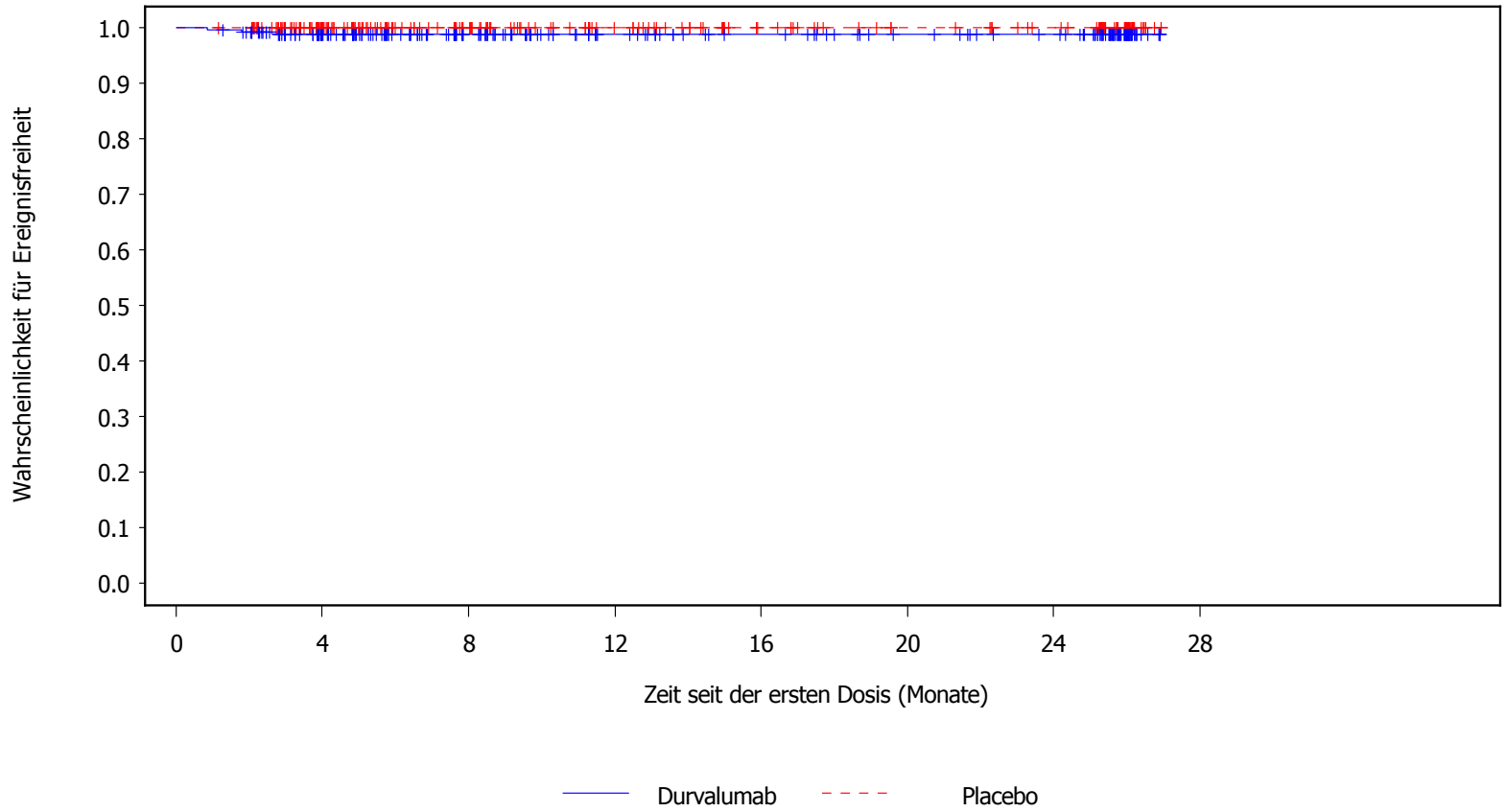
Anzahl an Patienten unter Risiko:

262	192	139	108	97	87	80	0	Durvalumab
265	193	140	106	85	74	67	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdi 05JUN2025:07:

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 2.3.88 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI GT: Thyroiditis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	206	153	119	106	96	89	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdj 05JUN2025:07:

Anhang 4-G8.5.2: UESI jeglichen Schweregrades - gesamt und nach GT - Subgruppenanalysen

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Table 5.5.1 ADRIATIC: Summary of subgroup analysis of time to first UESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	14 (38,9)	16,7 [6,4; NE]	37	11 (29,7)	NE [NE; NE]	1,32	[0,60; 2,98]	0,4872
Stadium III	226	120 (53,1)	8,2 [5,1;12,9]	228	62 (27,2)	NE [NE; NE]	2,28	[1,69; 3,12]	<0,0001*
Interaktions p-Wert									0,2112
TNM Status (eCRF) - DEU									
Stadium I/II	33	12 (36,4)	NE [NE; NE]	34	10 (29,4)	NE [NE; NE]	1,22	[0,53; 2,89]	0,6442
Stadium III	229	122 (53,3)	7,9 [4,7;12,0]	231	63 (27,3)	NE [NE; NE]	2,29	[1,70; 3,12]	<0,0001*
Interaktions p-Wert									0,1708
Erhalt einer PCI (IVRS) - DEU									
Ja	141	78 (55,3)	8,3 [5,1;12,9]	143	44 (30,8)	NE [NE; NE]	2,01	[1,40; 2,93]	0,0002*
Nein	121	56 (46,3)	12,0 [5,7; NE]	122	29 (23,8)	NE [NE; NE]	2,29	[1,48; 3,64]	0,0002*
Interaktions p-Wert									0,6526
Erhalt einer PCI (eCRF) - DEU									
Ja	141	78 (55,3)	8,3 [5,1;12,9]	142	43 (30,3)	NE [NE; NE]	2,05	[1,42; 2,99]	0,0001*
Nein	121	56 (46,3)	12,0 [5,7; NE]	123	30 (24,4)	NE [NE; NE]	2,23	[1,44; 3,52]	0,0003*
Interaktions p-Wert									0,7713
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	15 (48,4)	12,0 [2,9; NE]	32	5 (15,6)	NE [NE; NE]	3,61	[1,40; 11,11]	0,0070*
>=14 bis <28 Tage	79	37 (46,8)	9,2 [6,4; NE]	80	27 (33,8)	NE [NE; NE]	1,56	[0,95; 2,59]	0,0759
>=28 Tage	152	82 (53,9)	8,3 [4,7;13,1]	153	41 (26,8)	NE [NE; NE]	2,32	[1,60; 3,40]	<0,0001*
Interaktions p-Wert									0,2468
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	8 (50,0)	12,0 [1,8; NE]	24	5 (20,8)	NE [NE; NE]	2,36	[0,79; 7,80]	0,1259
>=28 bis <56 Tage	103	47 (45,6)	13,2 [4,7; NE]	103	29 (28,2)	NE [NE; NE]	1,80	[1,14; 2,89]	0,0115*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttesubae1.sas gttesubae1eaa
05JUN2025:07:12

Nutzenbewertung nach AMNOG

Table 5.5.1 ADRIATIC: Summary of subgroup analysis of time to first UESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	55 (56,1)	8,3 [5,3;10,9]	76	20 (26,3)	NE [NE; NE]	2,34	[1,43; 3,99]	0,0006*
>=84 Tage	45	24 (53,3)	6,4 [1,9; NE]	62	19 (30,6)	NE [NE; NE]	2,43	[1,33; 4,49]	0,0039*
Interaktions p-Wert									0,8379
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	50 (56,2)	7,7 [4,6;13,1]	88	24 (27,3)	NE [NE; NE]	2,24	[1,39; 3,71]	0,0008*
Cisplatin	173	84 (48,6)	9,2 [5,7;23,0]	177	49 (27,7)	NE [NE; NE]	2,06	[1,46; 2,95]	<0,0001*
Interaktions p-Wert									0,7841
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	96 (49,7)	9,2 [6,4;13,8]	186	45 (24,2)	NE [NE; NE]	2,31	[1,63; 3,32]	<0,0001*
Zweimal täglich	69	38 (55,1)	5,7 [2,8; NE]	79	28 (35,4)	NE [NE; NE]	1,88	[1,16; 3,08]	0,0109*
Interaktions p-Wert									0,5004
Bestes Ansprechen auf cCRT - DEU									
CR	31	19 (61,3)	7,7 [1,8;23,0]	34	11 (32,4)	NE [NE; NE]	2,26	[1,09; 4,92]	0,0275*
PR	189	91 (48,1)	9,0 [5,5; NE]	199	59 (29,6)	NE [NE; NE]	1,85	[1,33; 2,57]	0,0002*
SD	42	24 (57,1)	9,2 [2,9;19,8]	32	3 (9,4)	NE [NE; NE]	7,21	[2,52; 30,35]	<0,0001*
Interaktions p-Wert									0,0466*
Geschlecht - DEU									
Männer	178	88 (49,4)	9,2 [6,4;15,0]	187	45 (24,1)	NE [NE; NE]	2,38	[1,67; 3,44]	<0,0001*
Frauen	84	46 (54,8)	9,0 [2,9;19,8]	78	28 (35,9)	NE [NE; NE]	1,68	[1,06; 2,73]	0,0272*
Interaktions p-Wert									0,2535
Altersgruppe - DEU									
<65 Jahre	159	82 (51,6)	7,9 [4,7;19,8]	161	41 (25,5)	NE [NE; NE]	2,38	[1,65; 3,49]	<0,0001*
>=65 Jahre	103	52 (50,5)	10,2 [5,7;16,7]	104	32 (30,8)	NE [NE; NE]	1,81	[1,17; 2,84]	0,0074*
Interaktions p-Wert									0,3531

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Table 5.5.1 ADRIATIC: Summary of subgroup analysis of time to first UESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	41 (52,6)	7,7 [3,7; NE]	72	19 (26,4)	NE [NE; NE]	2,28	[1,34; 4,01]	0,0021*
TC or IC >=1%	84	43 (51,2)	9,2 [4,6; NE]	98	33 (33,7)	NE [NE; NE]	1,69	[1,07; 2,67]	0,0232*
Interaktions p-Wert									0,4045
Raucherstatus - DEU									
Raucher	239	121 (50,6)	9,2 [5,7;13,8]	239	66 (27,6)	NE [NE; NE]	2,11	[1,57; 2,86]	<0,0001*
Nichtraucher	23	13 (56,5)	9,0 [1,8; NE]	26	7 (26,9)	NE [NE; NE]	2,32	[0,95; 6,17]	0,0652
Interaktions p-Wert									0,8472
Abstammung - DEU									
Weiß	128	72 (56,3)	5,3 [3,4;12,0]	137	33 (24,1)	NE [NE; NE]	2,87	[1,91; 4,38]	<0,0001*
Schwarz/Afroamerikanisch	1	1 (100)	2,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	61 (46,6)	10,9 [7,9; NE]	121	39 (32,2)	NE [NE; NE]	1,57	[1,06; 2,37]	0,0249*
Andere	2	0	NE [NE; NE]	4	1 (25,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,0411*
Geographische Region - DEU									
Asien	129	61 (47,3)	10,9 [7,9; NE]	120	38 (31,7)	NE [NE; NE]	1,63	[1,09; 2,46]	0,0170*
Europa	94	53 (56,4)	5,7 [2,8;12,9]	112	25 (22,3)	NE [NE; NE]	2,96	[1,86; 4,84]	<0,0001*
Nordamerika	39	20 (51,3)	6,4 [2,9; NE]	33	10 (30,3)	NE [NE; NE]	2,16	[1,03; 4,81]	0,0405*
Interaktions p-Wert									0,1671
ECOG-Status zu Baseline - DEU									
0	131	58 (44,3)	15,0 [7,7; NE]	131	36 (27,5)	NE [NE; NE]	1,68	[1,11; 2,56]	0,0133*
1	131	76 (58,0)	5,7 [3,0; 9,2]	134	37 (27,6)	NE [NE; NE]	2,67	[1,81; 3,99]	<0,0001*
Interaktions p-Wert									0,1129

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.2 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	1 (2,8)	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	2 (0,9)	NE [NE; NE]	228	2 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	1 (3,0)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	2 (0,9)	NE [NE; NE]	231	2 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	143	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	142	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	2 (1,3)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.2 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	2 (2,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	2 (1,2)	NE [NE; NE]	177	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	2 (1,0)	NE [NE; NE]	186	2 (1,1)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	1 (1,4)	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
PR	189	2 (1,1)	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	3 (1,7)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	2 (1,3)	NE [NE; NE]	161	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.2 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	3 (1,3)	NE [NE; NE]	239	2 (0,8)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	2 (1,5)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	2 (1,5)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	2 (1,6)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	2 (1,8)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	2 (1,5)	NE [NE; NE]	134	2 (1,5)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.3 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	4 (11,1)	NE [NE; NE]	37	5 (13,5)	NE [NE; NE]	0,85	[0,21; 3,22]	0,8115
Stadium III	226	38 (16,8)	NE [NE; NE]	228	24 (10,5)	NE [NE; NE]	1,53	[0,92; 2,58]	0,1009
Interaktions p-Wert									0,4168
TNM Status (eCRF) - DEU									
Stadium I/II	33	3 (9,1)	NE [NE; NE]	34	5 (14,7)	NE [NE; NE]	0,62	[0,13; 2,52]	0,5030
Stadium III	229	39 (17,0)	NE [NE; NE]	231	24 (10,4)	NE [NE; NE]	1,58	[0,95; 2,66]	0,0755
Interaktions p-Wert									0,2182
Erhalt einer PCI (IVRS) - DEU									
Ja	141	27 (19,1)	NE [NE; NE]	143	16 (11,2)	NE [NE; NE]	1,66	[0,90; 3,14]	0,1041
Nein	121	15 (12,4)	NE [NE; NE]	122	13 (10,7)	NE [NE; NE]	1,12	[0,53; 2,40]	0,7586
Interaktions p-Wert									0,4311
Erhalt einer PCI (eCRF) - DEU									
Ja	141	27 (19,1)	NE [NE; NE]	142	16 (11,3)	NE [NE; NE]	1,64	[0,89; 3,11]	0,1109
Nein	121	15 (12,4)	NE [NE; NE]	123	13 (10,6)	NE [NE; NE]	1,14	[0,54; 2,43]	0,7347
Interaktions p-Wert									0,4570
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	2,80	[0,36; 56,58]	0,3394
>=14 bis <28 Tage	79	10 (12,7)	NE [NE; NE]	80	10 (12,5)	NE [NE; NE]	0,99	[0,41; 2,42]	0,9872
>=28 Tage	152	29 (19,1)	NE [NE; NE]	153	18 (11,8)	NE [NE; NE]	1,58	[0,88; 2,89]	0,1229
Interaktions p-Wert									0,5643
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	1 (6,3)	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	1,22	[0,05; 30,83]	0,8884
>=28 bis <56 Tage	103	12 (11,7)	NE [NE; NE]	103	8 (7,8)	NE [NE; NE]	1,45	[0,60; 3,71]	0,4074

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.3 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	18 (18,4)	NE [NE; NE]	76	9 (11,8)	NE [NE; NE]	1,41	[0,65; 3,30]	0,3879
>=84 Tage	45	11 (24,4)	NE [NE; NE]	62	11 (17,7)	NE [NE; NE]	1,59	[0,68; 3,71]	0,2804
Interaktions p-Wert									0,9962
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	16 (18,0)	NE [NE; NE]	88	7 (8,0)	NE [NE; NE]	2,13	[0,91; 5,55]	0,0824
Cisplatin	173	26 (15,0)	NE [NE; NE]	177	22 (12,4)	NE [NE; NE]	1,18	[0,67; 2,11]	0,5590
Interaktions p-Wert									0,2666
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	28 (14,5)	NE [NE; NE]	186	17 (9,1)	NE [NE; NE]	1,52	[0,84; 2,84]	0,1656
Zweimal täglich	69	14 (20,3)	NE [NE; NE]	79	12 (15,2)	NE [NE; NE]	1,32	[0,61; 2,89]	0,4854
Interaktions p-Wert									0,7691
Bestes Ansprechen auf cCRT - DEU									
CR	31	9 (29,0)	NE [NE; NE]	34	4 (11,8)	NE [NE; NE]	2,50	[0,81; 9,23]	0,1113
PR	189	27 (14,3)	NE [NE; NE]	199	24 (12,1)	NE [NE; NE]	1,17	[0,68; 2,05]	0,5681
SD	42	6 (14,3)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	3,90	[0,67; 73,67]	0,1444
Interaktions p-Wert									0,2887
Geschlecht - DEU									
Männer	178	33 (18,5)	NE [NE; NE]	187	19 (10,2)	NE [NE; NE]	1,81	[1,04; 3,24]	0,0361*
Frauen	84	9 (10,7)	NE [NE; NE]	78	10 (12,8)	NE [NE; NE]	0,77	[0,30; 1,90]	0,5633
Interaktions p-Wert									0,1137
Altersgruppe - DEU									
<65 Jahre	159	22 (13,8)	NE [NE; NE]	161	16 (9,9)	NE [NE; NE]	1,30	[0,68; 2,51]	0,4255
>=65 Jahre	103	20 (19,4)	NE [NE; NE]	104	13 (12,5)	NE [NE; NE]	1,59	[0,80; 3,28]	0,1873
Interaktions p-Wert									0,6742

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.3 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	7 (9,0)	NE [NE; NE]	72	7 (9,7)	NE [NE; NE]	0,82	[0,28; 2,41]	0,7188
TC or IC >=1%	84	20 (23,8)	NE [NE; NE]	98	12 (12,2)	NE [NE; NE]	1,98	[0,98; 4,17]	0,0563
Interaktions p-Wert									0,1768
Raucherstatus - DEU									
Raucher	239	42 (17,6)	NE [NE; NE]	239	27 (11,3)	NE [NE; NE]	1,52	[0,94; 2,49]	0,0870
Nichtraucher	23	0	NE [NE; NE]	26	2 (7,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	21 (16,4)	NE [NE; NE]	137	13 (9,5)	NE [NE; NE]	1,72	[0,87; 3,53]	0,1171
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	21 (16,0)	NE [NE; NE]	121	16 (13,2)	NE [NE; NE]	1,16	[0,61; 2,25]	0,6617
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,4091
Geographische Region - DEU									
Asien	129	21 (16,3)	NE [NE; NE]	120	16 (13,3)	NE [NE; NE]	1,16	[0,61; 2,26]	0,6578
Europa	94	18 (19,1)	NE [NE; NE]	112	10 (8,9)	NE [NE; NE]	2,02	[0,95; 4,56]	0,0674
Nordamerika	39	3 (7,7)	NE [NE; NE]	33	3 (9,1)	NE [NE; NE]	0,93	[0,17; 5,04]	0,9313
Interaktions p-Wert									0,4804
ECOG-Status zu Baseline - DEU									
0	131	21 (16,0)	NE [NE; NE]	131	18 (13,7)	NE [NE; NE]	1,09	[0,58; 2,07]	0,7913
1	131	21 (16,0)	NE [NE; NE]	134	11 (8,2)	NE [NE; NE]	1,95	[0,96; 4,20]	0,0650
Interaktions p-Wert									0,2318

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.4 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.4 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.4 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.5 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	3 (8,3)	NE [NE; NE]	37	5 (13,5)	NE [NE; NE]	0,62	[0,13; 2,52]	0,5034
Stadium III	226	26 (11,5)	NE [NE; NE]	228	19 (8,3)	NE [NE; NE]	1,31	[0,73; 2,40]	0,3678
Interaktions p-Wert									0,3337
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	4 (11,8)	NE [NE; NE]	0,51	[0,07; 2,62]	0,4249
Stadium III	229	27 (11,8)	NE [NE; NE]	231	20 (8,7)	NE [NE; NE]	1,29	[0,73; 2,34]	0,3790
Interaktions p-Wert									0,2952
Erhalt einer PCI (IVRS) - DEU									
Ja	141	17 (12,1)	NE [NE; NE]	143	14 (9,8)	NE [NE; NE]	1,14	[0,56; 2,35]	0,7153
Nein	121	12 (9,9)	NE [NE; NE]	122	10 (8,2)	NE [NE; NE]	1,20	[0,52; 2,85]	0,6633
Interaktions p-Wert									0,9224
Erhalt einer PCI (eCRF) - DEU									
Ja	141	17 (12,1)	NE [NE; NE]	142	13 (9,2)	NE [NE; NE]	1,22	[0,60; 2,57]	0,5847
Nein	121	12 (9,9)	NE [NE; NE]	123	11 (8,9)	NE [NE; NE]	1,10	[0,48; 2,54]	0,8172
Interaktions p-Wert									0,8514
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	9 (11,4)	NE [NE; NE]	80	7 (8,8)	NE [NE; NE]	1,30	[0,48; 3,63]	0,6032
>=28 Tage	152	17 (11,2)	NE [NE; NE]	153	17 (11,1)	NE [NE; NE]	0,95	[0,48; 1,87]	0,8760
Interaktions p-Wert									0,6051
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	9 (8,7)	NE [NE; NE]	103	11 (10,7)	NE [NE; NE]	0,79	[0,32; 1,90]	0,5925

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.5 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	15 (15,3)	NE [NE; NE]	76	7 (9,2)	NE [NE; NE]	1,54	[0,65; 4,03]	0,3374
>=84 Tage	45	5 (11,1)	NE [NE; NE]	62	6 (9,7)	NE [NE; NE]	1,23	[0,35; 4,07]	0,7371
Interaktions p-Wert									0,5662
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	10 (11,2)	NE [NE; NE]	88	6 (6,8)	NE [NE; NE]	1,51	[0,56; 4,45]	0,4162
Cisplatin	173	19 (11,0)	NE [NE; NE]	177	18 (10,2)	NE [NE; NE]	1,06	[0,55; 2,03]	0,8697
Interaktions p-Wert									0,5537
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	23 (11,9)	NE [NE; NE]	186	14 (7,5)	NE [NE; NE]	1,53	[0,80; 3,04]	0,2052
Zweimal täglich	69	6 (8,7)	NE [NE; NE]	79	10 (12,7)	NE [NE; NE]	0,64	[0,22; 1,72]	0,3778
Interaktions p-Wert									0,1514
Bestes Ansprechen auf cCRT - DEU									
CR	31	8 (25,8)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	4,84	[1,21; 32,06]	0,0241*
PR	189	17 (9,0)	NE [NE; NE]	199	21 (10,6)	NE [NE; NE]	0,82	[0,43; 1,55]	0,5395
SD	42	4 (9,5)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	2,61	[0,39; 50,96]	0,3513
Interaktions p-Wert									0,0541
Geschlecht - DEU									
Männer	178	16 (9,0)	NE [NE; NE]	187	13 (7,0)	NE [NE; NE]	1,27	[0,61; 2,68]	0,5236
Frauen	84	13 (15,5)	NE [NE; NE]	78	11 (14,1)	NE [NE; NE]	0,98	[0,44; 2,24]	0,9627
Interaktions p-Wert									0,6440
Altersgruppe - DEU									
<65 Jahre	159	18 (11,3)	NE [NE; NE]	161	15 (9,3)	NE [NE; NE]	1,14	[0,57; 2,29]	0,7114
>=65 Jahre	103	11 (10,7)	NE [NE; NE]	104	9 (8,7)	NE [NE; NE]	1,22	[0,50; 3,02]	0,6593
Interaktions p-Wert									0,9044

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.5 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	7 (9,0)	NE [NE; NE]	72	6 (8,3)	NE [NE; NE]	1,00	[0,33; 3,10]	0,9985
TC or IC >=1%	84	8 (9,5)	NE [NE; NE]	98	11 (11,2)	NE [NE; NE]	0,77	[0,30; 1,91]	0,5777
Interaktions p-Wert									0,7230
Raucherstatus - DEU									
Raucher	239	28 (11,7)	NE [NE; NE]	239	22 (9,2)	NE [NE; NE]	1,23	[0,71; 2,17]	0,4660
Nichtraucher	23	1 (4,3)	NE [NE; NE]	26	2 (7,7)	NE [NE; NE]	0,49	[0,02; 5,08]	0,5444
Interaktions p-Wert									0,4462
Abstammung - DEU									
Weiß	128	16 (12,5)	NE [NE; NE]	137	14 (10,2)	NE [NE; NE]	1,20	[0,58; 2,49]	0,6163
Schwarz/Afroamerikanisch	1	1 (100)	8,4 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	12 (9,2)	NE [NE; NE]	121	10 (8,3)	NE [NE; NE]	1,05	[0,45; 2,49]	0,9064
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,8137
Geographische Region - DEU									
Asien	129	12 (9,3)	NE [NE; NE]	120	10 (8,3)	NE [NE; NE]	1,05	[0,45; 2,49]	0,9082
Europa	94	9 (9,6)	NE [NE; NE]	112	8 (7,1)	NE [NE; NE]	1,24	[0,47; 3,31]	0,6567
Nordamerika	39	8 (20,5)	NE [NE; NE]	33	6 (18,2)	NE [NE; NE]	1,24	[0,43; 3,76]	0,6939
Interaktions p-Wert									0,9578
ECOG-Status zu Baseline - DEU									
0	131	15 (11,5)	NE [NE; NE]	131	12 (9,2)	NE [NE; NE]	1,17	[0,55; 2,55]	0,6826
1	131	14 (10,7)	NE [NE; NE]	134	12 (9,0)	NE [NE; NE]	1,16	[0,54; 2,56]	0,6991
Interaktions p-Wert									0,9911

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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Table 5.5.6 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.6 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.6 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.7 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Nieren
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.7 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Nieren
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	0	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	1 (1,2)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.7 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Ereignisse der Nieren
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.8 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	2 (5,4)	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	4 (1,8)	NE [NE; NE]	228	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	4 (1,7)	NE [NE; NE]	231	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	3 (2,1)	NE [NE; NE]	NC	[NC]	NC
Nein	121	4 (3,3)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	3 (2,1)	NE [NE; NE]	NC	[NC]	NC
Nein	121	4 (3,3)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	1 (3,2)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	3 (2,0)	NE [NE; NE]	153	3 (2,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	1 (6,3)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.8 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	3 (3,1)	NE [NE; NE]	76	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	1 (1,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	3 (3,4)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	2 (1,1)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	4 (2,1)	NE [NE; NE]	186	2 (1,1)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	3 (1,6)	NE [NE; NE]	199	3 (1,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	2 (1,1)	NE [NE; NE]	187	3 (1,6)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	2 (2,4)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	4 (3,9)	NE [NE; NE]	104	2 (1,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.8 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	2 (2,6)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	3 (1,3)	NE [NE; NE]	239	3 (1,3)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	1 (4,3)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	2 (1,6)	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	2 (1,5)	NE [NE; NE]	121	2 (1,7)	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	2 (1,6)	NE [NE; NE]	120	2 (1,7)	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	1 (2,6)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	2 (1,5)	NE [NE; NE]	NC	[NC]	NC
1	131	3 (2,3)	NE [NE; NE]	134	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.9 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hyperthyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	2 (5,6)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	2,14	[0,20; 45,96]	0,5223
Stadium III	226	25 (11,1)	NE [NE; NE]	228	3 (1,3)	NE [NE; NE]	8,70	[3,05; 36,54]	<0,0001*
Interaktions p-Wert									0,3358
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	2,12	[0,20; 45,56]	0,5272
Stadium III	229	25 (10,9)	NE [NE; NE]	231	3 (1,3)	NE [NE; NE]	8,71	[3,06; 36,60]	<0,0001*
Interaktions p-Wert									0,3326
Erhalt einer PCI (IVRS) - DEU									
Ja	141	13 (9,2)	NE [NE; NE]	143	3 (2,1)	NE [NE; NE]	4,51	[1,45; 19,68]	0,0075*
Nein	121	14 (11,6)	NE [NE; NE]	122	1 (0,8)	NE [NE; NE]	14,76	[2,97;267,43]	0,0002*
Interaktions p-Wert									0,2999
Erhalt einer PCI (eCRF) - DEU									
Ja	141	13 (9,2)	NE [NE; NE]	142	3 (2,1)	NE [NE; NE]	4,48	[1,44; 19,53]	0,0078*
Nein	121	14 (11,6)	NE [NE; NE]	123	1 (0,8)	NE [NE; NE]	14,90	[3,00;270,02]	0,0002*
Interaktions p-Wert									0,2925
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	8 (25,8)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	9,00	[1,65;166,97]	0,0080*
>=14 bis <28 Tage	79	7 (8,9)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	12 (7,9)	NE [NE; NE]	153	3 (2,0)	NE [NE; NE]	4,11	[1,31; 18,03]	0,0141*
Interaktions p-Wert									0,5106
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	4 (25,0)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	12 (11,7)	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	12,43	[2,45;226,30]	0,0008*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.9 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hyperthyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	7 (7,1)	NE [NE; NE]	76	2 (2,6)	NE [NE; NE]	2,69	[0,65; 18,04]	0,1823
>=84 Tage	45	4 (8,9)	NE [NE; NE]	62	1 (1,6)	NE [NE; NE]	6,14	[0,91;120,14]	0,0636
Interaktions p-Wert									0,4824
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	8 (9,0)	NE [NE; NE]	88	2 (2,3)	NE [NE; NE]	3,93	[0,98; 26,04]	0,0529
Cisplatin	173	19 (11,0)	NE [NE; NE]	177	2 (1,1)	NE [NE; NE]	10,28	[2,99; 64,54]	<0,0001*
Interaktions p-Wert									0,3803
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	20 (10,4)	NE [NE; NE]	186	3 (1,6)	NE [NE; NE]	6,61	[2,27; 28,07]	0,0002*
Zweimal täglich	69	7 (10,1)	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	8,40	[1,49;156,93]	0,0126*
Interaktions p-Wert									0,8447
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	1,10	[0,04; 27,75]	0,9472
PR	189	22 (11,6)	NE [NE; NE]	199	3 (1,5)	NE [NE; NE]	8,13	[2,82; 34,36]	<0,0001*
SD	42	4 (9,5)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2135
Geschlecht - DEU									
Männer	178	19 (10,7)	NE [NE; NE]	187	3 (1,6)	NE [NE; NE]	6,81	[2,32; 28,99]	0,0002*
Frauen	84	8 (9,5)	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	7,90	[1,45;146,48]	0,0135*
Interaktions p-Wert									0,9034
Altersgruppe - DEU									
<65 Jahre	159	19 (11,9)	NE [NE; NE]	161	2 (1,2)	NE [NE; NE]	10,10	[2,93; 63,39]	<0,0001*
>=65 Jahre	103	8 (7,8)	NE [NE; NE]	104	2 (1,9)	NE [NE; NE]	4,10	[1,03; 27,14]	0,0455*
Interaktions p-Wert									0,4097

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.9 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hyperthyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	10 (12,8)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	9,59	[1,84;175,98]	0,0042*
TC or IC >=1%	84	6 (7,1)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	3,51	[0,81; 23,96]	0,0959
Interaktions p-Wert									0,4363
Raucherstatus - DEU									
Raucher	239	24 (10,0)	NE [NE; NE]	239	4 (1,7)	NE [NE; NE]	6,20	[2,40; 21,12]	<0,0001*
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	13 (10,2)	NE [NE; NE]	137	3 (2,2)	NE [NE; NE]	4,79	[1,54; 20,88]	0,0053*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	14 (10,7)	NE [NE; NE]	121	1 (0,8)	NE [NE; NE]	13,59	[2,73;246,34]	0,0003*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,3638
Geographische Region - DEU									
Asien	129	14 (10,9)	NE [NE; NE]	120	1 (0,8)	NE [NE; NE]	13,65	[2,75;247,41]	0,0003*
Europa	94	10 (10,6)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	3,99	[1,22; 17,81]	0,0208*
Nordamerika	39	3 (7,7)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,2856
ECOG-Status zu Baseline - DEU									
0	131	10 (7,6)	NE [NE; NE]	131	4 (3,1)	NE [NE; NE]	2,50	[0,84; 9,11]	0,1033
1	131	17 (13,0)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.10 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	2 (0,9)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	2 (0,9)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	2 (1,3)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.10 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	2 (1,0)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	0	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	2 (2,4)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	2 (1,3)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.10 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	2 (0,8)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	1 (100)	3,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	1 (2,6)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	2 (1,5)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.11 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypothyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	3 (8,3)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	3,49	[0,45; 70,48]	0,2418
Stadium III	226	39 (17,3)	NE [NE; NE]	228	9 (3,9)	NE [NE; NE]	4,49	[2,28; 9,89]	<0,0001*
Interaktions p-Wert									0,8375
TNM Status (eCRF) - DEU									
Stadium I/II	33	3 (9,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	3,39	[0,43; 68,57]	0,2528
Stadium III	229	39 (17,0)	NE [NE; NE]	231	9 (3,9)	NE [NE; NE]	4,52	[2,29; 9,94]	<0,0001*
Interaktions p-Wert									0,8172
Erhalt einer PCI (IVRS) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	143	5 (3,5)	NE [NE; NE]	5,19	[2,15; 15,42]	0,0001*
Nein	121	18 (14,9)	NE [NE; NE]	122	5 (4,1)	NE [NE; NE]	3,67	[1,47; 11,13]	0,0045*
Interaktions p-Wert									0,6246
Erhalt einer PCI (eCRF) - DEU									
Ja	141	24 (17,0)	NE [NE; NE]	142	4 (2,8)	NE [NE; NE]	6,48	[2,50; 22,04]	<0,0001*
Nein	121	18 (14,9)	NE [NE; NE]	123	6 (4,9)	NE [NE; NE]	3,07	[1,29; 8,46]	0,0105*
Interaktions p-Wert									0,2920
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	4 (12,9)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	11 (13,9)	NE [NE; NE]	80	6 (7,5)	NE [NE; NE]	1,89	[0,72; 5,48]	0,2002
>=28 Tage	152	27 (17,8)	NE [NE; NE]	153	4 (2,6)	NE [NE; NE]	7,22	[2,82; 24,42]	<0,0001*
Interaktions p-Wert									0,0652
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	1 (4,2)	NE [NE; NE]	2,38	[0,23; 51,23]	0,4638
>=28 bis <56 Tage	103	15 (14,6)	NE [NE; NE]	103	3 (2,9)	NE [NE; NE]	5,07	[1,67; 21,89]	0,0029*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.11 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypothyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	18 (18,4)	NE [NE; NE]	76	4 (5,3)	NE [NE; NE]	3,69	[1,38; 12,77]	0,0079*
>=84 Tage	45	7 (15,6)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	5,57	[1,35; 37,39]	0,0166*
Interaktions p-Wert									0,9255
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	14 (15,7)	NE [NE; NE]	88	6 (6,8)	NE [NE; NE]	2,19	[0,88; 6,18]	0,0947
Cisplatin	173	28 (16,2)	NE [NE; NE]	177	4 (2,3)	NE [NE; NE]	7,85	[3,08; 26,50]	<0,0001*
Interaktions p-Wert									0,0738
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	28 (14,5)	NE [NE; NE]	186	7 (3,8)	NE [NE; NE]	3,87	[1,79; 9,62]	0,0003*
Zweimal täglich	69	14 (20,3)	NE [NE; NE]	79	3 (3,8)	NE [NE; NE]	6,09	[1,99; 26,41]	0,0009*
Interaktions p-Wert									0,5451
Bestes Ansprechen auf cCRT - DEU									
CR	31	3 (9,7)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	1,63	[0,27; 12,36]	0,5894
PR	189	30 (15,9)	NE [NE; NE]	199	7 (3,5)	NE [NE; NE]	4,82	[2,25; 11,95]	<0,0001*
SD	42	9 (21,4)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	6,65	[1,25;122,56]	0,0230*
Interaktions p-Wert									0,5237
Geschlecht - DEU									
Männer	178	23 (12,9)	NE [NE; NE]	187	4 (2,1)	NE [NE; NE]	6,11	[2,35; 20,85]	<0,0001*
Frauen	84	19 (22,6)	NE [NE; NE]	78	6 (7,7)	NE [NE; NE]	3,28	[1,38; 9,00]	0,0060*
Interaktions p-Wert									0,3790
Altersgruppe - DEU									
<65 Jahre	159	29 (18,2)	NE [NE; NE]	161	5 (3,1)	NE [NE; NE]	6,17	[2,61; 18,15]	<0,0001*
>=65 Jahre	103	13 (12,6)	NE [NE; NE]	104	5 (4,8)	NE [NE; NE]	2,70	[1,02; 8,42]	0,0456*
Interaktions p-Wert									0,2499

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.11 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Hypothyreose Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	13 (16,7)	NE [NE; NE]	72	2 (2,8)	NE [NE; NE]	6,31	[1,74; 40,36]	0,0032*
TC or IC >=1%	84	13 (15,5)	NE [NE; NE]	98	4 (4,1)	NE [NE; NE]	3,85	[1,36; 13,68]	0,0098*
Interaktions p-Wert									0,5976
Raucherstatus - DEU									
Raucher	239	35 (14,6)	NE [NE; NE]	239	9 (3,8)	NE [NE; NE]	3,99	[2,00; 8,83]	<0,0001*
Nichtraucher	23	7 (30,4)	NE [NE; NE]	26	1 (3,8)	NE [NE; NE]	9,86	[1,75;184,25]	0,0067*
Interaktions p-Wert									0,3854
Abstammung - DEU									
Weiß	128	21 (16,4)	NE [NE; NE]	137	6 (4,4)	NE [NE; NE]	3,93	[1,68; 10,71]	0,0011*
Schwarz/Afroamerikanisch	1	1 (100)	2,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	20 (15,3)	NE [NE; NE]	121	4 (3,3)	NE [NE; NE]	4,88	[1,85; 16,77]	0,0008*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7623
Geographische Region - DEU									
Asien	129	20 (15,5)	NE [NE; NE]	120	3 (2,5)	NE [NE; NE]	6,52	[2,24; 27,69]	0,0002*
Europa	94	15 (16,0)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	5,97	[1,97; 25,79]	0,0009*
Nordamerika	39	7 (17,9)	NE [NE; NE]	33	4 (12,1)	NE [NE; NE]	1,65	[0,50; 6,29]	0,4184
Interaktions p-Wert									0,2375
ECOG-Status zu Baseline - DEU									
0	131	18 (13,7)	NE [NE; NE]	131	4 (3,1)	NE [NE; NE]	4,50	[1,68; 15,57]	0,0019*
1	131	24 (18,3)	NE [NE; NE]	134	6 (4,5)	NE [NE; NE]	4,45	[1,94; 12,01]	0,0002*
Interaktions p-Wert									0,9876

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.12 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.12 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.5.12 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.13 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	3 (1,3)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	3 (1,3)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	2 (1,3)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.5.13 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	3 (1,7)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	3 (1,6)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	3 (1,6)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	2 (2,4)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	2 (1,3)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.13 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	2 (0,8)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	1 (4,3)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	1 (100)	3,7 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	1 (2,6)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	2 (1,5)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.14 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	5 (13,9)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	5,45	[0,88;104,31]	0,0708
Stadium III	226	38 (16,8)	NE [NE; NE]	228	16 (7,0)	NE [NE; NE]	2,40	[1,37; 4,43]	0,0021*
Interaktions p-Wert									0,4388
TNM Status (eCRF) - DEU									
Stadium I/II	33	5 (15,2)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	5,39	[0,87;103,20]	0,0728
Stadium III	229	38 (16,6)	NE [NE; NE]	231	16 (6,9)	NE [NE; NE]	2,41	[1,37; 4,45]	0,0020*
Interaktions p-Wert									0,4467
Erhalt einer PCI (IVRS) - DEU									
Ja	141	22 (15,6)	NE [NE; NE]	143	13 (9,1)	NE [NE; NE]	1,71	[0,87; 3,49]	0,1180
Nein	121	21 (17,4)	NE [NE; NE]	122	4 (3,3)	NE [NE; NE]	5,45	[2,07; 18,67]	0,0003*
Interaktions p-Wert									0,0605
Erhalt einer PCI (eCRF) - DEU									
Ja	141	22 (15,6)	NE [NE; NE]	142	13 (9,2)	NE [NE; NE]	1,70	[0,87; 3,46]	0,1243
Nein	121	21 (17,4)	NE [NE; NE]	123	4 (3,3)	NE [NE; NE]	5,51	[2,10; 18,87]	0,0002*
Interaktions p-Wert									0,0561
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	2 (6,3)	NE [NE; NE]	1,53	[0,25; 11,62]	0,6376
>=14 bis <28 Tage	79	15 (19,0)	NE [NE; NE]	80	6 (7,5)	NE [NE; NE]	2,58	[1,05; 7,24]	0,0385*
>=28 Tage	152	25 (16,4)	NE [NE; NE]	153	9 (5,9)	NE [NE; NE]	2,83	[1,37; 6,41]	0,0043*
Interaktions p-Wert									0,8310
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	3 (18,8)	NE [NE; NE]	24	3 (12,5)	NE [NE; NE]	1,41	[0,26; 7,63]	0,6746
>=28 bis <56 Tage	103	19 (18,4)	NE [NE; NE]	103	8 (7,8)	NE [NE; NE]	2,38	[1,08; 5,76]	0,0316*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.14 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	14 (14,3)	NE [NE; NE]	76	4 (5,3)	NE [NE; NE]	2,63	[0,94; 9,27]	0,0658
>=84 Tage	45	7 (15,6)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	5,51	[1,33; 36,95]	0,0173*
Interaktions p-Wert									0,6622
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	13 (14,6)	NE [NE; NE]	88	7 (8,0)	NE [NE; NE]	1,72	[0,70; 4,57]	0,2385
Cisplatin	173	30 (17,3)	NE [NE; NE]	177	10 (5,6)	NE [NE; NE]	3,24	[1,64; 6,97]	0,0005*
Interaktions p-Wert									0,2908
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	30 (15,5)	NE [NE; NE]	186	11 (5,9)	NE [NE; NE]	2,62	[1,35; 5,47]	0,0037*
Zweimal täglich	69	13 (18,8)	NE [NE; NE]	79	6 (7,6)	NE [NE; NE]	2,59	[1,03; 7,38]	0,0440*
Interaktions p-Wert									0,9866
Bestes Ansprechen auf cCRT - DEU									
CR	31	5 (16,1)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	2,84	[0,61; 19,82]	0,1873
PR	189	33 (17,5)	NE [NE; NE]	199	14 (7,0)	NE [NE; NE]	2,56	[1,40; 4,94]	0,0020*
SD	42	5 (11,9)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	3,51	[0,57; 67,22]	0,1946
Interaktions p-Wert									0,9567
Geschlecht - DEU									
Männer	178	30 (16,9)	NE [NE; NE]	187	11 (5,9)	NE [NE; NE]	2,91	[1,50; 6,08]	0,0012*
Frauen	84	13 (15,5)	NE [NE; NE]	78	6 (7,7)	NE [NE; NE]	2,02	[0,80; 5,75]	0,1409
Interaktions p-Wert									0,5486
Altersgruppe - DEU									
<65 Jahre	159	29 (18,2)	NE [NE; NE]	161	10 (6,2)	NE [NE; NE]	2,97	[1,50; 6,42]	0,0015*
>=65 Jahre	103	14 (13,6)	NE [NE; NE]	104	7 (6,7)	NE [NE; NE]	2,04	[0,85; 5,38]	0,1123
Interaktions p-Wert									0,5259

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.5.14 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	17 (21,8)	NE [NE; NE]	72	6 (8,3)	NE [NE; NE]	2,64	[1,10; 7,32]	0,0296*
TC or IC >=1%	84	15 (17,9)	NE [NE; NE]	98	9 (9,2)	NE [NE; NE]	1,94	[0,86; 4,62]	0,1095
Interaktions p-Wert									0,6253
Raucherstatus - DEU									
Raucher	239	37 (15,5)	NE [NE; NE]	239	13 (5,4)	NE [NE; NE]	2,89	[1,58; 5,65]	0,0004*
Nichtraucher	23	6 (26,1)	NE [NE; NE]	26	4 (15,4)	NE [NE; NE]	1,64	[0,47; 6,42]	0,4385
Interaktions p-Wert									0,4380
Abstammung - DEU									
Weiß	128	18 (14,1)	NE [NE; NE]	137	4 (2,9)	NE [NE; NE]	4,98	[1,86; 17,25]	0,0009*
Schwarz/Afroamerikanisch	1	1 (100)	12,8 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	24 (18,3)	NE [NE; NE]	121	12 (9,9)	NE [NE; NE]	1,86	[0,95; 3,85]	0,0707
Andere	2	0	NE [NE; NE]	4	1 (25,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,1187
Geographische Region - DEU									
Asien	129	24 (18,6)	NE [NE; NE]	120	12 (10,0)	NE [NE; NE]	1,87	[0,95; 3,87]	0,0692
Europa	94	12 (12,8)	NE [NE; NE]	112	4 (3,6)	NE [NE; NE]	3,55	[1,24; 12,70]	0,0175*
Nordamerika	39	7 (17,9)	NE [NE; NE]	33	1 (3,0)	NE [NE; NE]	6,39	[1,14;119,52]	0,0333*
Interaktions p-Wert									0,3657
ECOG-Status zu Baseline - DEU									
0	131	13 (9,9)	NE [NE; NE]	131	6 (4,6)	NE [NE; NE]	2,14	[0,85; 6,09]	0,1099
1	131	30 (22,9)	NE [NE; NE]	134	11 (8,2)	NE [NE; NE]	2,89	[1,49; 6,04]	0,0013*
Interaktions p-Wert									0,6217

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.15 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Thyroiditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	3 (1,3)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	3 (1,3)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	2 (1,3)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.5.15 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Thyroiditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	2 (1,2)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	0	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	3 (4,3)	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	2 (1,1)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	2 (1,1)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	1 (1,2)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	2 (1,3)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.5.15 ADRIATIC: Summary of subgroup analysis of time to first UESI GT: Thyroiditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	3 (1,3)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	2 (1,6)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	1 (2,6)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	2 (1,5)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Anhang 4-G8.5.3: UESI jeglichen Schweregrades - gesamt und nach GT - Subgruppenanalysen Kaplan-Meier-Plot

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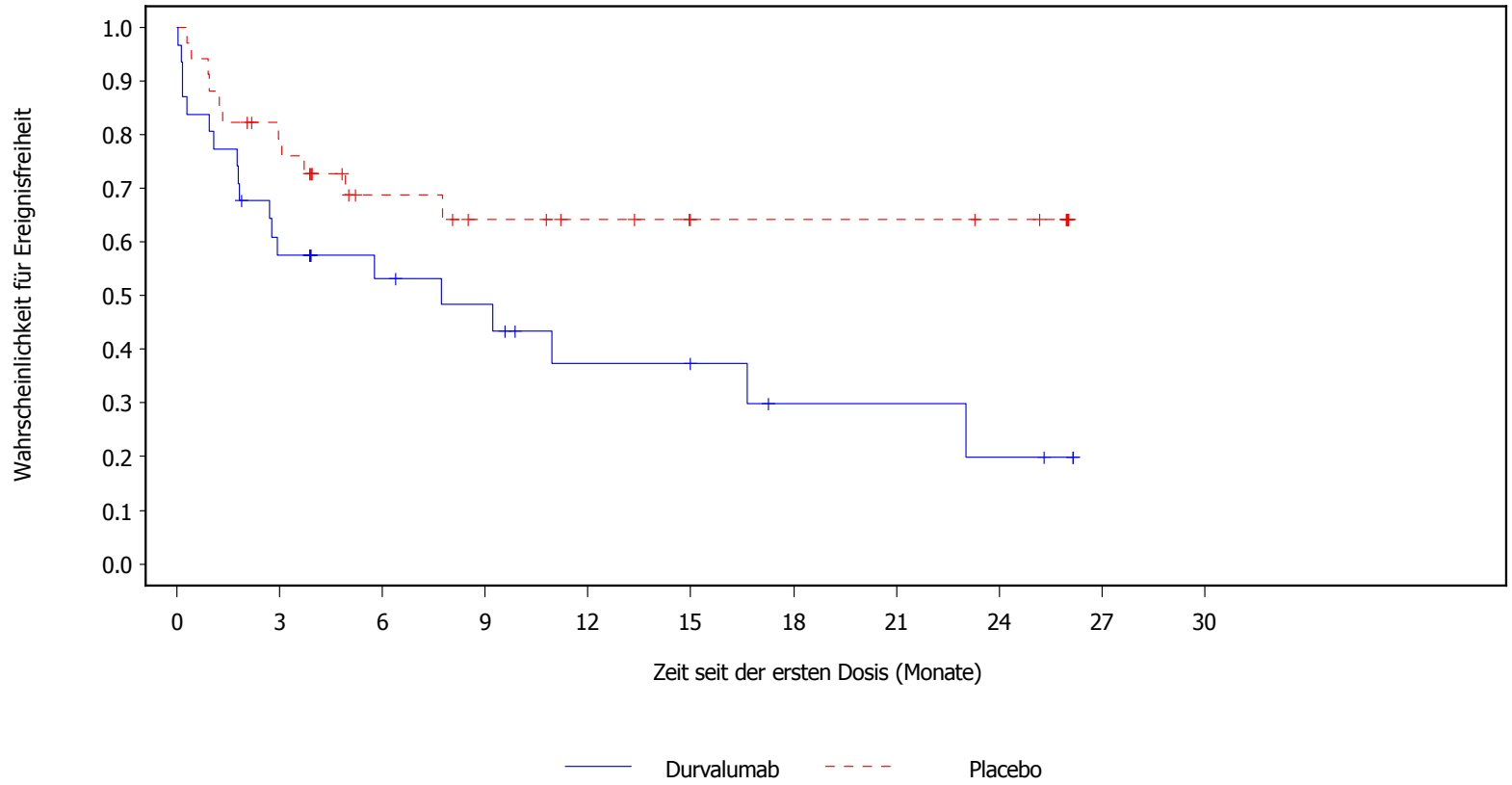
Figure 5.12.1 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Bestes Ansprechen auf cCRT - DEU=CR
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

31	17	12	10	6	5	3	3	2	0	0	Durvalumab
34	25	15	12	10	7	7	7	6	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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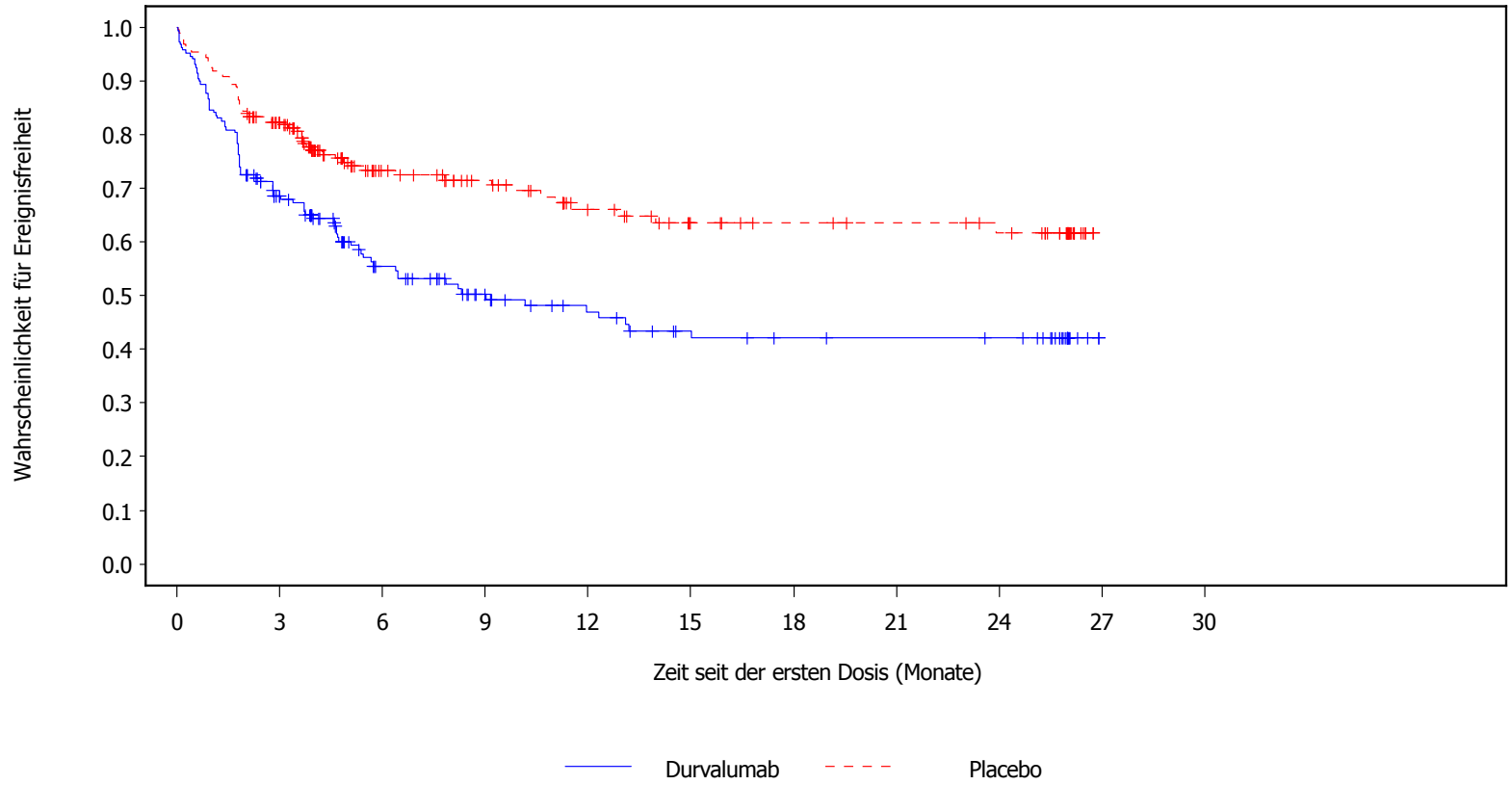
Figure 5.12.2 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Bestes Ansprechen auf cCRT - DEU=PR
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

189	116	69	50	40	32	29	28	27	0	0	Durvalumab
199	148	85	71	53	42	38	36	33	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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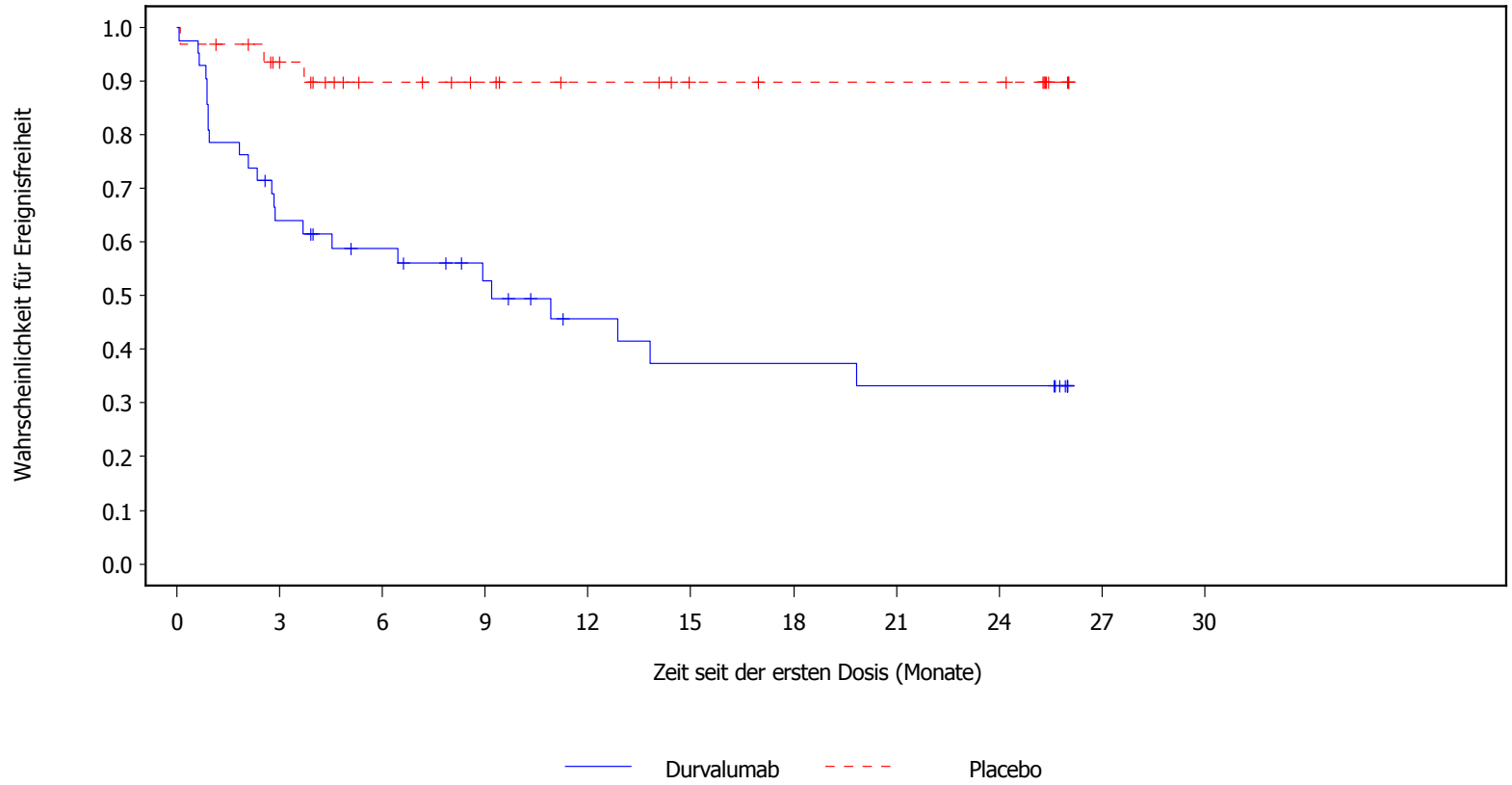
Figure 5.12.3 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Bestes Ansprechen auf cCRT - DEU=SD
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

42	26	21	16	11	9	9	8	8	0	0	Durvalumab
32	25	18	15	12	9	8	8	8	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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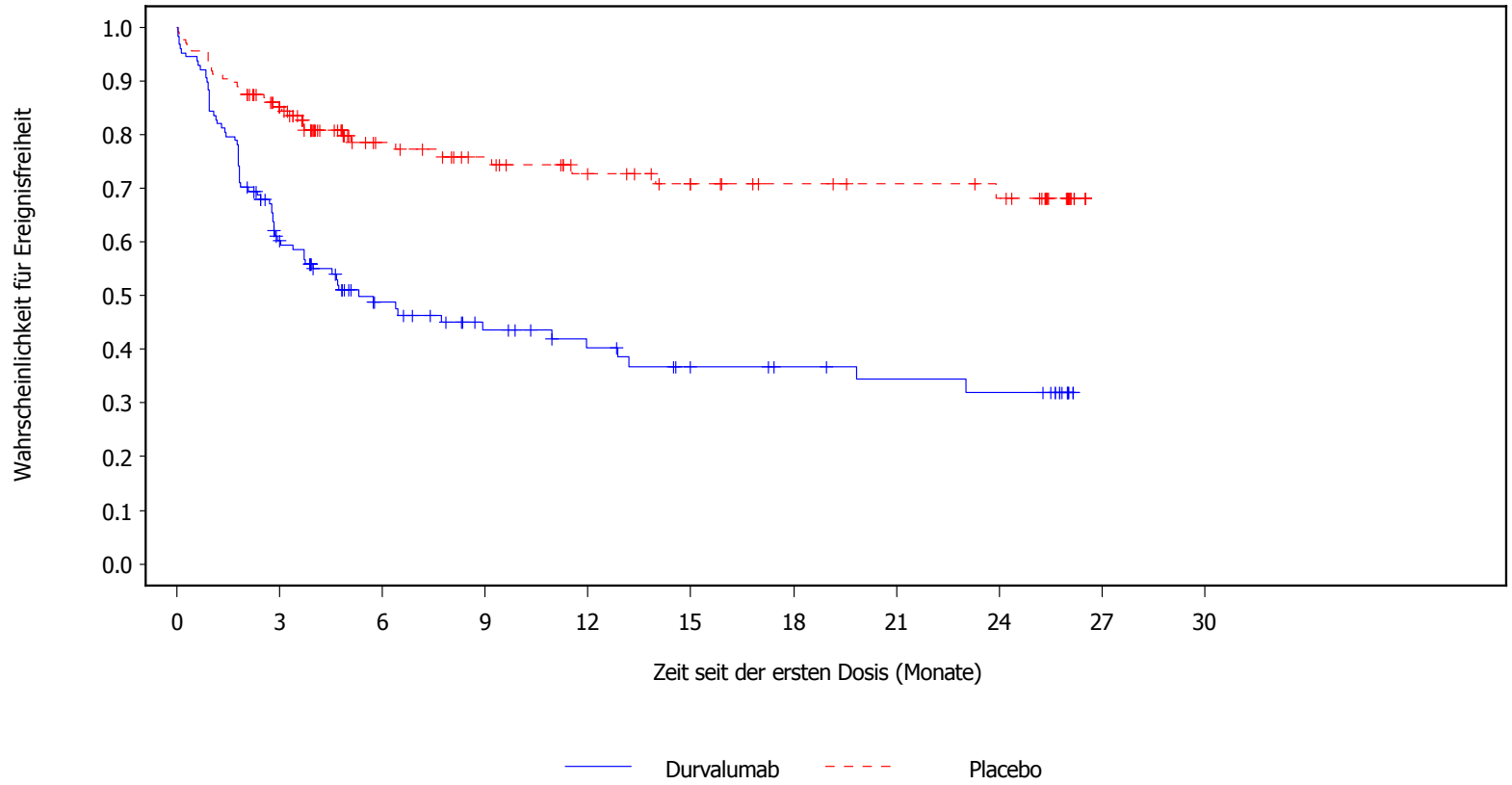
Figure 5.12.4 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Abstammung - DEU=Weiß
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

128	69	41	30	24	18	16	14	13	0	0	Durvalumab
137	103	61	52	41	34	30	28	26	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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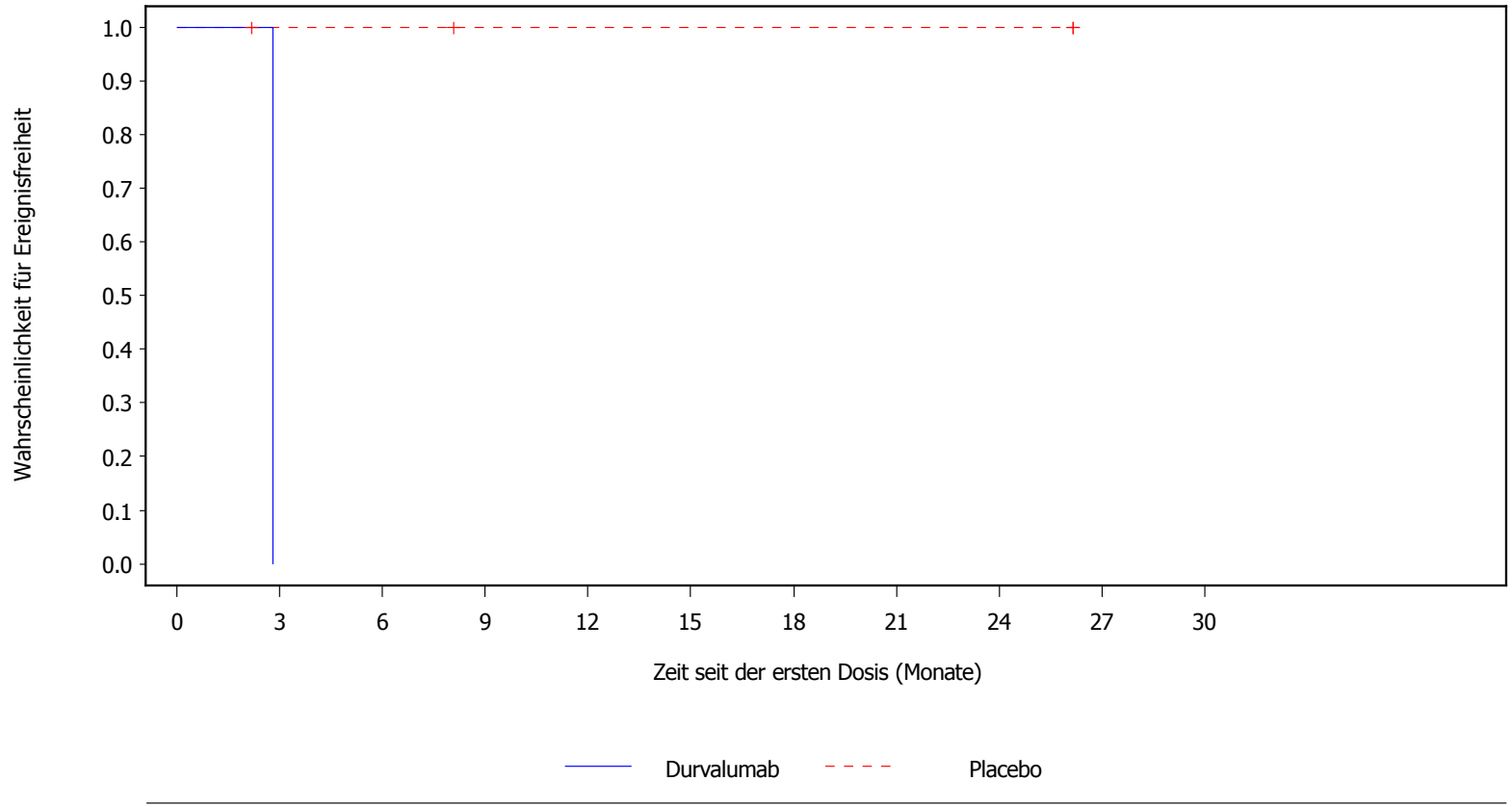
Figure 5.12.5 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Abstammung - DEU=Schwarz/Afroamerikanisch
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

1	0	0	0	0	0	0	0	0	0	Durvalumab
3	2	2	1	1	1	1	1	1	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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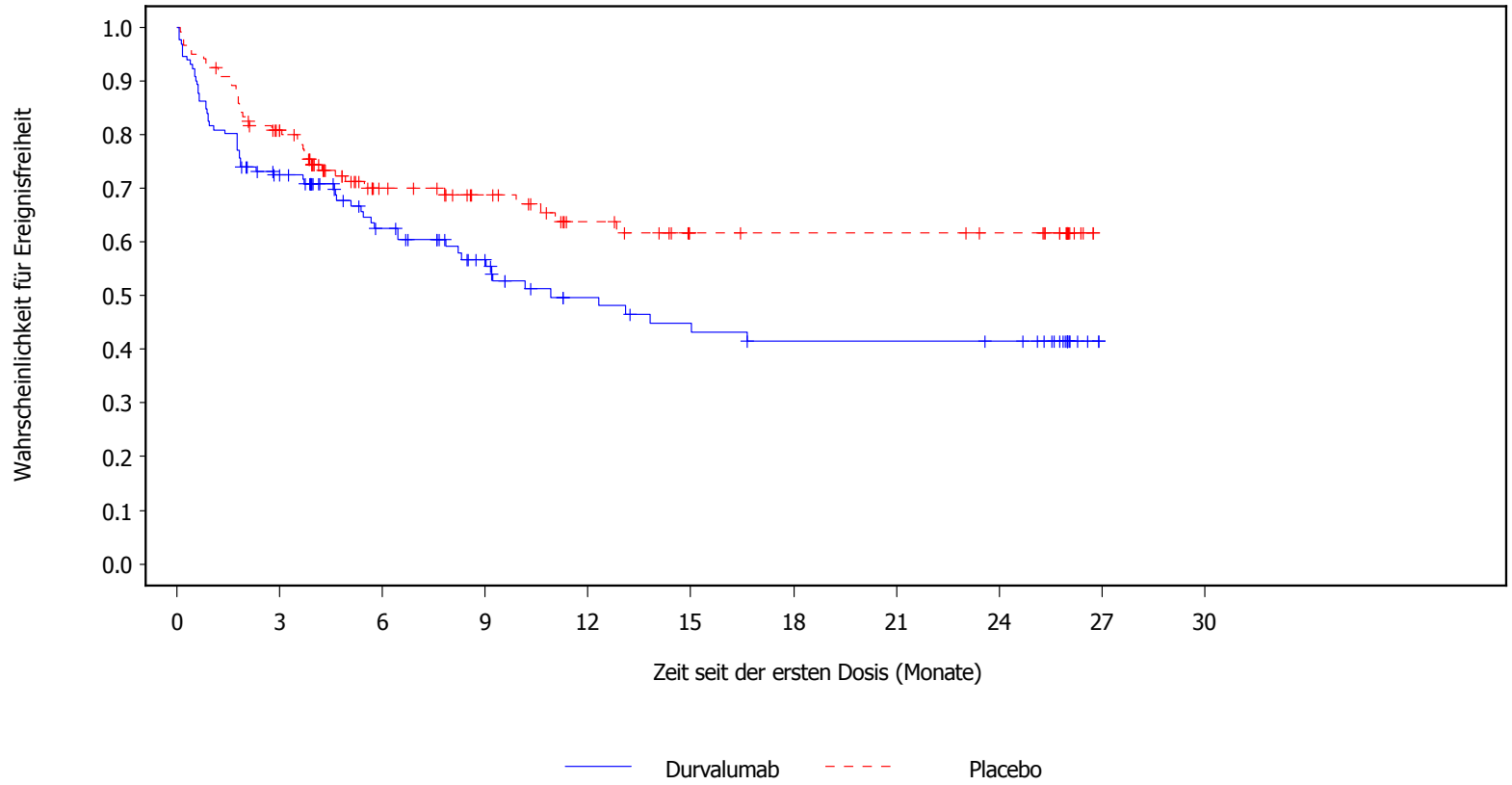
Figure 5.12.6 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Abstammung - DEU=Asiatisch
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

131	88	59	44	31	27	24	24	23	0	0	Durvalumab
121	90	55	45	33	23	22	22	20	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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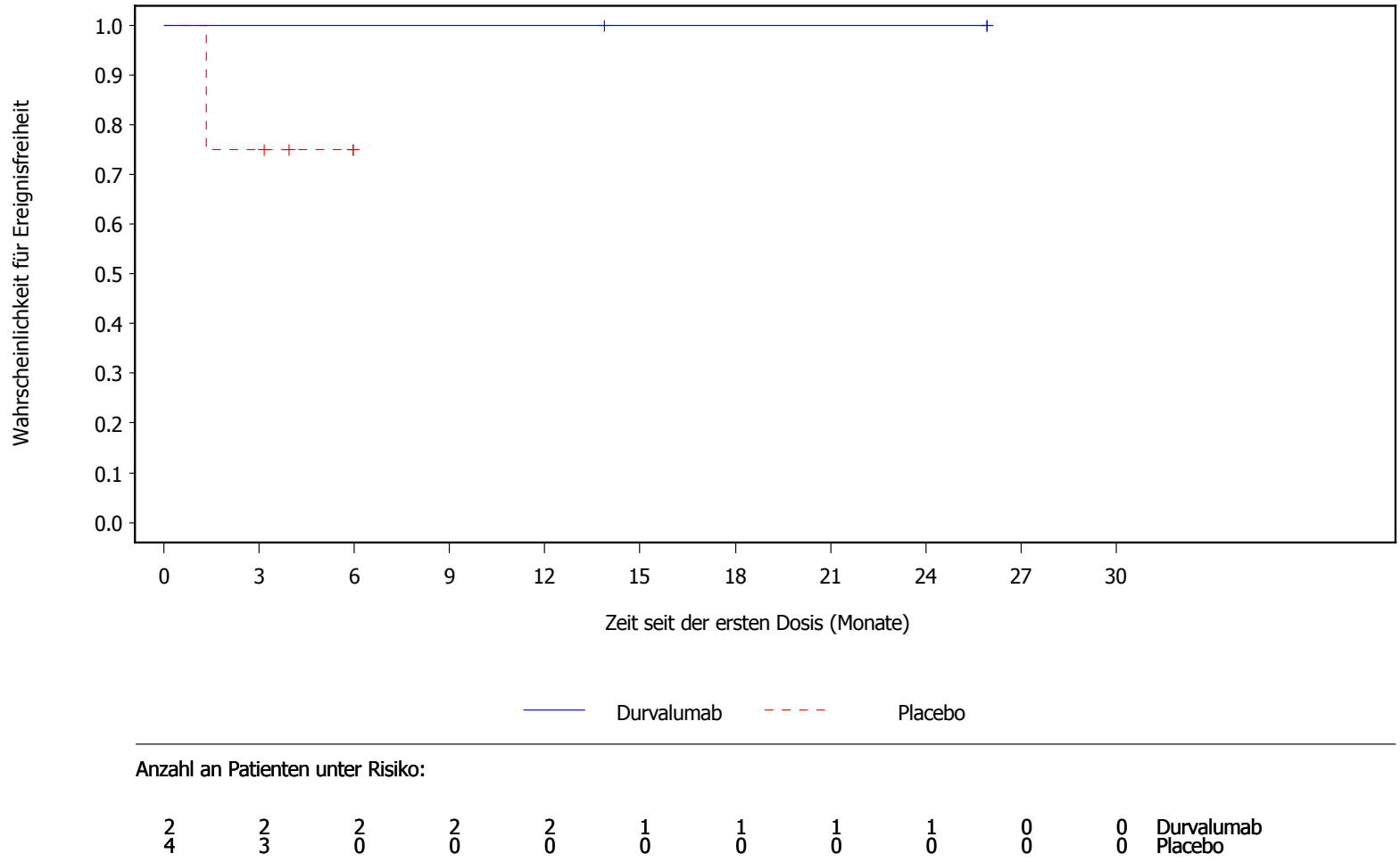
Figure 5.12.7 ADRIATIC Subgroup Analysis: Kaplan-Meier plot of UESI for Abstammung - DEU=Andere
Safety Analysis Set, DCO 15JAN2024



Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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Anhang 4-G8.6: Schwere UESI (CTCAE Grad >= 3) - gesamt und nach GT

Table 2.2.6 ADRIATIC: Summary of analysis of time to first adverse event of special interest with max. CTCAE grade 3 or higher (total, and by grouped term)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UESI mit CTCAE Grad >=3	262	16 (6,1)	NE [NE; NE]	265	4 (1,5)	NE [NE; NE]	3,86	[1,41; 13,47]	0,0093*
UESI G>=3 GT: Andere seltene/verschiedene	262	0	NE [NE; NE]	265	1 (0,4)	NE [NE; NE]	NC	NC	0,3201
UESI G>=3 GT: Dermatitis/Hautausschlag	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3747
UESI G>=3 GT: Diabetes mellitus Typ 1	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3699
UESI G>=3 GT: Durchfall/Colitis	262	5 (1,9)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,0326*
UESI G>=3 GT: Ereignisse der Bauchspeicheldrüse	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3295
UESI G>=3 GT: Hepatische Ereignisse	262	1 (0,4)	NE [NE; NE]	265	1 (0,4)	NE [NE; NE]	0,88	[0,03; 22,18]	0,9266
UESI G>=3 GT: Hypophysitis	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3173
UESI G>=3 GT: Nebenniereninsuffizienz	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3146

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.

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Nutzenbewertung nach AMNOG

Table 2.2.6 ADRIATIC: Summary of analysis of time to first adverse event of special interest with max. CTCAE grade 3 or higher (total, and by grouped term)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
UESI G>=3 GT: Pneumonitis	262	6 (2,3)	NE [NE; NE]	265	2 (0,8)	NE [NE; NE]	2,99	[0,69; 20,42]	0,1584

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1af
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Anhang 4-G8.6.1: Schwere UESI (CTCAE Grad >= 3) - gesamt und nach GT - Kaplan-Meier-Plot

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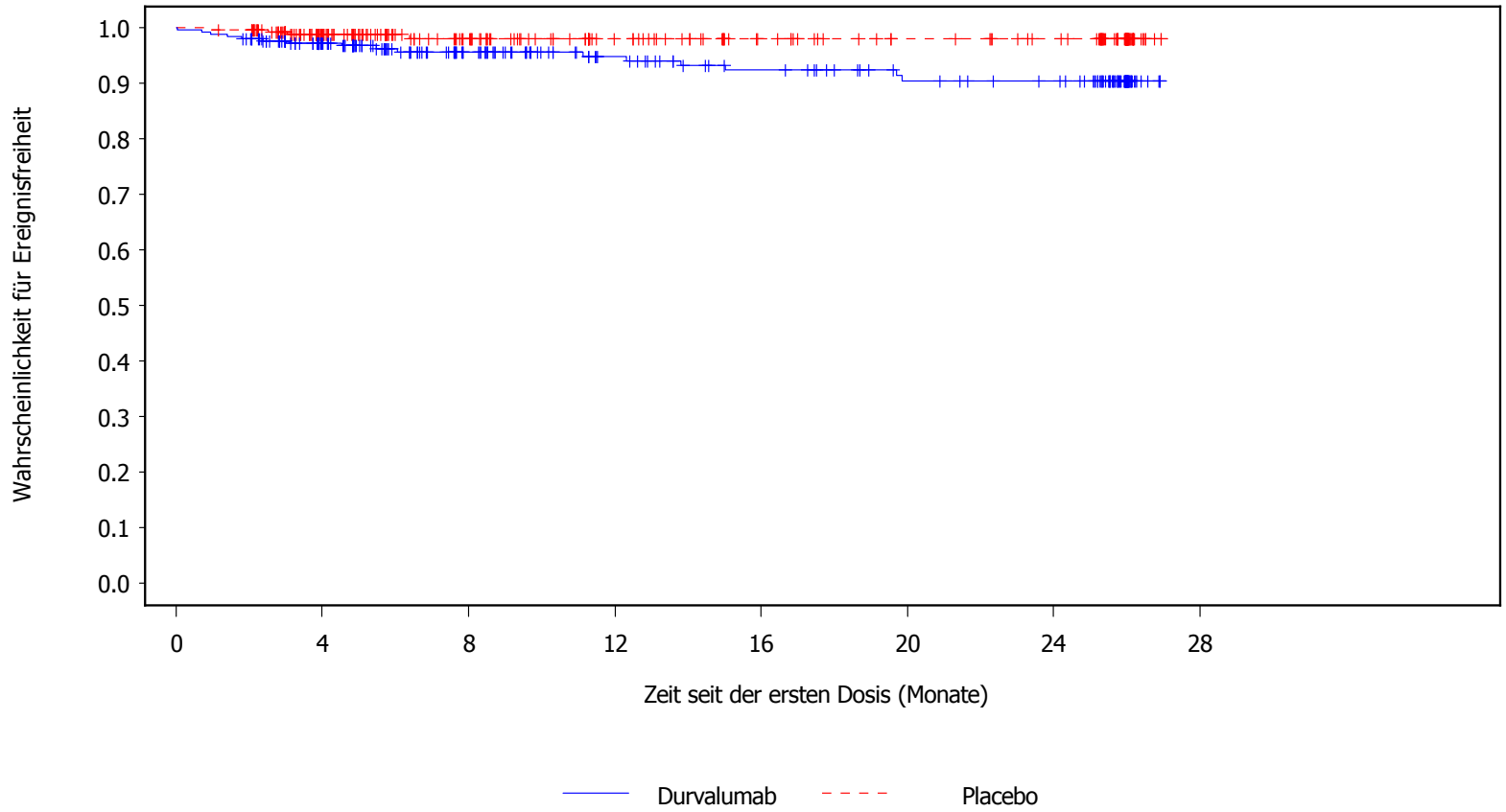
Figure 2.3.89 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	206	153	118	103	91	86	0	Durvalumab
265	202	146	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdk 05JUN2025:07:

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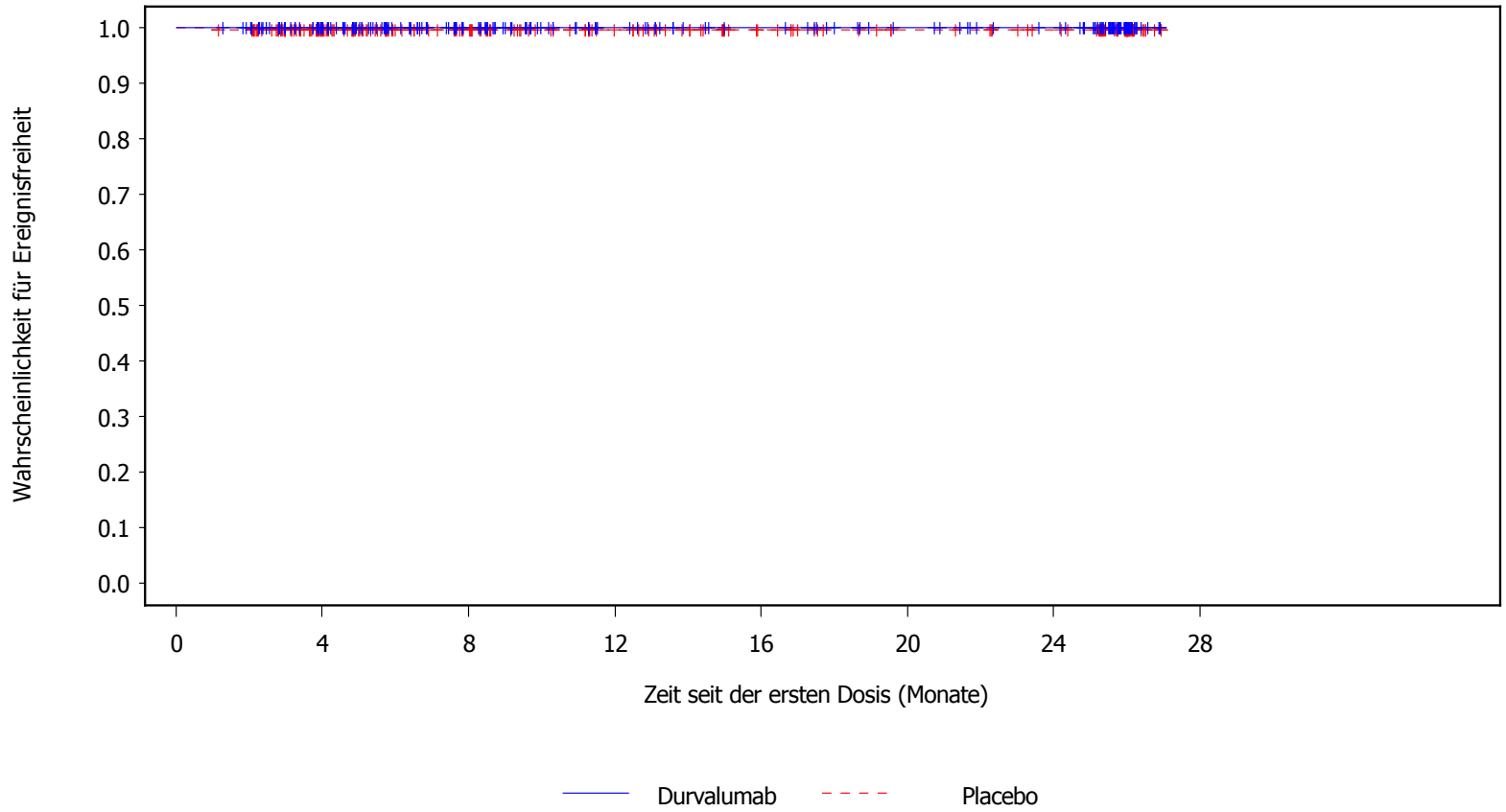
Figure 2.3.90 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	109	99	91	0	Durvalumab
265	204	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdl 05JUN2025:07:

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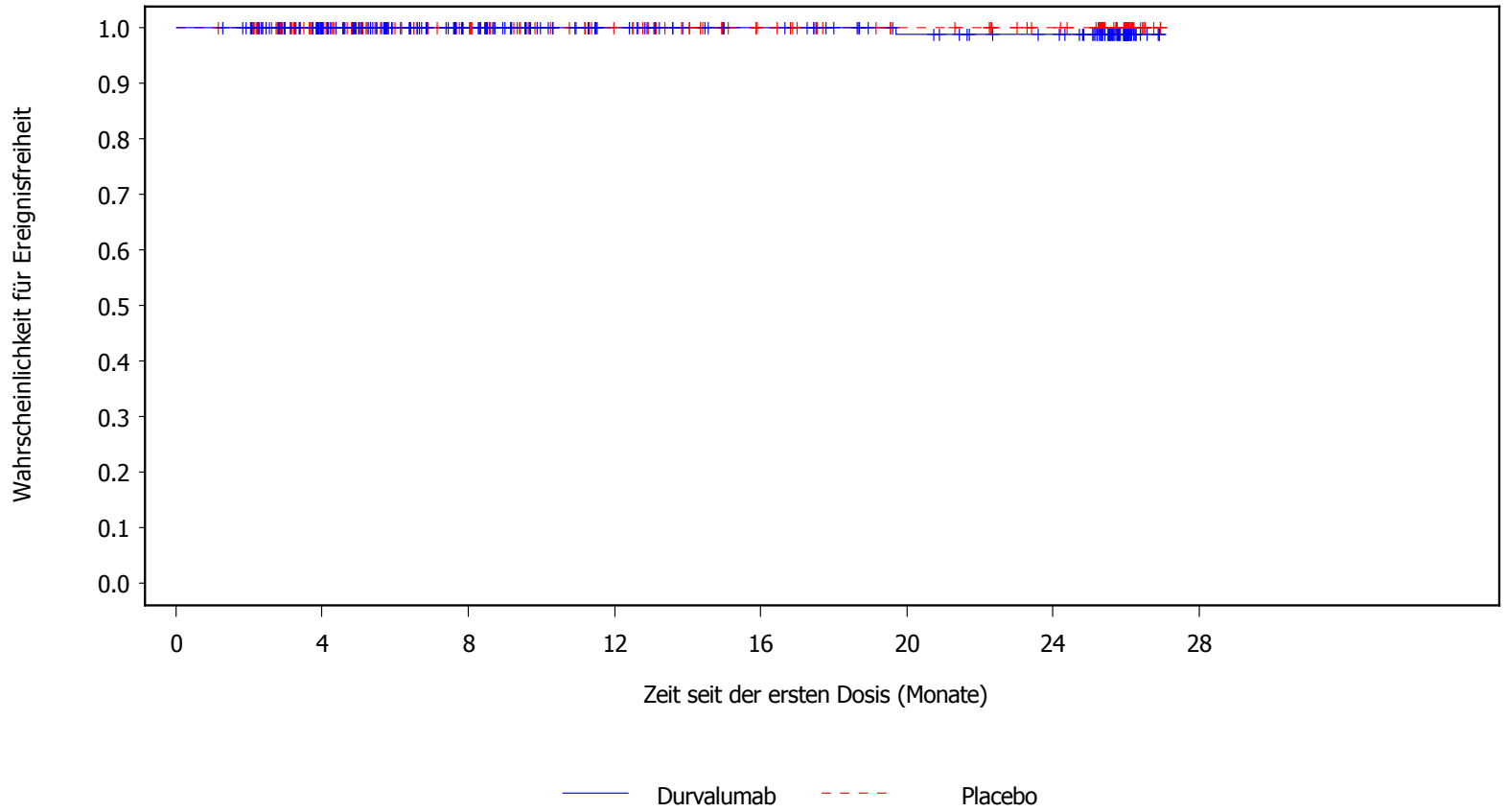
Figure 2.3.91 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	109	98	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdm 05JUN2025:07:

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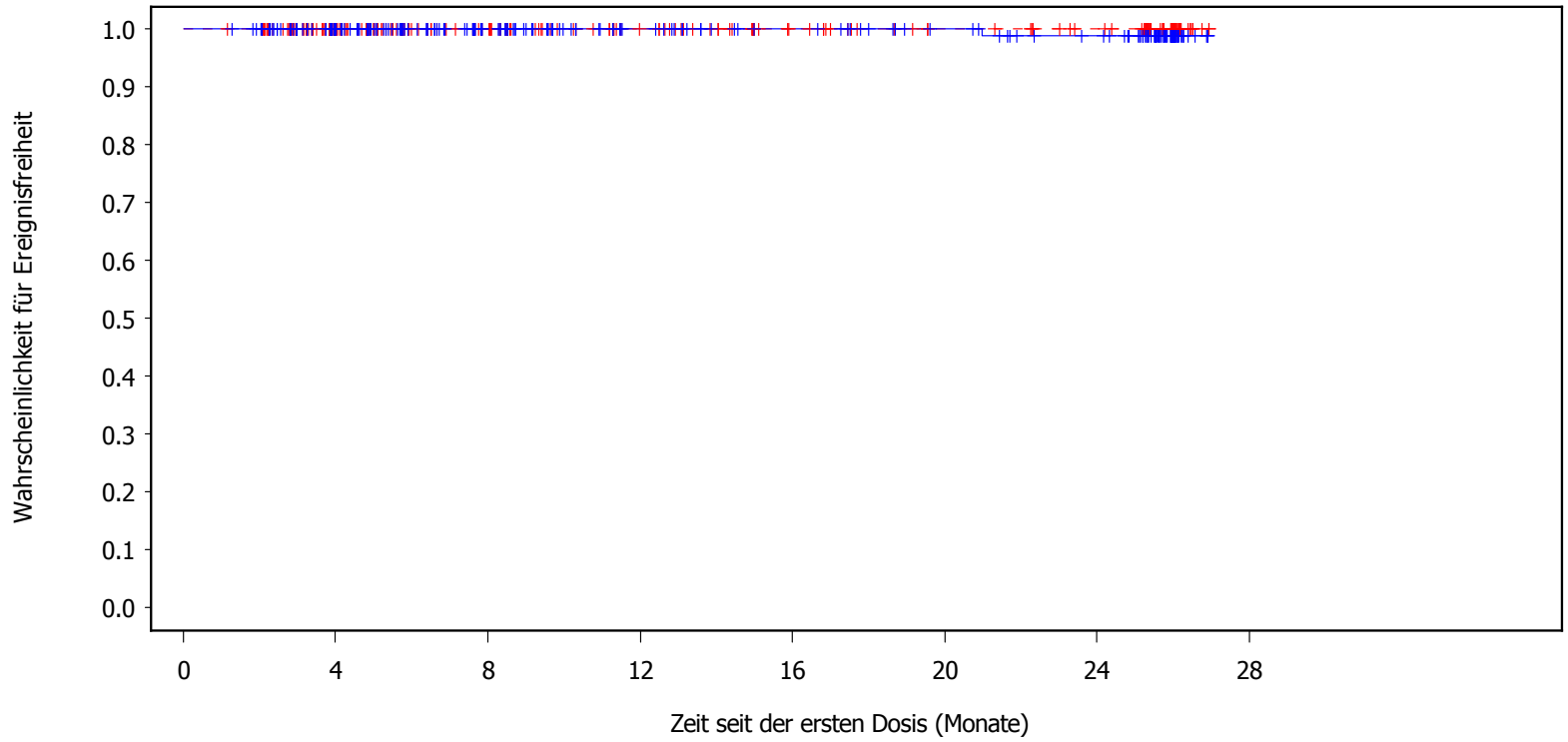
Figure 2.3.92 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	109	99	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdn 05JUN2025:07:

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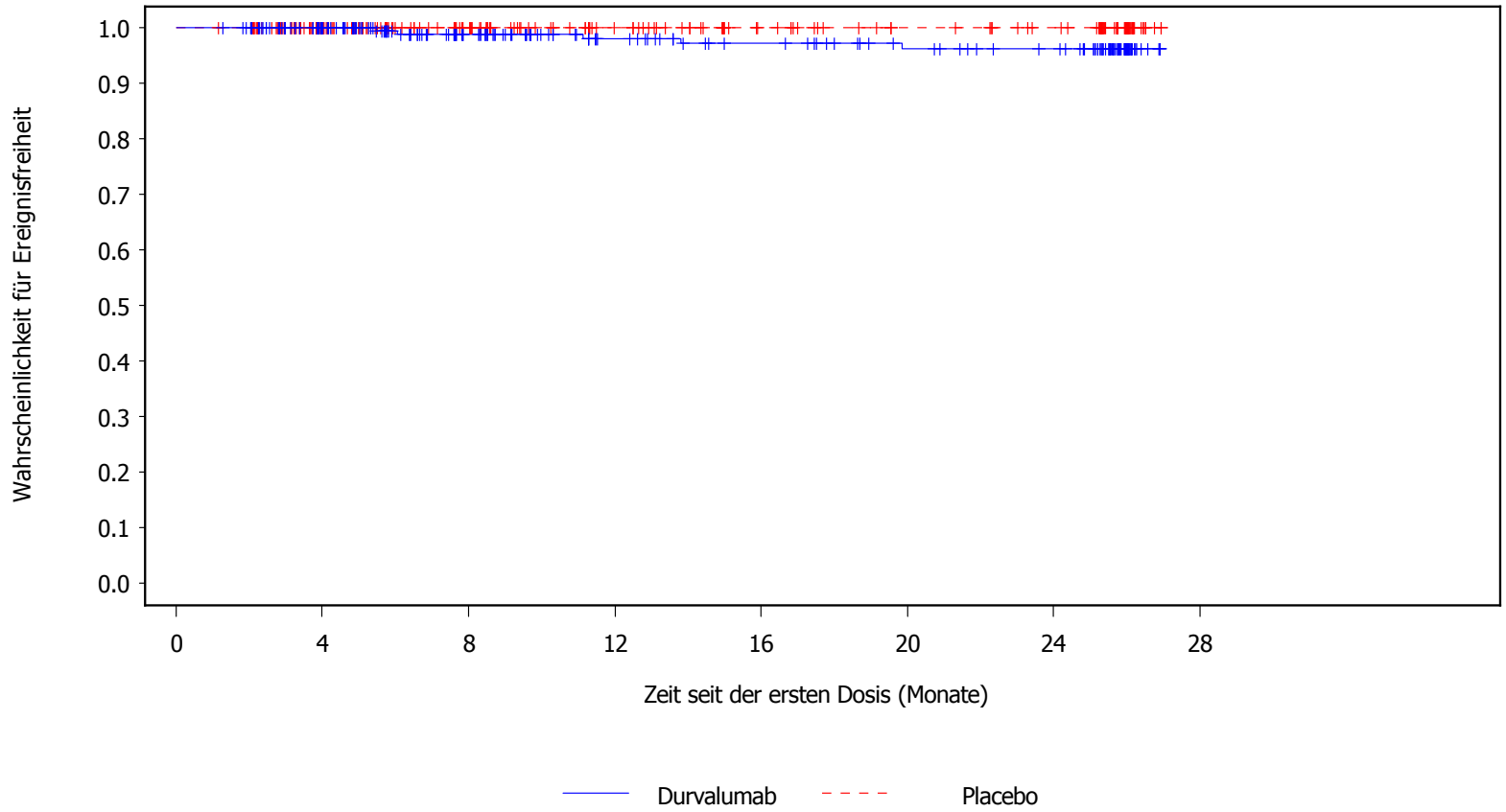
Figure 2.3.93 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

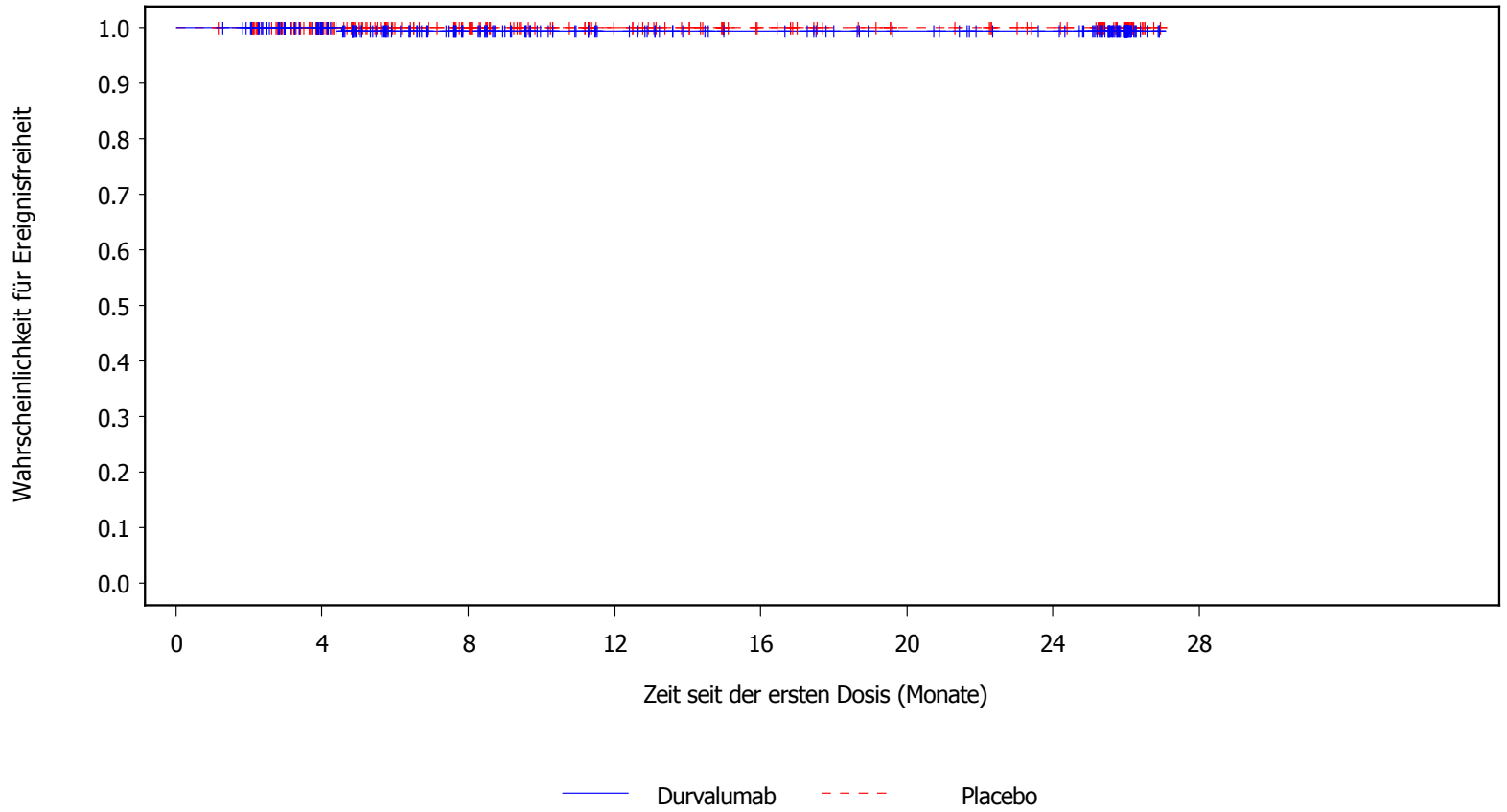


Anzahl an Patienten unter Risiko:

262	209	154	119	106	95	88	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdo 05JUN2025:07:

Figure 2.3.94 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdp 05JUN2025:07:

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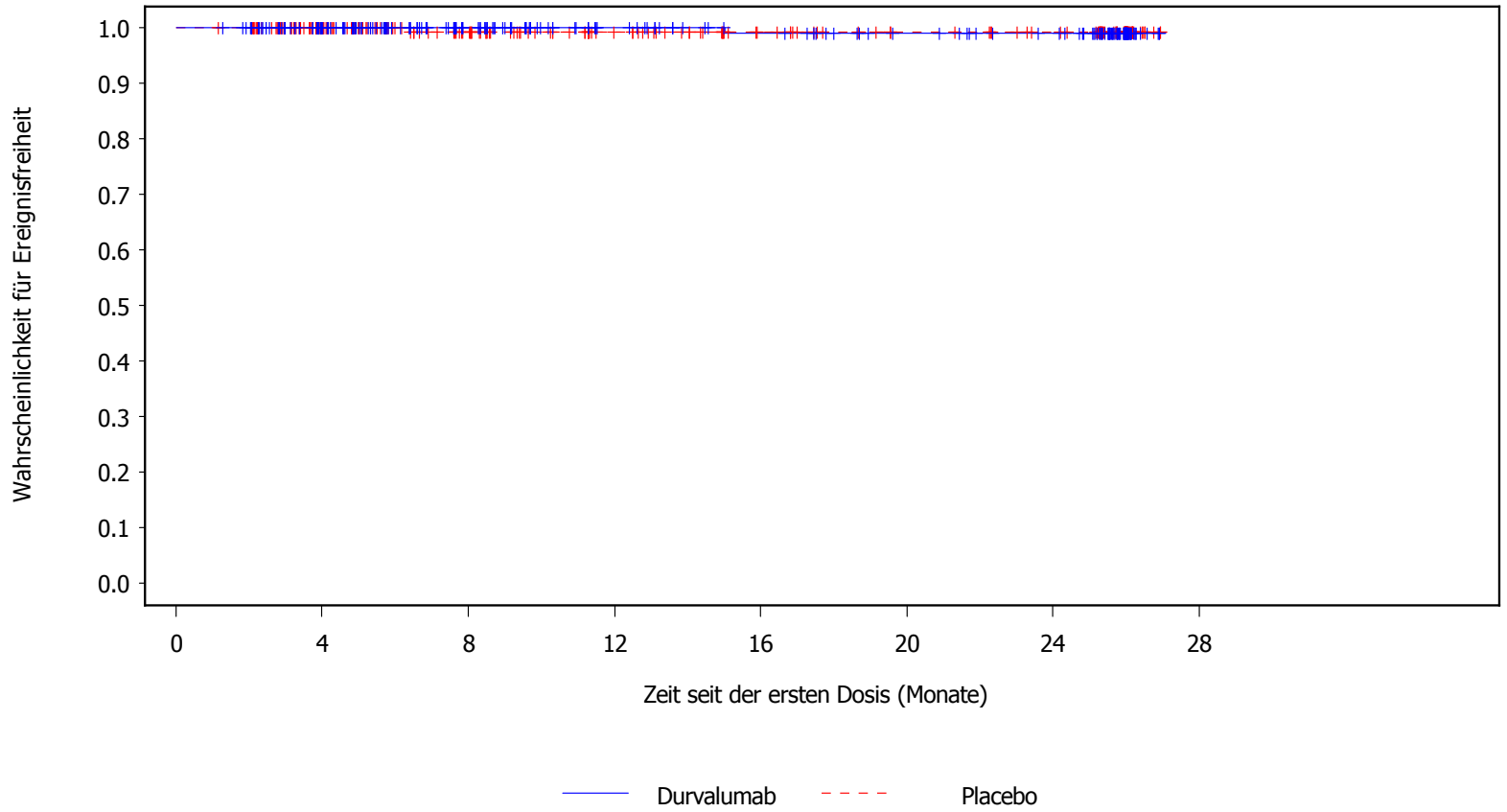
Figure 2.3.95 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

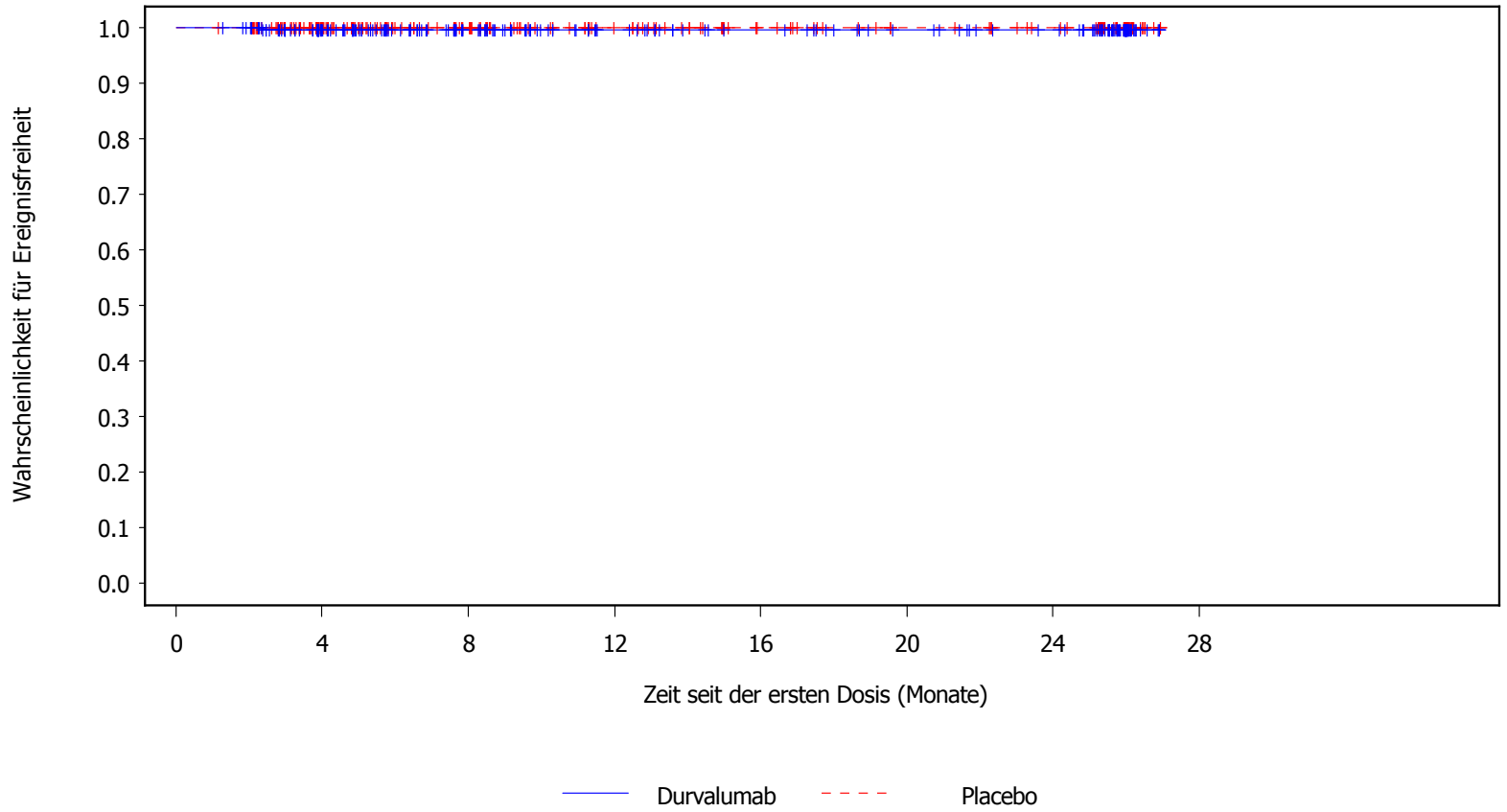


Anzahl an Patienten unter Risiko:

262	209	156	122	108	98	91	0	Durvalumab
265	205	146	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdq 05JUN2025:07:

Figure 2.3.96 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

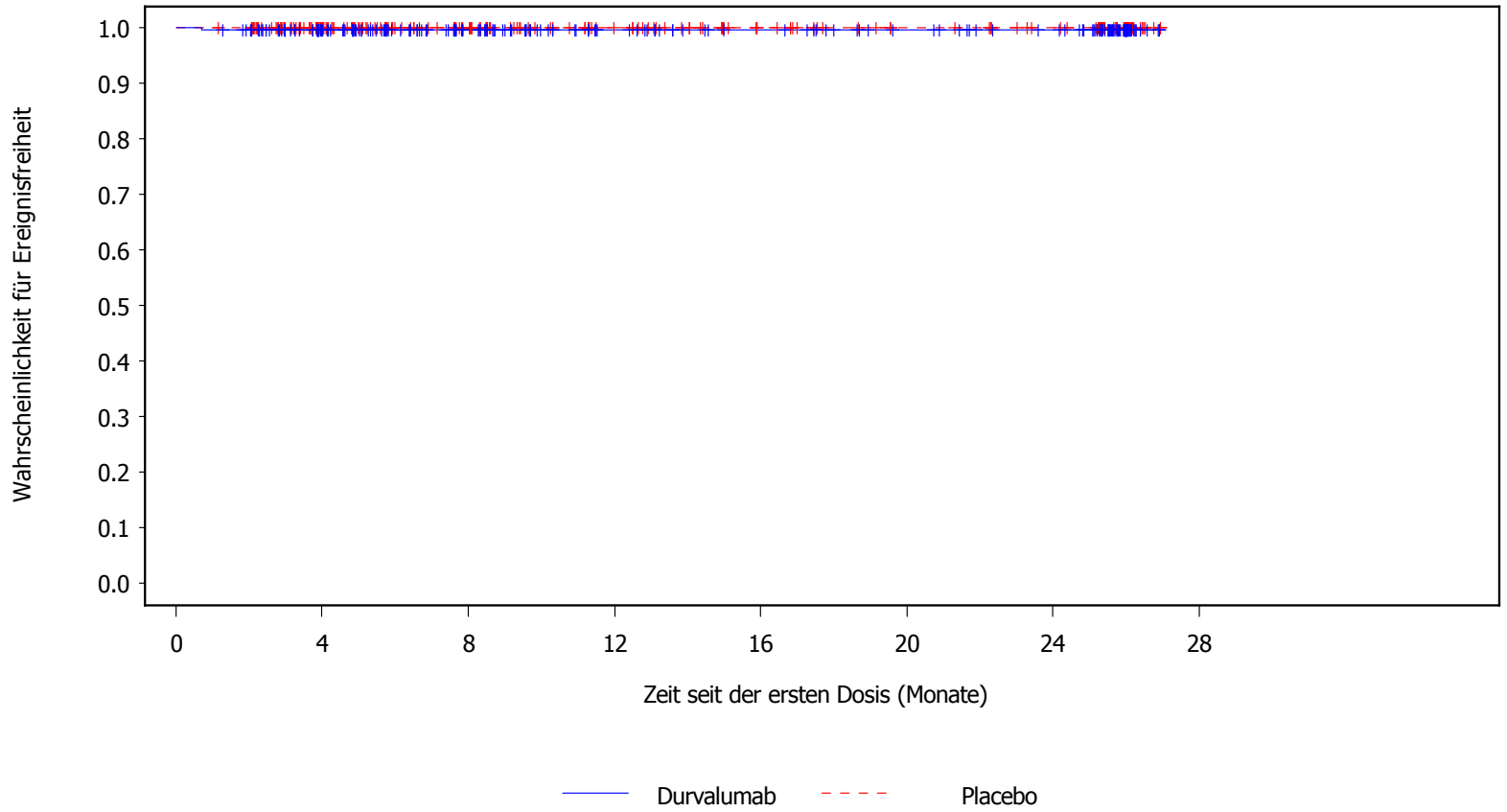


Anzahl an Patienten unter Risiko:

262	208	155	121	108	98	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdr 05JUN2025:07:

Figure 2.3.97 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

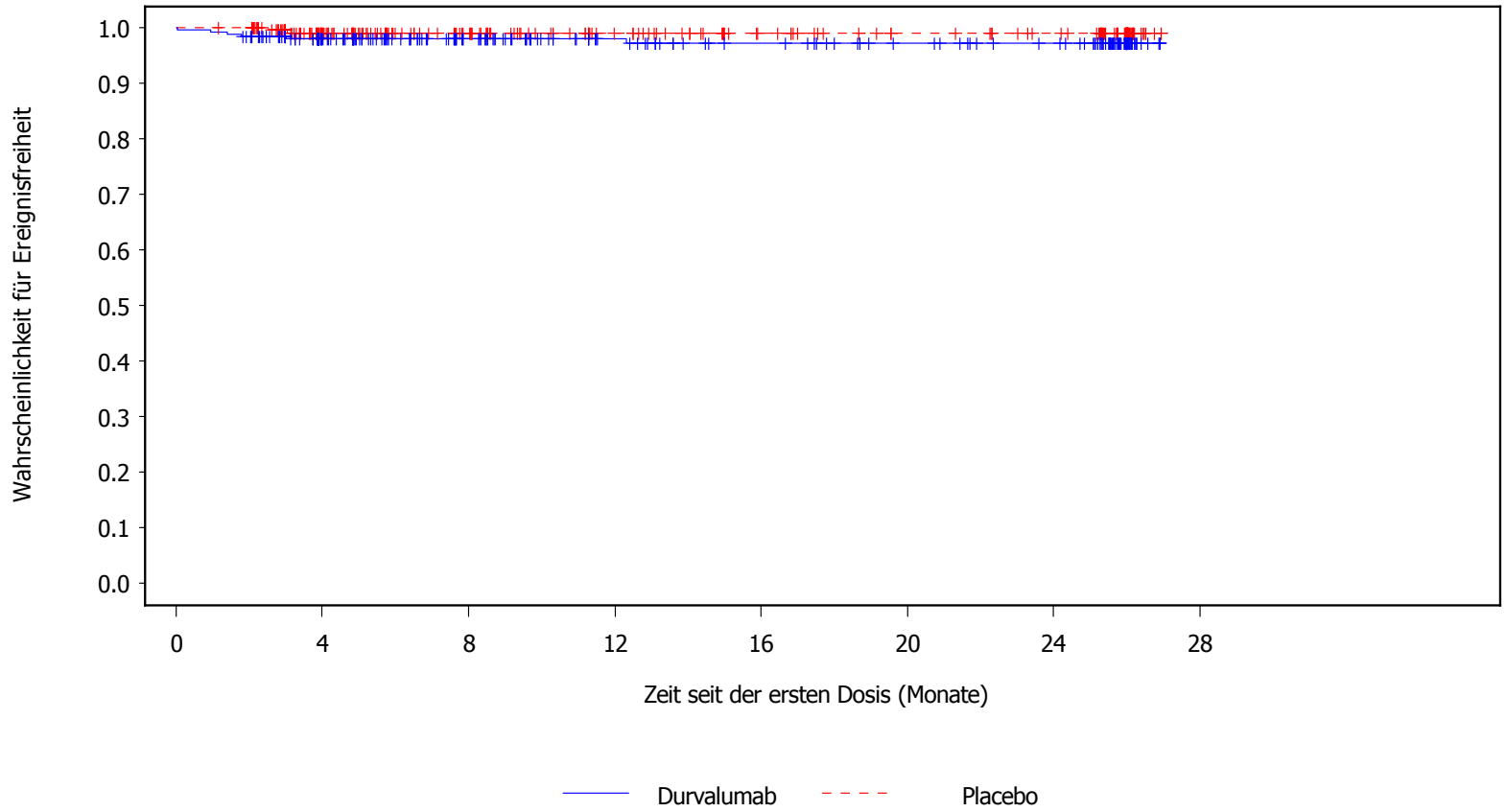


Anzahl an Patienten unter Risiko:

262	208	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bds 05JUN2025:07:

Figure 2.3.98 ADRIATIC: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	156	122	108	98	90	0	Durvalumab
265	203	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdt 05JUN2025:07:

Anhang 4-G8.6.2: Schwere UESI (CTCAE Grad >= 3) - gesamt und nach GT - Subgruppenanalysen

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Table 5.6.1 ADRIATIC: Summary of subgroup analysis of time to first UESI mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	2 (5,6)	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	2,33	[0,22; 50,03]	0,4763
Stadium III	226	14 (6,2)	NE [NE; NE]	228	3 (1,3)	NE [NE; NE]	4,36	[1,42; 18,94]	0,0082*
Interaktions p-Wert									0,6560
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	2,28	[0,22; 49,02]	0,4871
Stadium III	229	14 (6,1)	NE [NE; NE]	231	3 (1,3)	NE [NE; NE]	4,39	[1,43; 19,03]	0,0079*
Interaktions p-Wert									0,6434
Erhalt einer PCI (IVRS) - DEU									
Ja	141	10 (7,1)	NE [NE; NE]	143	4 (2,8)	NE [NE; NE]	2,43	[0,81; 8,85]	0,1158
Nein	121	6 (5,0)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	10 (7,1)	NE [NE; NE]	142	4 (2,8)	NE [NE; NE]	2,41	[0,80; 8,77]	0,1193
Nein	121	6 (5,0)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	5 (6,3)	NE [NE; NE]	80	2 (2,5)	NE [NE; NE]	2,48	[0,54; 17,33]	0,2529
>=28 Tage	152	8 (5,3)	NE [NE; NE]	153	2 (1,3)	NE [NE; NE]	3,86	[0,97; 25,59]	0,0562
Interaktions p-Wert									0,7014
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	1 (6,3)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	7 (6,8)	NE [NE; NE]	103	3 (2,9)	NE [NE; NE]	2,26	[0,63; 10,49]	0,2177

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.6.1 ADRIATIC: Summary of subgroup analysis of time to first UESI mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	6 (6,1)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	2 (4,4)	NE [NE; NE]	62	1 (1,6)	NE [NE; NE]	2,97	[0,28; 63,97]	0,3557
Interaktions p-Wert									0,8442
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	8 (9,0)	NE [NE; NE]	88	2 (2,3)	NE [NE; NE]	3,57	[0,89; 23,66]	0,0737
Cisplatin	173	8 (4,6)	NE [NE; NE]	177	2 (1,1)	NE [NE; NE]	4,02	[1,01; 26,62]	0,0489*
Interaktions p-Wert									0,9158
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	12 (6,2)	NE [NE; NE]	186	3 (1,6)	NE [NE; NE]	3,64	[1,16; 15,99]	0,0258*
Zweimal täglich	69	4 (5,8)	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	4,41	[0,65; 86,31]	0,1350
Interaktions p-Wert									0,8807
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	2 (5,9)	NE [NE; NE]	0,54	[0,03; 5,63]	0,6041
PR	189	11 (5,8)	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	11,39	[2,22;208,15]	0,0015*
SD	42	4 (9,5)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	2,52	[0,37; 49,38]	0,3687
Interaktions p-Wert									0,1142
Geschlecht - DEU									
Männer	178	9 (5,1)	NE [NE; NE]	187	2 (1,1)	NE [NE; NE]	4,55	[1,17; 29,83]	0,0270*
Frauen	84	7 (8,3)	NE [NE; NE]	78	2 (2,6)	NE [NE; NE]	3,05	[0,74; 20,48]	0,1300
Interaktions p-Wert									0,7218
Altersgruppe - DEU									
<65 Jahre	159	12 (7,5)	NE [NE; NE]	161	1 (0,6)	NE [NE; NE]	11,33	[2,23;206,37]	0,0013*
>=65 Jahre	103	4 (3,9)	NE [NE; NE]	104	3 (2,9)	NE [NE; NE]	1,33	[0,29; 6,76]	0,7068
Interaktions p-Wert									0,0724

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.1 ADRIATIC: Summary of subgroup analysis of time to first UESI mit CTCAE Grad >=3
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	7 (9,0)	NE [NE; NE]	72	2 (2,8)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	4 (4,8)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	15 (6,3)	NE [NE; NE]	239	4 (1,7)	NE [NE; NE]	3,60	[1,31; 12,64]	0,0118*
Nichtraucher	23	1 (4,3)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	8 (6,3)	NE [NE; NE]	137	3 (2,2)	NE [NE; NE]	2,82	[0,82; 12,88]	0,1036
Schwarz/Afroamerikanisch	1	1 (100)	11,1 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	7 (5,3)	NE [NE; NE]	121	1 (0,8)	NE [NE; NE]	6,06	[1,08;113,22]	0,0397*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5308
Geographische Region - DEU									
Asien	129	7 (5,4)	NE [NE; NE]	120	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Europa	94	5 (5,3)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	4 (10,3)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	6 (4,6)	NE [NE; NE]	131	3 (2,3)	NE [NE; NE]	1,87	[0,49; 8,86]	0,3636
1	131	10 (7,6)	NE [NE; NE]	134	1 (0,7)	NE [NE; NE]	9,96	[1,91;182,73]	0,0035*
Interaktions p-Wert									0,1559

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.2 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	0	NE [NE; NE]	228	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	0	NE [NE; NE]	231	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.2 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	0	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	0	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.2 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	0	NE [NE; NE]	239	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.3 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.3 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.3 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Dermatitis/Hautausschlag
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.4 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.4 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.4 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Diabetes mellitus Typ 1
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.5 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	5 (2,2)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	5 (2,2)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	3 (2,1)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	3 (2,1)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	1 (3,2)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	2 (2,5)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	2 (1,3)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	2 (1,9)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.5 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	2 (2,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	2 (2,2)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	3 (1,7)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	4 (2,1)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	1 (1,4)	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	3 (1,6)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	2 (4,8)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	3 (1,7)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	2 (2,4)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	4 (2,5)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.5 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	5 (2,1)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	1 (100)	11,1 [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	3 (2,3)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	3 (2,3)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	2 (5,1)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	2 (1,5)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	3 (2,3)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.6 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.6 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.6 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Ereignisse der Bauchspeicheldrüse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.7 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	1 (3,2)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	1 (6,3)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.7 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.7 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.8 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.8 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	0	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	1 (1,2)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.8 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.9 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.9 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.9 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.10 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	2 (5,6)	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	4 (1,8)	NE [NE; NE]	228	2 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	4 (1,7)	NE [NE; NE]	231	2 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	4 (2,8)	NE [NE; NE]	143	2 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	4 (2,8)	NE [NE; NE]	142	2 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nein	121	2 (1,7)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	1 (3,2)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	4 (2,6)	NE [NE; NE]	153	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	3 (2,9)	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.10 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	2 (2,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	1 (1,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	3 (3,4)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	3 (1,7)	NE [NE; NE]	177	1 (0,6)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	3 (1,6)	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	3 (4,3)	NE [NE; NE]	79	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
PR	189	6 (3,2)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	2 (1,1)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	4 (4,8)	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	4 (2,5)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	2 (1,9)	NE [NE; NE]	104	2 (1,9)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.6.10 ADRIATIC: Summary of subgroup analysis of time to first UESI G>=3 GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	3 (3,8)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	2 (2,4)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	5 (2,1)	NE [NE; NE]	239	2 (0,8)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	1 (4,3)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	4 (3,1)	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	2 (1,5)	NE [NE; NE]	121	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	2 (1,6)	NE [NE; NE]	120	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Europa	94	2 (2,1)	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	2 (5,1)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	2 (1,5)	NE [NE; NE]	131	2 (1,5)	NE [NE; NE]	NC	[NC]	NC
1	131	4 (3,1)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Anhang 4-G8.7: SUESI - gesamt und nach GT

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Table 2.2.7 ADRIATIC: Summary of analysis of time to first serious adverse event of special interest (total, and by grouped term)
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [c]
SUESI	262	25 (9,5)	NE [NE; NE]	265	8 (3,0)	NE [NE; NE]	3,15	[1,49; 7,47]	0,0029*
SUESI GT: Andere seltene/verschiedene	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3144
SUESI GT: Durchfall/Colitis	262	2 (0,8)	NE [NE; NE]	265	1 (0,4)	NE [NE; NE]	1,80	[0,17; 38,76]	0,6270
SUESI GT: Hepatische Ereignisse	262	1 (0,4)	NE [NE; NE]	265	1 (0,4)	NE [NE; NE]	0,88	[0,03; 22,18]	0,9266
SUESI GT: Hypophysitis	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3173
SUESI GT: Myokarditis	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3145
SUESI GT: Nebenniereninsuffizienz	262	1 (0,4)	NE [NE; NE]	265	0	NE [NE; NE]	NC	NC	0,3146
SUESI GT: Pneumonitis	262	18 (6,9)	NE [NE; NE]	265	6 (2,3)	NE [NE; NE]	3,05	[1,28; 8,42]	0,0128*

The time to event endpoint is defined as the time from first dose of study treatment to first onset of the respective AE if the AE has occurred by 90 days following the date of last dose of study treatment.
Any patient that has not experienced the AE will be censored at the earliest of the date of Durva/Placebo discontinuation+90 days, administration of subsequent therapy, death or date of data cut-off.
All AEs are coded using MedDRA version 26.1.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified Cox proportional hazard model including treatment only. Efron method for handling ties. 95% CI from profile likelihood estimation. [c] Determined using unstratified log-rank test.
NC = not calculable. Hazard ratio <1 favours Durva. * p<0.05.
root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1ag
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Anhang 4-G8.7.1: SUESI - gesamt und nach GT - Kaplan-Meier-Plot

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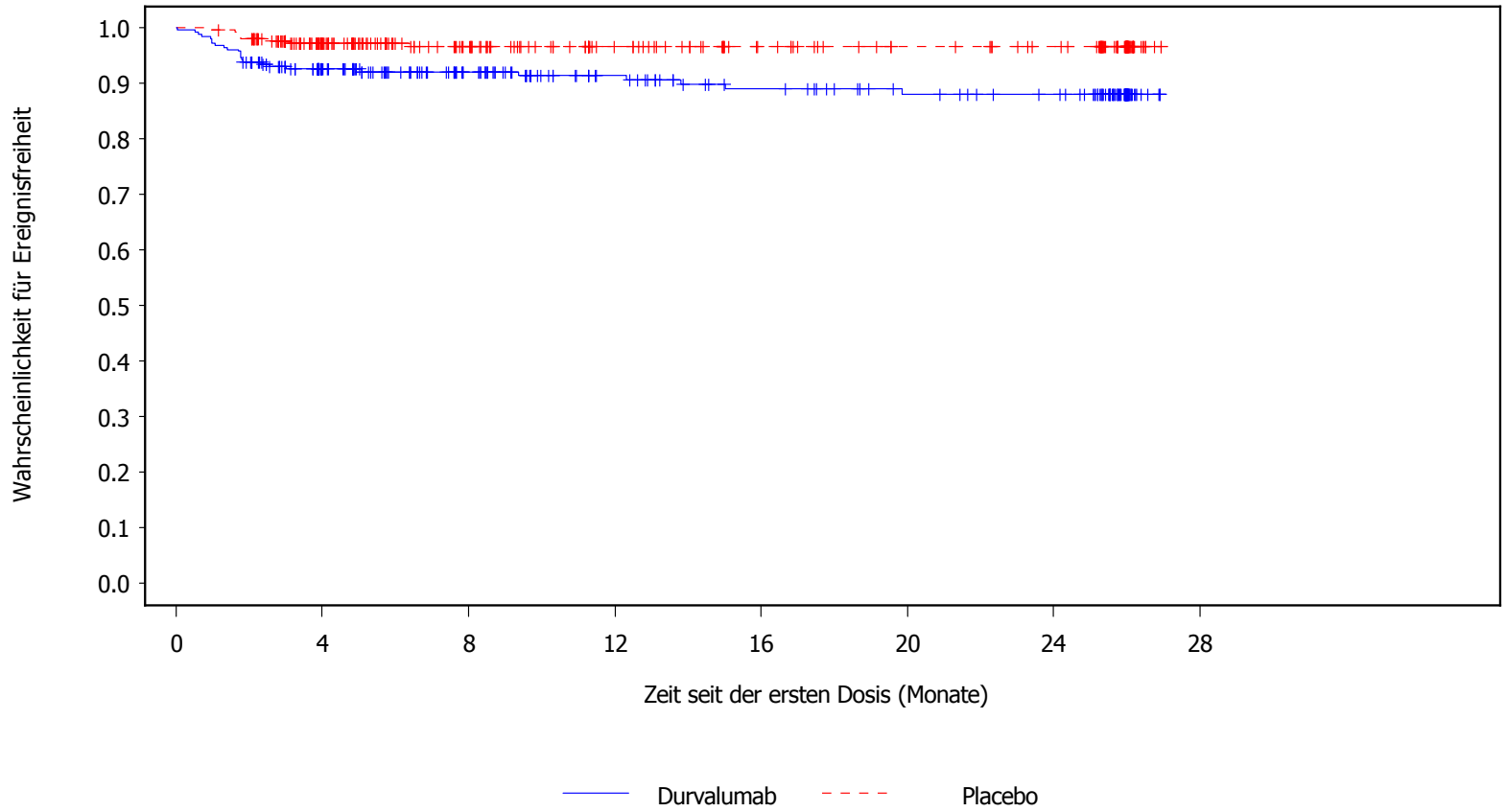
Figure 2.3.99 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	200	153	119	103	92	86	0	Durvalumab
265	201	145	111	89	77	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdu 05JUN2025:07:

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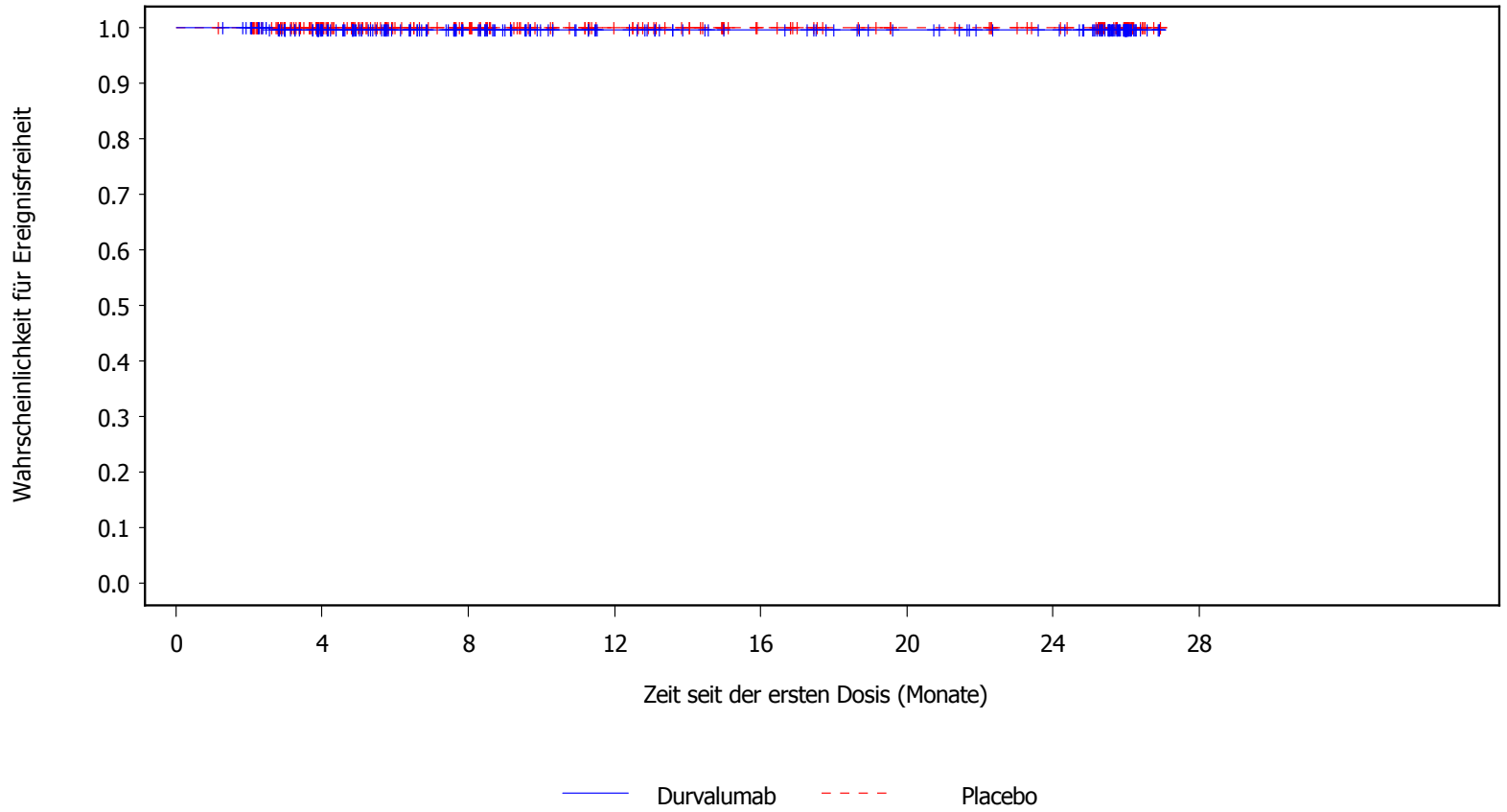
Figure 2.3.100 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdv 05JUN2025:07:

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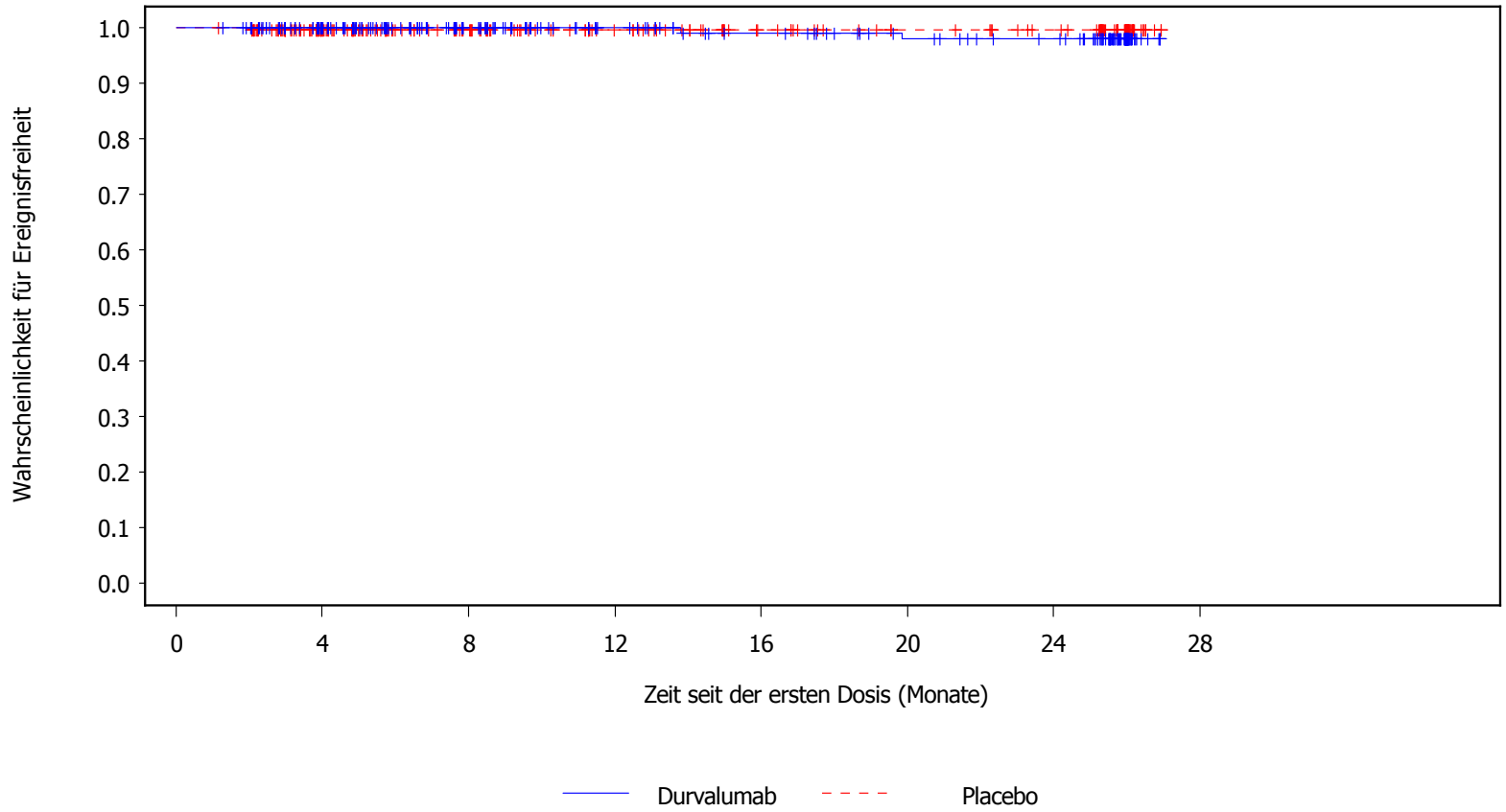
Figure 2.3.101 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	108	97	90	0	Durvalumab
265	204	146	111	89	77	70	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdw 05JUN2025:07:

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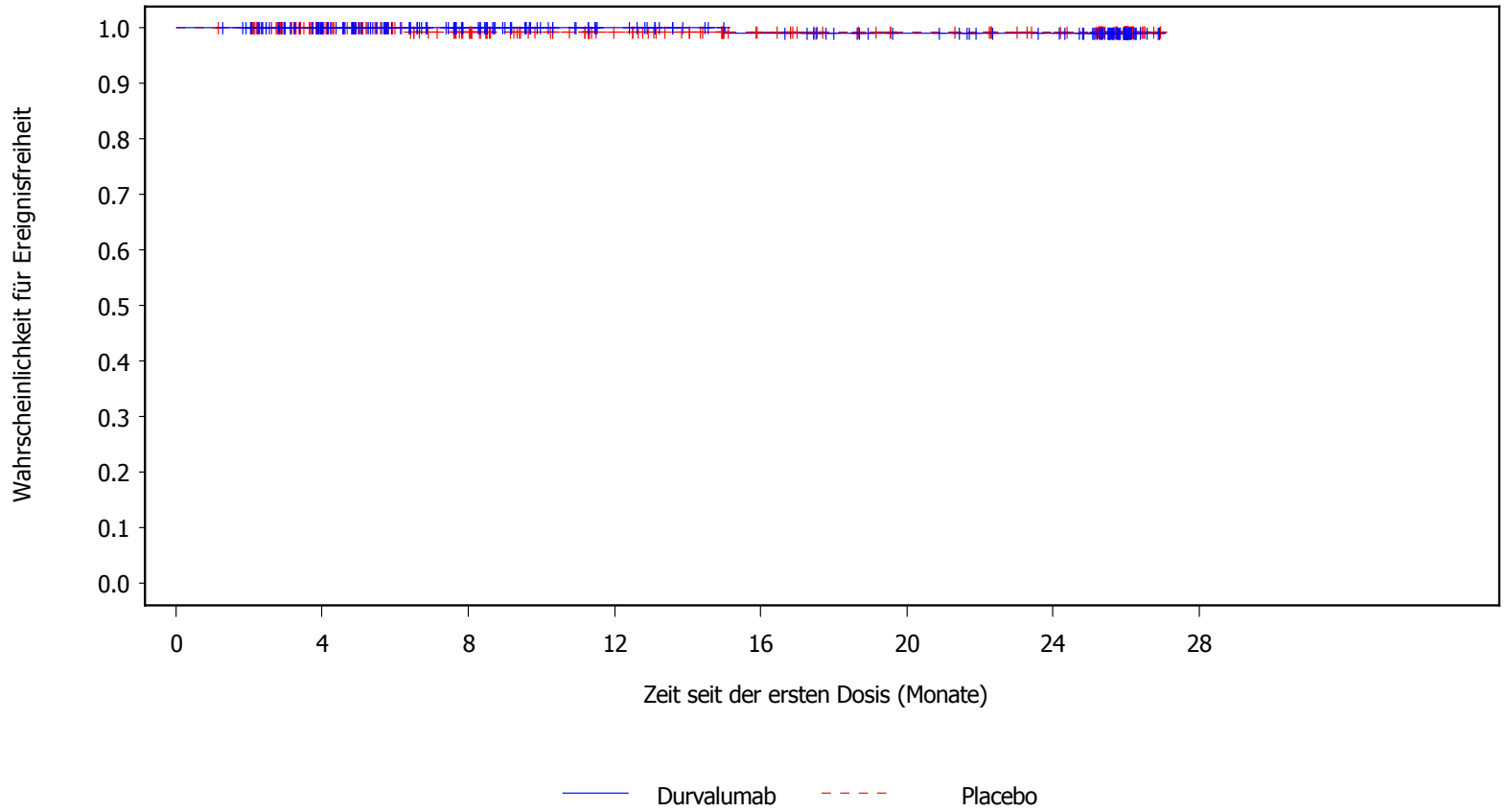
Figure 2.3.102 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	209	156	122	108	98	91	0	Durvalumab
265	205	146	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdx 05JUN2025:07:

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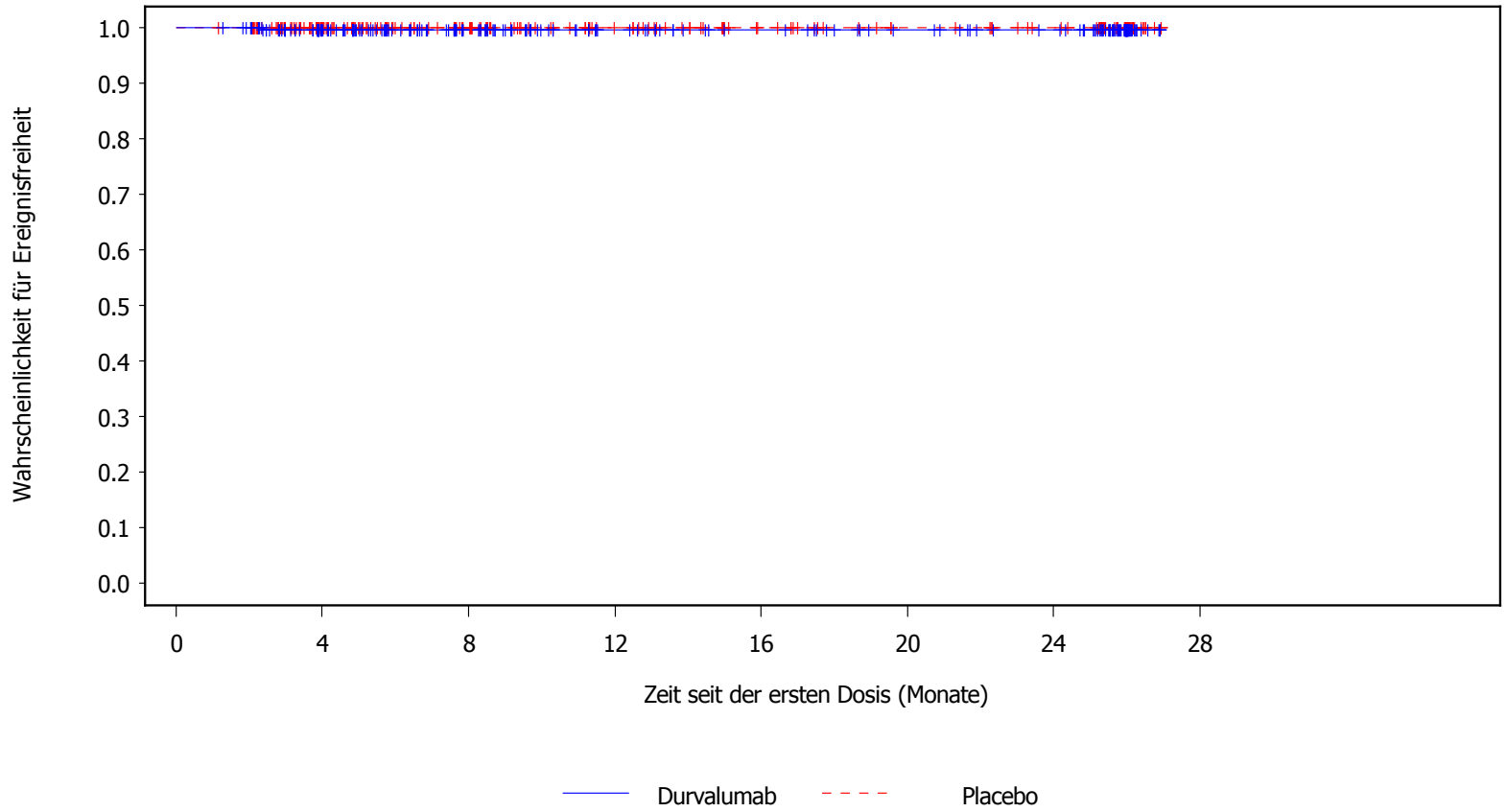
Figure 2.3.103 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	155	121	108	98	90	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdy 05JUN2025:07:

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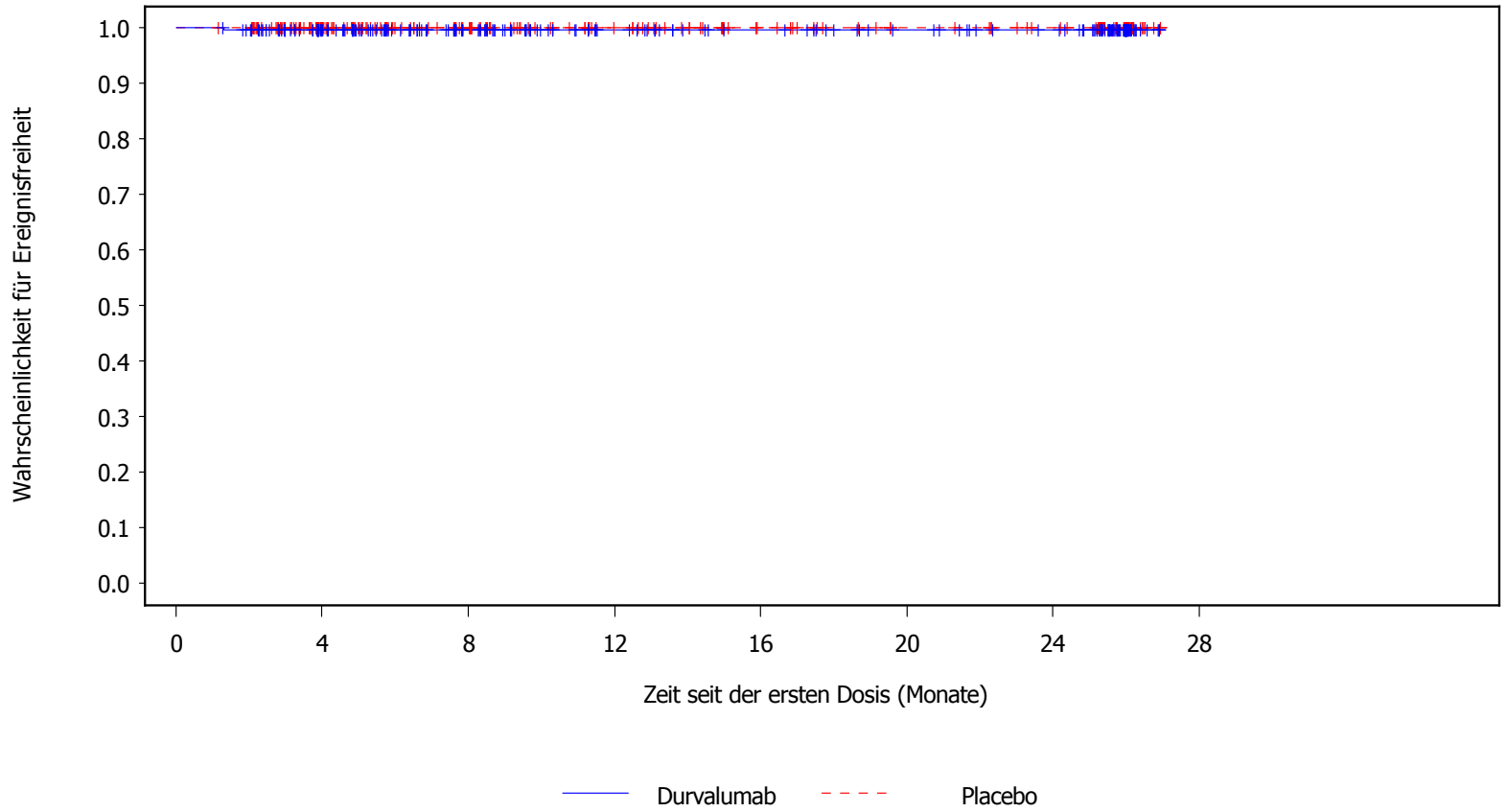
Figure 2.3.104 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bdz 05JUN2025:07:

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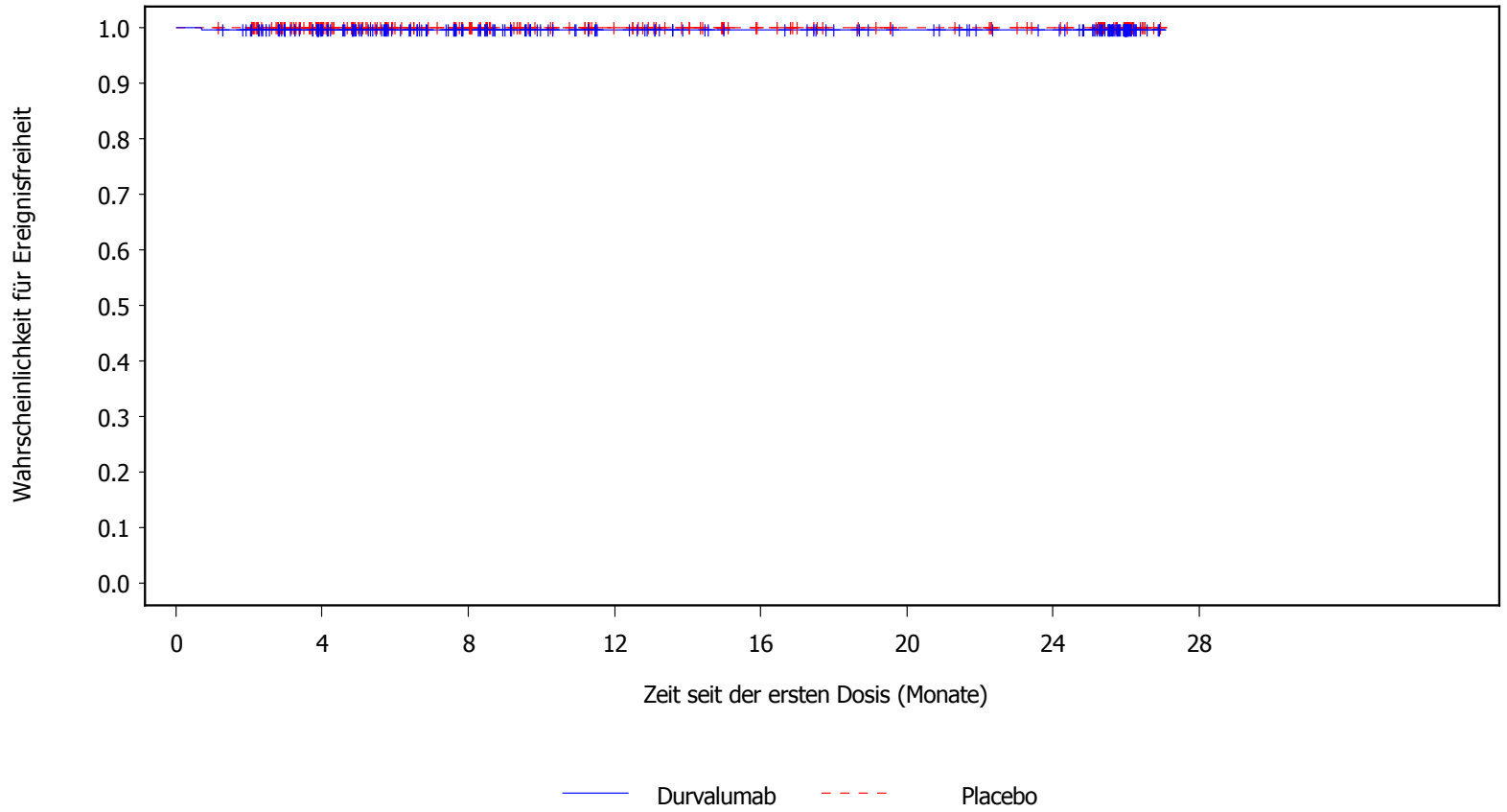
Figure 2.3.105 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	208	156	122	109	99	91	0	Durvalumab
265	205	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1bea 05JUN2025:07:

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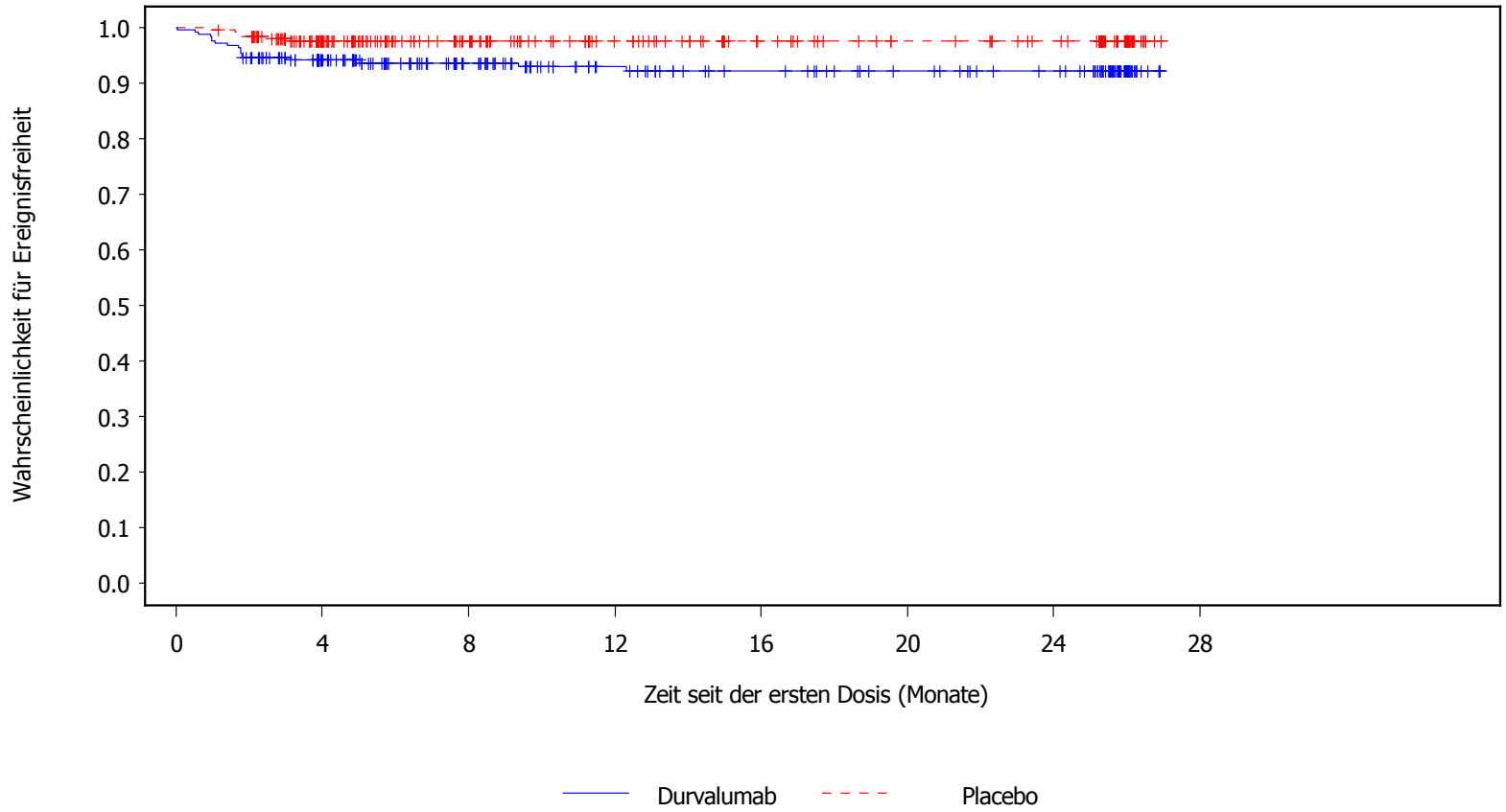
Figure 2.3.106 ADRIATIC: Kaplan-Meier plot of time to first occurrence of SUESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024



Anzahl an Patienten unter Risiko:

262	204	154	120	106	96	88	0	Durvalumab
265	202	147	112	90	78	71	0	Placebo

root/cdar/d419/_Payer/ar/restricted_adriatic_payer1_germany/restricted_tlf/prod/program/ttemainae1.sas gttemainae1beb 05JUN2025:07:

Anhang 4-G8.7.2: SUESI - gesamt und nach GT - Subgruppenanalysen

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Table 5.7.1 ADRIATIC: Summary of subgroup analysis of time to first SUESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	3 (8,3)	NE [NE; NE]	37	2 (5,4)	NE [NE; NE]	1,60	[0,26; 12,13]	0,6036
Stadium III	226	22 (9,7)	NE [NE; NE]	228	6 (2,6)	NE [NE; NE]	3,67	[1,58; 9,96]	0,0018*
Interaktions p-Wert									0,4269
TNM Status (eCRF) - DEU									
Stadium I/II	33	3 (9,1)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	3,23	[0,41; 65,38]	0,2728
Stadium III	229	22 (9,6)	NE [NE; NE]	231	7 (3,0)	NE [NE; NE]	3,14	[1,41; 7,94]	0,0044*
Interaktions p-Wert									0,9804
Erhalt einer PCI (IVRS) - DEU									
Ja	141	18 (12,8)	NE [NE; NE]	143	8 (5,6)	NE [NE; NE]	2,28	[1,02; 5,56]	0,0433*
Nein	121	7 (5,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	18 (12,8)	NE [NE; NE]	142	8 (5,6)	NE [NE; NE]	2,26	[1,02; 5,52]	0,0454*
Nein	121	7 (5,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	4 (12,9)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	6 (7,6)	NE [NE; NE]	80	4 (5,0)	NE [NE; NE]	1,51	[0,43; 5,91]	0,5191
>=28 Tage	152	15 (9,9)	NE [NE; NE]	153	4 (2,6)	NE [NE; NE]	3,79	[1,38; 13,30]	0,0086*
Interaktions p-Wert									0,2824
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	3 (18,8)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	11 (10,7)	NE [NE; NE]	103	5 (4,9)	NE [NE; NE]	2,20	[0,80; 6,99]	0,1282

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.1 ADRIATIC: Summary of subgroup analysis of time to first SUESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	7 (7,1)	NE [NE; NE]	76	1 (1,3)	NE [NE; NE]	5,24	[0,93; 98,06]	0,0616
>=84 Tage	45	4 (8,9)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	2,95	[0,58; 21,26]	0,1950
Interaktions p-Wert									0,7421
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	11 (12,4)	NE [NE; NE]	88	4 (4,5)	NE [NE; NE]	2,60	[0,89; 9,39]	0,0826
Cisplatin	173	14 (8,1)	NE [NE; NE]	177	4 (2,3)	NE [NE; NE]	3,65	[1,31; 12,88]	0,0120*
Interaktions p-Wert									0,6771
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	17 (8,8)	NE [NE; NE]	186	5 (2,7)	NE [NE; NE]	3,25	[1,28; 9,88]	0,0116*
Zweimal täglich	69	8 (11,6)	NE [NE; NE]	79	3 (3,8)	NE [NE; NE]	3,09	[0,89; 14,11]	0,0758
Interaktions p-Wert									0,9534
Bestes Ansprechen auf cCRT - DEU									
CR	31	3 (9,7)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	3,33	[0,43; 67,32]	0,2604
PR	189	19 (10,1)	NE [NE; NE]	199	6 (3,0)	NE [NE; NE]	3,39	[1,43; 9,31]	0,0046*
SD	42	3 (7,1)	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	2,07	[0,27; 41,84]	0,5065
Interaktions p-Wert									0,9284
Geschlecht - DEU									
Männer	178	18 (10,1)	NE [NE; NE]	187	7 (3,7)	NE [NE; NE]	2,70	[1,18; 6,94]	0,0184*
Frauen	84	7 (8,3)	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	6,47	[1,15;121,05]	0,0319*
Interaktions p-Wert									0,4170
Altersgruppe - DEU									
<65 Jahre	159	17 (10,7)	NE [NE; NE]	161	4 (2,5)	NE [NE; NE]	4,27	[1,58; 14,84]	0,0032*
>=65 Jahre	103	8 (7,8)	NE [NE; NE]	104	4 (3,8)	NE [NE; NE]	2,03	[0,64; 7,61]	0,2328
Interaktions p-Wert									0,3702

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Nutzenbewertung nach AMNOG

Table 5.7.1 ADRIATIC: Summary of subgroup analysis of time to first SUESI
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	9 (11,5)	NE [NE; NE]	72	4 (5,6)	NE [NE; NE]	2,05	[0,67; 7,58]	0,2149
TC or IC >=1%	84	8 (9,5)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	3,12	[0,90; 14,24]	0,0732
Interaktions p-Wert									0,6425
Raucherstatus - DEU									
Raucher	239	22 (9,2)	NE [NE; NE]	239	8 (3,3)	NE [NE; NE]	2,74	[1,27; 6,56]	0,0094*
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	10 (7,8)	NE [NE; NE]	137	3 (2,2)	NE [NE; NE]	3,61	[1,10; 16,10]	0,0328*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	15 (11,5)	NE [NE; NE]	121	5 (4,1)	NE [NE; NE]	2,75	[1,07; 8,46]	0,0359*
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,7442
Geographische Region - DEU									
Asien	129	15 (11,6)	NE [NE; NE]	120	5 (4,2)	NE [NE; NE]	2,79	[1,08; 8,57]	0,0335*
Europa	94	7 (7,4)	NE [NE; NE]	112	3 (2,7)	NE [NE; NE]	2,73	[0,76; 12,69]	0,1262
Nordamerika	39	3 (7,7)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,9821
ECOG-Status zu Baseline - DEU									
0	131	9 (6,9)	NE [NE; NE]	131	3 (2,3)	NE [NE; NE]	2,97	[0,88; 13,37]	0,0797
1	131	16 (12,2)	NE [NE; NE]	134	5 (3,7)	NE [NE; NE]	3,29	[1,29; 10,07]	0,0115*
Interaktions p-Wert									0,9011

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.2 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	1 (2,8)	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	0	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	1 (3,0)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	0	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.2 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	1 (2,2)	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	0	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	1 (1,4)	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	1 (3,2)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.2 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Andere seltene/verschiedene
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.3 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	2 (0,9)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	2 (0,9)	NE [NE; NE]	231	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	143	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	2 (1,4)	NE [NE; NE]	142	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	1 (1,3)	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.3 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	2 (1,0)	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	2 (4,8)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	1 (1,2)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.3 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Durchfall/Colitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	2 (0,8)	NE [NE; NE]	239	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	1 (2,6)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	2 (1,5)	NE [NE; NE]	134	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.4 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	1 (2,7)	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	0	NE [NE; NE]	143	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	0	NE [NE; NE]	142	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Nein	121	1 (0,8)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	1 (3,2)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	1 (6,3)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	1 (1,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.4 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.4 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hepatische Ereignisse
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	0	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	1 (0,8)	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	1 (0,8)	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	0	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.5 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	0	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.5 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	1 (1,0)	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	0	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	1 (2,4)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	0	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	1 (1,2)	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.5 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Hypophysitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	1 (1,2)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	0	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	1 (0,8)	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.6 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	0	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	1 (0,7)	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.6 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	1 (1,1)	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	0	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	0	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	1 (1,0)	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.6 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Myokarditis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	0	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.7 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	0	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	1 (0,4)	NE [NE; NE]	228	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	1 (0,4)	NE [NE; NE]	231	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	143	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	1 (0,7)	NE [NE; NE]	142	0	NE [NE; NE]	NC	[NC]	NC
Nein	121	0	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	1 (1,3)	NE [NE; NE]	80	0	NE [NE; NE]	NC	[NC]	NC
>=28 Tage	152	0	NE [NE; NE]	153	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	0	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	1 (1,0)	NE [NE; NE]	103	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.7 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	0	NE [NE; NE]	76	0	NE [NE; NE]	NC	[NC]	NC
>=84 Tage	45	0	NE [NE; NE]	62	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	0	NE [NE; NE]	88	0	NE [NE; NE]	NC	[NC]	NC
Cisplatin	173	1 (0,6)	NE [NE; NE]	177	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	1 (0,5)	NE [NE; NE]	186	0	NE [NE; NE]	NC	[NC]	NC
Zweimal täglich	69	0	NE [NE; NE]	79	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Bestes Ansprechen auf cCRT - DEU									
CR	31	0	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
PR	189	1 (0,5)	NE [NE; NE]	199	0	NE [NE; NE]	NC	[NC]	NC
SD	42	0	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geschlecht - DEU									
Männer	178	1 (0,6)	NE [NE; NE]	187	0	NE [NE; NE]	NC	[NC]	NC
Frauen	84	0	NE [NE; NE]	78	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Altersgruppe - DEU									
<65 Jahre	159	1 (0,6)	NE [NE; NE]	161	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	103	0	NE [NE; NE]	104	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.7 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Nebenniereninsuffizienz
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	1 (1,3)	NE [NE; NE]	72	0	NE [NE; NE]	NC	[NC]	NC
TC or IC >=1%	84	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Raucherstatus - DEU									
Raucher	239	1 (0,4)	NE [NE; NE]	239	0	NE [NE; NE]	NC	[NC]	NC
Nichtraucher	23	0	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	1 (0,8)	NE [NE; NE]	137	0	NE [NE; NE]	NC	[NC]	NC
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	0	NE [NE; NE]	121	0	NE [NE; NE]	NC	[NC]	NC
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Geographische Region - DEU									
Asien	129	0	NE [NE; NE]	120	0	NE [NE; NE]	NC	[NC]	NC
Europa	94	1 (1,1)	NE [NE; NE]	112	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	39	0	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
ECOG-Status zu Baseline - DEU									
0	131	1 (0,8)	NE [NE; NE]	131	0	NE [NE; NE]	NC	[NC]	NC
1	131	0	NE [NE; NE]	134	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.8 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
TNM Status (IVRS) - DEU									
Stadium I/II	36	2 (5,6)	NE [NE; NE]	37	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	226	16 (7,1)	NE [NE; NE]	228	6 (2,6)	NE [NE; NE]	2,72	[1,12; 7,57]	0,0268*
Interaktions p-Wert									NC
TNM Status (eCRF) - DEU									
Stadium I/II	33	2 (6,1)	NE [NE; NE]	34	0	NE [NE; NE]	NC	[NC]	NC
Stadium III	229	16 (7,0)	NE [NE; NE]	231	6 (2,6)	NE [NE; NE]	2,72	[1,12; 7,57]	0,0268*
Interaktions p-Wert									NC
Erhalt einer PCI (IVRS) - DEU									
Ja	141	12 (8,5)	NE [NE; NE]	143	6 (4,2)	NE [NE; NE]	2,04	[0,79; 5,86]	0,1416
Nein	121	6 (5,0)	NE [NE; NE]	122	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Erhalt einer PCI (eCRF) - DEU									
Ja	141	12 (8,5)	NE [NE; NE]	142	6 (4,2)	NE [NE; NE]	2,02	[0,79; 5,81]	0,1462
Nein	121	6 (5,0)	NE [NE; NE]	123	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Zeit vom Ende der cCRT bis Randomisierung - DEU									
<14 Tage	31	3 (9,7)	NE [NE; NE]	32	0	NE [NE; NE]	NC	[NC]	NC
>=14 bis <28 Tage	79	4 (5,1)	NE [NE; NE]	80	3 (3,8)	NE [NE; NE]	1,34	[0,30; 6,82]	0,6968
>=28 Tage	152	11 (7,2)	NE [NE; NE]	153	3 (2,0)	NE [NE; NE]	3,71	[1,16; 16,41]	0,0260*
Interaktions p-Wert									0,3112
Zeit vom Ende der Radiotherapie bis Randomisierung - DEU									
<28 Tage	16	2 (12,5)	NE [NE; NE]	24	0	NE [NE; NE]	NC	[NC]	NC
>=28 bis <56 Tage	103	8 (7,8)	NE [NE; NE]	103	3 (2,9)	NE [NE; NE]	2,67	[0,77; 12,17]	0,1249

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.8 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
>=56 bis <84 Tage	98	5 (5,1)	NE [NE; NE]	76	1 (1,3)	NE [NE; NE]	3,81	[0,62; 73,05]	0,1640
>=84 Tage	45	3 (6,7)	NE [NE; NE]	62	2 (3,2)	NE [NE; NE]	2,18	[0,36; 16,55]	0,3870
Interaktions p-Wert									0,9225
Vorherige platinbasierte Chemotherapie - DEU									
Carboplatin	89	7 (7,9)	NE [NE; NE]	88	2 (2,3)	NE [NE; NE]	3,39	[0,82; 22,72]	0,0956
Cisplatin	173	11 (6,4)	NE [NE; NE]	177	4 (2,3)	NE [NE; NE]	2,87	[0,98; 10,36]	0,0542
Interaktions p-Wert									0,8675
Vorheriges Radiochemotherapieregime - DEU									
Täglich	193	11 (5,7)	NE [NE; NE]	186	3 (1,6)	NE [NE; NE]	3,52	[1,10; 15,58]	0,0330*
Zweimal täglich	69	7 (10,1)	NE [NE; NE]	79	3 (3,8)	NE [NE; NE]	2,75	[0,76; 12,74]	0,1242
Interaktions p-Wert									0,7926
Bestes Ansprechen auf cCRT - DEU									
CR	31	2 (6,5)	NE [NE; NE]	34	1 (2,9)	NE [NE; NE]	2,21	[0,21; 47,41]	0,5049
PR	189	16 (8,5)	NE [NE; NE]	199	4 (2,0)	NE [NE; NE]	4,30	[1,58; 15,01]	0,0034*
SD	42	0	NE [NE; NE]	32	1 (3,1)	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,6298
Geschlecht - DEU									
Männer	178	13 (7,3)	NE [NE; NE]	187	5 (2,7)	NE [NE; NE]	2,74	[1,03; 8,53]	0,0428*
Frauen	84	5 (6,0)	NE [NE; NE]	78	1 (1,3)	NE [NE; NE]	4,72	[0,76; 90,38]	0,1013
Interaktions p-Wert									0,6421
Altersgruppe - DEU									
<65 Jahre	159	13 (8,2)	NE [NE; NE]	161	4 (2,5)	NE [NE; NE]	3,30	[1,17; 11,70]	0,0234*
>=65 Jahre	103	5 (4,9)	NE [NE; NE]	104	2 (1,9)	NE [NE; NE]	2,56	[0,55; 17,85]	0,2372
Interaktions p-Wert									0,8037

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.
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Table 5.7.8 ADRIATIC: Summary of subgroup analysis of time to first SUESI GT: Pneumonitis
Safety Analysis Set, DCO 15JAN2024

	Durvalumab (N=262)			Placebo (N=265)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PD-L1-Status - DEU									
TC and IC <1%	78	7 (9,0)	NE [NE; NE]	72	3 (4,2)	NE [NE; NE]	2,15	[0,60; 9,96]	0,2492
TC or IC >=1%	84	7 (8,3)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	2,73	[0,76; 12,65]	0,1269
Interaktions p-Wert									0,8062
Raucherstatus - DEU									
Raucher	239	15 (6,3)	NE [NE; NE]	239	6 (2,5)	NE [NE; NE]	2,51	[1,02; 7,04]	0,0450*
Nichtraucher	23	3 (13,0)	NE [NE; NE]	26	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									NC
Abstammung - DEU									
Weiß	128	6 (4,7)	NE [NE; NE]	137	1 (0,7)	NE [NE; NE]	6,46	[1,10;122,02]	0,0372*
Schwarz/Afroamerikanisch	1	0	NE [NE; NE]	3	0	NE [NE; NE]	NC	[NC]	NC
Asiatisch	131	12 (9,2)	NE [NE; NE]	121	5 (4,1)	NE [NE; NE]	2,24	[0,83; 7,05]	0,1126
Andere	2	0	NE [NE; NE]	4	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,3470
Geographische Region - DEU									
Asien	129	12 (9,3)	NE [NE; NE]	120	5 (4,2)	NE [NE; NE]	2,25	[0,84; 7,08]	0,1105
Europa	94	4 (4,3)	NE [NE; NE]	112	1 (0,9)	NE [NE; NE]	4,71	[0,70; 92,17]	0,1173
Nordamerika	39	2 (5,1)	NE [NE; NE]	33	0	NE [NE; NE]	NC	[NC]	NC
Interaktions p-Wert									0,5343
ECOG-Status zu Baseline - DEU									
0	131	6 (4,6)	NE [NE; NE]	131	2 (1,5)	NE [NE; NE]	3,00	[0,69; 20,44]	0,1486
1	131	12 (9,2)	NE [NE; NE]	134	4 (3,0)	NE [NE; NE]	3,11	[1,08; 11,13]	0,0343*
Interaktions p-Wert									0,9699

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 90 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 26.1. Includes AEs with onset date on or after the date of first dose and up to and including 90 days following discontinuation of study treatment. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Durva. * p<0.05.

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