

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4A

Anhang 4-G: Weitere Ergebnisse

*Erstlinienbehandlung des nicht resezierbaren oder
metastasierenden Urothelkarzinoms*

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Anhang 4-G1: Ansprechraten, Zeit bis zum Ansprechen und Dauer des Ansprechens

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.4 die Ansprechraten, die Zeit bis zum Ansprechen und die Dauer des Ansprechens

Alle Ergebnisse im Anhang 4G beziehen sich auf den Datenschnitt vom 08. August 2023.

Cisplatin geeignet

Tabelle 4G-1: Zusammenfassung der Ansprechraten (Cisplatin geeignet)

Response Evaluation	EV+Pembro			Plat+Gem		
	n	(%)	(95% CI) ^a	n	(%)	(95% CI) ^a
Participants in population	240			242		
Complete Response (CR)	77	32.1	(26.2, 38.4)	36	14.9	(10.6, 20.0)
Partial Response (PR)	92	38.3	(32.2, 44.8)	89	36.8	(30.7, 43.2)
Objective Response Rate (CR+PR)	169	70.4	(64.2, 76.1)	125	51.7	(45.2, 58.1)
Stable Disease (SD)	38	15.8	(11.5, 21.1)	74	30.6	(24.8, 36.8)
Non-CR/Non-PD	1	0.4	(0.0, 2.3)	1	0.4	(0.0, 2.3)
Disease Control Rate (CR+PR+SD)	208	86.7	(81.7, 90.7)	200	82.6	(77.3, 87.2)
Progressive Disease (PD)	24	10.0	(6.5, 14.5)	27	11.2	(7.5, 15.8)
Non-evaluable (NE)	0	0.0	(0.0, 0.0)	1	0.4	(0.0, 2.3)
No Assessment	8	3.3	(1.4, 6.5)	14	5.8	(3.2, 9.5)

Database Cutoff Date: 08AUG2023
Number of participants: intention-to-treat population, cisplatin eligible
a: Based on binomial exact confidence interval method for binomial data
Best overall response according to RECIST v1.1. CR or PR was confirmed with repeat scans ≥ 28 days after initial response
Not evaluable - Subjects had post-baseline assessment and the best overall response was determined to be not evaluable per RECIST v1.1
No assessment - Subjects had no response assessment post-baseline
Non-CR/Non-PD is preferred over Stable Disease for participants with no target lesion per RECIST v1.1
CI: Confidence Interval; RECIST: Response Evaluation Criteria In Solid Tumors

Tabelle 4G-2: Zeit bis zum Ansprechen und Dauer des Ansprechens für Patient:innen mit bestätigtem Ansprechen (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro N ^b = 240	Plat+Gem N ^b = 242
Number of participants with response ^c	169	125
Time to Response (Months)		
Mean (SD)	2.2 (0.6)	2.4 (0.9)
Median (Q1; Q3)	2.10 (1.97; 2.17)	2.10 (2.04; 2.20)
Min; Max	1.64; 6.24	1.71; 6.60
Response Duration (Months)		
Median ^d (Q1; Q3)	Not reached (8.31; Not reached)	8.34 (4.40; 17.15)
Min ^e ; Max ^e	2.10+; 26.55+	2.07+; 30.92+
Number (%^d) of Participants with Extended Response Duration		
≥ 6 Months	138 (87.1)	62 (61.3)
≥ 12 Months	72 (66.9)	29 (41.2)
≥ 18 Months	26 (62.0)	4 (19.8)
a: Database Cutoff Date: 08AUG2023 b: Number of participants: intention-to-treat population, cisplatin eligible c: Includes participants with confirmed complete response or partial response d: From product-limit (Kaplan-Meier) method for censored data e: '+' indicates there is no progressive disease by the time of last disease assessment Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation		

Cisplatin ungeeignet

Tabelle 4G-3: Zusammenfassung der Ansprechraten (Cisplatin ungeeignet)

Response Evaluation	EV+Pembro			Plat+Gem		
	n	(%)	(95% CI) ^a	n	(%)	(95% CI) ^a
Participants in population	202			202		
Complete Response (CR)	51	25.2	(19.4, 31.8)	19	9.4	(5.8, 14.3)
Partial Response (PR)	77	38.1	(31.4, 45.2)	52	25.7	(19.9, 32.3)
Objective Response Rate (CR+PR)	128	63.4	(56.3, 70.0)	71	35.1	(28.6, 42.2)
Stable Disease (SD)	44	21.8	(16.3, 28.1)	75	37.1	(30.5, 44.2)
Non-CR/Non-PD	3	1.5	(0.3, 4.3)	1	0.5	(0.0, 2.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Disease Control Rate (CR+PR+SD)	175	86.6	(81.2, 91.0)	147	72.8	(66.1, 78.8)
Progressive Disease (PD)	14	6.9	(3.8, 11.4)	33	16.3	(11.5, 22.2)
Non-evaluable (NE)	0	0.0	(0.0, 0.0)	3	1.5	(0.3, 4.3)
No Assessment	13	6.4	(3.5, 10.8)	19	9.4	(5.8, 14.3)
Database Cutoff Date: 08AUG2023 Number of participants: intention-to-treat population, cisplatin ineligible a: Based on binomial exact confidence interval method for binomial data Best overall response according to RECIST v1.1. CR or PR was confirmed with repeat scans ≥ 28 days after initial response Not evaluable - Subjects had post-baseline assessment and the best overall response was determined to be not evaluable per RECIST v1.1 No assessment - Subjects had no response assessment post-baseline Non-CR/Non-PD is preferred over Stable Disease for participants with no target lesion per RECIST v1.1 CI: Confidence Interval; RECIST: Response Evaluation Criteria In Solid Tumors						

Tabelle 4G-4: Zeit bis zum Ansprechen und Dauer des Ansprechens für Patient:innen mit bestätigtem Ansprechen (Cisplatin ungeeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro N ^b = 202	Plat+Gem N ^b = 202
Number of participants with response ^c	128	71
Time to Response (Months)		
Mean (SD)	2.3 (1.1)	2.5 (1.2)
Median (Q1; Q3)	2.10 (1.97; 2.20)	2.10 (2.00; 2.23)
Min; Max	1.31; 12.25	1.64; 8.31
Response Duration (Months)		
Median ^d (Q1; Q3)	Not reached (8.31; Not reached)	6.44 (4.21; 12.45)
Min ^e ; Max ^e	2.04+; 28.32+	1.48+; 22.34+
Number (%^d) of Participants with Extended Response Duration		
≥ 6 Months	96 (84.4)	37 (59.3)
≥ 12 Months	53 (68.1)	10 (25.7)
≥ 18 Months	18 (56.4)	4 (16.5)
a: Database Cutoff Date: 08AUG2023 b: Number of participants: intention-to-treat population, cisplatin ineligible c: Includes participants with confirmed complete response or partial response d: From product-limit (Kaplan-Meier) method for censored data e: '+' indicates there is no progressive disease by the time of last disease assessment Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation		

Anhang 4-G2: Rücklaufquoten des EORTC QLQ-C30, BPI-SF und EQ-5D VAS

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Rücklaufquoten des EORTC QLQ-C30, die Rücklaufquoten des BPI-SF und die Rücklaufquoten der EQ-5D VAS für die Studie KEYNOTE A39 dargestellt.

Cisplatin geeignet

Tabelle 4G-5: Rücklaufquoten mit Gründen für das Fehlen von Werten im EORTC QLQ-C30 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro N ^b = 240 n (%)	Plat+Gem N ^b = 242 n (%)
Baseline	Expected to Complete Questionnaires	240 (100.0)	242 (100.0)
	Completed ^c	206 (85.8)	188 (77.7)
	Compliance (% in those expected to complete questionnaires) ^d	206 (85.8)	188 (77.7)
	Not completed	34 (14.2)	54 (22.3)
	With visit, no record	34 (14.2)	54 (22.3)
	Missing by Design	0 (0.0)	0 (0.0)
Week 1	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	190 (79.2)	173 (71.5)
	Compliance (% in those expected to complete questionnaires) ^d	190 (79.5)	173 (73.6)
	Not completed	49 (20.4)	62 (25.6)
	With visit, no record	49 (20.4)	62 (25.6)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
Week 2	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	203 (84.6)	171 (70.7)
	Compliance (% in those expected to complete questionnaires) ^d	203 (84.9)	171 (72.8)
	Not completed	36 (15.0)	64 (26.4)
	With visit, no record	36 (15.0)	64 (26.4)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
Week 3	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	198 (82.5)	184 (76.0)
	Compliance (% in those expected to complete questionnaires) ^d	198 (82.8)	184 (78.3)
	Not completed	41 (17.1)	51 (21.1)
	With visit, no record	41 (17.1)	51 (21.1)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
Week 4	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	194 (80.8)	183 (75.6)
	Compliance (% in those expected to complete questionnaires) ^d	194 (81.2)	183 (77.9)
	Not completed	45 (18.8)	52 (21.5)
	With visit, no record	45 (18.8)	52 (21.5)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to death	0 (0.0)	1 (0.4)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 5	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	190 (79.2)	187 (77.3)
	Compliance (% in those expected to complete questionnaires) ^d	190 (79.8)	187 (80.3)
	Not completed	48 (20.0)	46 (19.0)
	With visit, no record	48 (20.0)	46 (19.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 6	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	188 (78.3)	174 (71.9)
	Compliance (% in those expected to complete questionnaires) ^d	188 (79.0)	174 (74.7)
	Not completed	50 (20.8)	59 (24.4)
	With visit, no record	50 (20.8)	59 (24.4)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 7	Expected to Complete Questionnaires	236 (98.3)	233 (96.3)
	Completed ^c	195 (81.3)	186 (76.9)
	Compliance (% in those expected to complete questionnaires) ^d	195 (82.6)	186 (79.8)
	Not completed	41 (17.1)	47 (19.4)
	With visit, no record	41 (17.1)	47 (19.4)
	Missing by Design	4 (1.7)	9 (3.7)
	Discontinued due to death	2 (0.8)	3 (1.2)
	Discontinued due to withdrawal by participant	1 (0.4)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 8	Expected to Complete Questionnaires	235 (97.9)	230 (95.0)
	Completed ^c	191 (79.6)	167 (69.0)
	Compliance (% in those expected to complete questionnaires) ^d	191 (81.3)	167 (72.6)
	Not completed	44 (18.3)	63 (26.0)
	With visit, no record	44 (18.3)	63 (26.0)
	Missing by Design	5 (2.1)	12 (5.0)
	Discontinued due to death	3 (1.3)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 9	Expected to Complete Questionnaires	234 (97.5)	230 (95.0)
	Completed ^c	197 (82.1)	177 (73.1)
	Compliance (% in those expected to complete questionnaires) ^d	197 (84.2)	177 (77.0)
	Not completed	37 (15.4)	53 (21.9)
	With visit, no record	37 (15.4)	53 (21.9)
	Missing by Design	6 (2.5)	12 (5.0)
	Discontinued due to death	4 (1.7)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 10	Expected to Complete Questionnaires	234 (97.5)	228 (94.2)
	Completed ^c	191 (79.6)	166 (68.6)
	Compliance (% in those expected to complete questionnaires) ^d	191 (81.6)	166 (72.8)
	Not completed	43 (17.9)	62 (25.6)
	With visit, no record	43 (17.9)	62 (25.6)
	Missing by Design	6 (2.5)	14 (5.8)
	Discontinued due to death	4 (1.7)	7 (2.9)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 11	Expected to Complete Questionnaires	233 (97.1)	226 (93.4)
	Completed ^c	194 (80.8)	168 (69.4)
	Compliance (% in those expected to complete questionnaires) ^d	194 (83.3)	168 (74.3)
	Not completed	39 (16.3)	58 (24.0)
	With visit, no record	39 (16.3)	58 (24.0)
	Missing by Design	7 (2.9)	16 (6.6)
	Discontinued due to death	4 (1.7)	9 (3.7)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 12	Expected to Complete Questionnaires	233 (97.1)	223 (92.1)
	Completed ^c	186 (77.5)	159 (65.7)
	Compliance (% in those expected to complete questionnaires) ^d	186 (79.8)	159 (71.3)
	Not completed	47 (19.6)	64 (26.4)
	With visit, no record	47 (19.6)	64 (26.4)
	Missing by Design	7 (2.9)	19 (7.9)
	Discontinued due to death	4 (1.7)	12 (5.0)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 14	Expected to Complete Questionnaires	231 (96.3)	221 (91.3)
	Completed ^c	185 (77.1)	153 (63.2)
	Compliance (% in those expected to complete questionnaires) ^d	185 (80.1)	153 (69.2)
	Not completed	46 (19.2)	68 (28.1)
	With visit, no record	46 (19.2)	68 (28.1)
	Missing by Design	9 (3.8)	21 (8.7)
	Discontinued due to death	6 (2.5)	15 (6.2)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 17	Expected to Complete Questionnaires	227 (94.6)	217 (89.7)
	Completed ^c	178 (74.2)	155 (64.0)
	Compliance (% in those expected to complete questionnaires) ^d	178 (78.4)	155 (71.4)
	Not completed	49 (20.4)	62 (25.6)
	With visit, no record	49 (20.4)	62 (25.6)
	Missing by Design	13 (5.4)	25 (10.3)
	Discontinued due to death	10 (4.2)	18 (7.4)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 20	Expected to Complete Questionnaires	226 (94.2)	211 (87.2)
	Completed ^c	167 (69.6)	126 (52.1)
	Compliance (% in those expected to complete questionnaires) ^d	167 (73.9)	126 (59.7)
	Not completed	59 (24.6)	85 (35.1)
	With visit, no record	59 (24.6)	85 (35.1)
	Missing by Design	14 (5.8)	31 (12.8)
	Discontinued due to death	11 (4.6)	24 (9.9)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 23	Expected to Complete Questionnaires	223 (92.9)	206 (85.1)
	Completed ^c	162 (67.5)	115 (47.5)
	Compliance (% in those expected to complete questionnaires) ^d	162 (72.6)	115 (55.8)
	Not completed	61 (25.4)	91 (37.6)
	With visit, no record	61 (25.4)	91 (37.6)
	Missing by Design	17 (7.1)	36 (14.9)
	Discontinued due to death	14 (5.8)	29 (12.0)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 26	Expected to Complete Questionnaires	220 (91.7)	200 (82.6)
	Completed ^c	156 (65.0)	108 (44.6)
	Compliance (% in those expected to complete questionnaires) ^d	156 (70.9)	108 (54.0)
	Not completed	64 (26.7)	92 (38.0)
	With visit, no record	64 (26.7)	92 (38.0)
	Missing by Design	20 (8.3)	42 (17.4)
	Discontinued due to death	17 (7.1)	35 (14.5)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 29	Expected to Complete Questionnaires	215 (89.6)	198 (81.8)
	Completed ^c	157 (65.4)	100 (41.3)
	Compliance (% in those expected to complete questionnaires) ^d	157 (73.0)	100 (50.5)
	Not completed	58 (24.2)	98 (40.5)
	With visit, no record	58 (24.2)	98 (40.5)
	Missing by Design	25 (10.4)	44 (18.2)
	Discontinued due to death	21 (8.8)	37 (15.3)
	Discontinued due to withdrawal by participant	3 (1.3)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 32	Expected to Complete Questionnaires	214 (89.2)	187 (77.3)
	Completed ^c	135 (56.3)	83 (34.3)
	Compliance (% in those expected to complete questionnaires) ^d	135 (63.1)	83 (44.4)
	Not completed	79 (32.9)	104 (43.0)
	With visit, no record	79 (32.9)	104 (43.0)
	Missing by Design	26 (10.8)	55 (22.7)
	Discontinued due to death	22 (9.2)	47 (19.4)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 35	Expected to Complete Questionnaires	211 (87.9)	180 (74.4)
	Completed ^c	132 (55.0)	76 (31.4)
	Compliance (% in those expected to complete questionnaires) ^d	132 (62.6)	76 (42.2)
	Not completed	79 (32.9)	104 (43.0)
	With visit, no record	79 (32.9)	104 (43.0)
	Missing by Design	29 (12.1)	62 (25.6)
	Discontinued due to death	25 (10.4)	54 (22.3)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 38	Expected to Complete Questionnaires	208 (86.7)	174 (71.9)
	Completed ^c	132 (55.0)	74 (30.6)
	Compliance (% in those expected to complete questionnaires) ^d	132 (63.5)	74 (42.5)
	Not completed	76 (31.7)	100 (41.3)
	With visit, no record	76 (31.7)	100 (41.3)
	Missing by Design	32 (13.3)	68 (28.1)
	Discontinued due to death	27 (11.3)	59 (24.4)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 41	Expected to Complete Questionnaires	202 (84.2)	164 (67.8)
	Completed ^c	129 (53.8)	65 (26.9)
	Compliance (% in those expected to complete questionnaires) ^d	129 (63.9)	65 (39.6)
	Not completed	73 (30.4)	99 (40.9)
	With visit, no record	73 (30.4)	99 (40.9)
	Missing by Design	38 (15.8)	78 (32.2)
	Discontinued due to death	30 (12.5)	65 (26.9)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	4 (1.7)	5 (2.1)
Week 44	Expected to Complete Questionnaires	190 (79.2)	148 (61.2)
	Completed ^c	108 (45.0)	60 (24.8)
	Compliance (% in those expected to complete questionnaires) ^d	108 (56.8)	60 (40.5)
	Not completed	82 (34.2)	88 (36.4)
	With visit, no record	82 (34.2)	88 (36.4)
	Missing by Design	50 (20.8)	94 (38.8)
	Discontinued due to death	33 (13.8)	68 (28.1)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	13 (5.4)	18 (7.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 47	Expected to Complete Questionnaires	172 (71.7)	142 (58.7)
	Completed ^c	100 (41.7)	56 (23.1)
	Compliance (% in those expected to complete questionnaires) ^d	100 (58.1)	56 (39.4)
	Not completed	72 (30.0)	86 (35.5)
	With visit, no record	72 (30.0)	86 (35.5)
	Missing by Design	68 (28.3)	100 (41.3)
	Discontinued due to death	39 (16.3)	71 (29.3)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
Visit not scheduled	25 (10.4)	21 (8.7)	
Week 50	Expected to Complete Questionnaires	162 (67.5)	132 (54.5)
	Completed ^c	89 (37.1)	51 (21.1)
	Compliance (% in those expected to complete questionnaires) ^d	89 (54.9)	51 (38.6)
	Not completed	73 (30.4)	81 (33.5)
	With visit, no record	73 (30.4)	81 (33.5)
	Missing by Design	78 (32.5)	110 (45.5)
	Discontinued due to death	41 (17.1)	73 (30.2)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
Visit not scheduled	33 (13.8)	29 (12.0)	
Week 53	Expected to Complete Questionnaires	149 (62.1)	122 (50.4)
	Completed ^c	79 (32.9)	46 (19.0)
	Compliance (% in those expected to complete questionnaires) ^d	79 (53.0)	46 (37.7)
	Not completed	70 (29.2)	76 (31.4)
	With visit, no record	70 (29.2)	76 (31.4)
	Missing by Design	91 (37.9)	120 (49.6)
	Discontinued due to death	44 (18.3)	77 (31.8)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
Visit not scheduled	43 (17.9)	35 (14.5)	
Week 56	Expected to Complete Questionnaires	140 (58.3)	117 (48.3)
	Completed ^c	81 (33.8)	39 (16.1)
	Compliance (% in those expected to complete questionnaires) ^d	81 (57.9)	39 (33.3)
	Not completed	59 (24.6)	78 (32.2)
	With visit, no record	59 (24.6)	78 (32.2)
	Missing by Design	100 (41.7)	125 (51.7)
	Discontinued due to death	48 (20.0)	79 (32.6)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
Visit not scheduled	48 (20.0)	38 (15.7)	
Week 59	Expected to Complete Questionnaires	132 (55.0)	107 (44.2)
	Completed ^c	72 (30.0)	37 (15.3)
	Compliance (% in those expected to complete questionnaires) ^d	72 (54.5)	37 (34.6)
	Not completed	60 (25.0)	70 (28.9)
	With visit, no record	60 (25.0)	70 (28.9)
	Missing by Design	108 (45.0)	135 (55.8)
	Discontinued due to death	49 (20.4)	82 (33.9)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
Visit not scheduled	54 (22.5)	45 (18.6)	
Week 62	Expected to Complete Questionnaires	127 (52.9)	100 (41.3)
	Completed ^c	65 (27.1)	32 (13.2)
	Compliance (% in those expected to complete questionnaires) ^d	65 (51.2)	32 (32.0)
	Not completed	62 (25.8)	68 (28.1)
	With visit, no record	62 (25.8)	68 (28.1)
	Missing by Design	113 (47.1)	142 (58.7)
	Discontinued due to death	50 (20.8)	86 (35.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
Visit not scheduled	58 (24.2)	48 (19.8)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 65	Expected to Complete Questionnaires	112 (46.7)	92 (38.0)
	Completed ^c	58 (24.2)	30 (12.4)
	Compliance (% in those expected to complete questionnaires) ^d	58 (51.8)	30 (32.6)
	Not completed	54 (22.5)	62 (25.6)
	With visit, no record	54 (22.5)	62 (25.6)
	Missing by Design	128 (53.3)	150 (62.0)
	Discontinued due to death	53 (22.1)	87 (36.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	70 (29.2)	55 (22.7)
Week 68	Expected to Complete Questionnaires	105 (43.8)	83 (34.3)
	Completed ^c	53 (22.1)	25 (10.3)
	Compliance (% in those expected to complete questionnaires) ^d	53 (50.5)	25 (30.1)
	Not completed	52 (21.7)	58 (24.0)
	With visit, no record	52 (21.7)	58 (24.0)
	Missing by Design	135 (56.3)	159 (65.7)
	Discontinued due to death	55 (22.9)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	75 (31.3)	59 (24.4)
Week 71	Expected to Complete Questionnaires	98 (40.8)	79 (32.6)
	Completed ^c	51 (21.3)	22 (9.1)
	Compliance (% in those expected to complete questionnaires) ^d	51 (52.0)	22 (27.8)
	Not completed	47 (19.6)	57 (23.6)
	With visit, no record	47 (19.6)	57 (23.6)
	Missing by Design	142 (59.2)	163 (67.4)
	Discontinued due to death	56 (23.3)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	81 (33.8)	63 (26.0)
Week 74	Expected to Complete Questionnaires	92 (38.3)	66 (27.3)
	Completed ^c	47 (19.6)	21 (8.7)
	Compliance (% in those expected to complete questionnaires) ^d	47 (51.1)	21 (31.8)
	Not completed	45 (18.8)	45 (18.6)
	With visit, no record	45 (18.8)	45 (18.6)
	Missing by Design	148 (61.7)	176 (72.7)
	Discontinued due to death	57 (23.8)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	86 (35.8)	70 (28.9)
Week 77	Expected to Complete Questionnaires	82 (34.2)	62 (25.6)
	Completed ^c	44 (18.3)	18 (7.4)
	Compliance (% in those expected to complete questionnaires) ^d	44 (53.7)	18 (29.0)
	Not completed	38 (15.8)	44 (18.2)
	With visit, no record	38 (15.8)	44 (18.2)
	Missing by Design	158 (65.8)	180 (74.4)
	Discontinued due to death	58 (24.2)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	95 (39.6)	74 (30.6)
Week 80	Expected to Complete Questionnaires	73 (30.4)	55 (22.7)
	Completed ^c	40 (16.7)	14 (5.8)
	Compliance (% in those expected to complete questionnaires) ^d	40 (54.8)	14 (25.5)
	Not completed	33 (13.8)	41 (16.9)
	With visit, no record	33 (13.8)	41 (16.9)
	Missing by Design	167 (69.6)	187 (77.3)
	Discontinued due to death	59 (24.6)	103 (42.6)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	103 (42.9)	76 (31.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 83	Expected to Complete Questionnaires	70 (29.2)	49 (20.2)
	Completed ^c	37 (15.4)	13 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	37 (52.9)	13 (26.5)
	Not completed	33 (13.8)	36 (14.9)
	With visit, no record	33 (13.8)	36 (14.9)
	Missing by Design	170 (70.8)	193 (79.8)
	Discontinued due to death	59 (24.6)	104 (43.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	106 (44.2)	81 (33.5)
Week 86	Expected to Complete Questionnaires	63 (26.3)	40 (16.5)
	Completed ^c	34 (14.2)	12 (5.0)
	Compliance (% in those expected to complete questionnaires) ^d	34 (54.0)	12 (30.0)
	Not completed	29 (12.1)	28 (11.6)
	With visit, no record	29 (12.1)	28 (11.6)
	Missing by Design	177 (73.8)	202 (83.5)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	112 (46.7)	87 (36.0)
Week 89	Expected to Complete Questionnaires	57 (23.8)	38 (15.7)
	Completed ^c	33 (13.8)	11 (4.5)
	Compliance (% in those expected to complete questionnaires) ^d	33 (57.9)	11 (28.9)
	Not completed	24 (10.0)	27 (11.2)
	With visit, no record	24 (10.0)	27 (11.2)
	Missing by Design	183 (76.3)	204 (84.3)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	118 (49.2)	89 (36.8)
Week 92	Expected to Complete Questionnaires	49 (20.4)	33 (13.6)
	Completed ^c	27 (11.3)	8 (3.3)
	Compliance (% in those expected to complete questionnaires) ^d	27 (55.1)	8 (24.2)
	Not completed	22 (9.2)	25 (10.3)
	With visit, no record	22 (9.2)	25 (10.3)
	Missing by Design	191 (79.6)	209 (86.4)
	Discontinued due to death	61 (25.4)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	125 (52.1)	93 (38.4)
Week 95	Expected to Complete Questionnaires	41 (17.1)	30 (12.4)
	Completed ^c	22 (9.2)	9 (3.7)
	Compliance (% in those expected to complete questionnaires) ^d	22 (53.7)	9 (30.0)
	Not completed	19 (7.9)	21 (8.7)
	With visit, no record	19 (7.9)	21 (8.7)
	Missing by Design	199 (82.9)	212 (87.6)
	Discontinued due to death	62 (25.8)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	132 (55.0)	96 (39.7)
Week 98	Expected to Complete Questionnaires	35 (14.6)	27 (11.2)
	Completed ^c	18 (7.5)	6 (2.5)
	Compliance (% in those expected to complete questionnaires) ^d	18 (51.4)	6 (22.2)
	Not completed	17 (7.1)	21 (8.7)
	With visit, no record	17 (7.1)	21 (8.7)
	Missing by Design	205 (85.4)	215 (88.8)
	Discontinued due to death	63 (26.3)	108 (44.6)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	137 (57.1)	98 (40.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 101	Expected to Complete Questionnaires	30 (12.5)	25 (10.3)
	Completed ^c	14 (5.8)	5 (2.1)
	Compliance (% in those expected to complete questionnaires) ^d	14 (46.7)	5 (20.0)
	Not completed	16 (6.7)	20 (8.3)
	With visit, no record	16 (6.7)	20 (8.3)
	Missing by Design	210 (87.5)	217 (89.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	140 (58.3)	100 (41.3)	
Week 104	Expected to Complete Questionnaires	26 (10.8)	20 (8.3)
	Completed ^c	10 (4.2)	4 (1.7)
	Compliance (% in those expected to complete questionnaires) ^d	10 (38.5)	4 (20.0)
	Not completed	16 (6.7)	16 (6.6)
	With visit, no record	16 (6.7)	16 (6.6)
	Missing by Design	214 (89.2)	222 (91.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	144 (60.0)	105 (43.4)	
Week 107	Expected to Complete Questionnaires	24 (10.0)	16 (6.6)
	Completed ^c	8 (3.3)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	8 (33.3)	3 (18.8)
	Not completed	16 (6.7)	13 (5.4)
	With visit, no record	16 (6.7)	13 (5.4)
	Missing by Design	216 (90.0)	226 (93.4)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	146 (60.8)	109 (45.0)	
Week 110	Expected to Complete Questionnaires	21 (8.8)	15 (6.2)
	Completed ^c	6 (2.5)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	6 (28.6)	3 (20.0)
	Not completed	15 (6.3)	12 (5.0)
	With visit, no record	15 (6.3)	12 (5.0)
	Missing by Design	219 (91.3)	227 (93.8)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	149 (62.1)	110 (45.5)	
Week 113	Expected to Complete Questionnaires	18 (7.5)	15 (6.2)
	Completed ^c	8 (3.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	8 (44.4)	2 (13.3)
	Not completed	10 (4.2)	13 (5.4)
	With visit, no record	10 (4.2)	13 (5.4)
	Missing by Design	222 (92.5)	227 (93.8)
	Discontinued due to death	66 (27.5)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	150 (62.5)	110 (45.5)	
Week 116	Expected to Complete Questionnaires	15 (6.3)	14 (5.8)
	Completed ^c	5 (2.1)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	5 (33.3)	3 (21.4)
	Not completed	10 (4.2)	11 (4.5)
	With visit, no record	10 (4.2)	11 (4.5)
	Missing by Design	225 (93.8)	228 (94.2)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	152 (63.3)	111 (45.9)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 119	Expected to Complete Questionnaires	11 (4.6)	12 (5.0)
	Completed ^c	5 (2.1)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	5 (45.5)	1 (8.3)
	Not completed	6 (2.5)	11 (4.5)
	With visit, no record	6 (2.5)	11 (4.5)
	Missing by Design	229 (95.4)	230 (95.0)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	156 (65.0)	113 (46.7)	
Week 122	Expected to Complete Questionnaires	9 (3.8)	9 (3.7)
	Completed ^c	4 (1.7)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	4 (44.4)	3 (33.3)
	Not completed	5 (2.1)	6 (2.5)
	With visit, no record	5 (2.1)	6 (2.5)
	Missing by Design	231 (96.3)	233 (96.3)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	158 (65.8)	115 (47.5)	
Week 125	Expected to Complete Questionnaires	8 (3.3)	6 (2.5)
	Completed ^c	3 (1.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	3 (37.5)	2 (33.3)
	Not completed	5 (2.1)	4 (1.7)
	With visit, no record	5 (2.1)	4 (1.7)
	Missing by Design	232 (96.7)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	159 (66.3)	118 (48.8)	
Week 128	Expected to Complete Questionnaires	6 (2.5)	6 (2.5)
	Completed ^c	1 (0.4)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	1 (16.7)	3 (50.0)
	Not completed	5 (2.1)	3 (1.2)
	With visit, no record	5 (2.1)	3 (1.2)
	Missing by Design	234 (97.5)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	161 (67.1)	118 (48.8)	
Week 131	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	
Week 134	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 137	Expected to Complete Questionnaires	2 (0.8)	5 (2.1)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (50.0)	2 (40.0)
	Not completed	1 (0.4)	3 (1.2)
	With visit, no record	1 (0.4)	3 (1.2)
	Missing by Design	238 (99.2)	237 (97.9)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	164 (68.3)	118 (48.8)	
Week 140	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 143	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 146	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	
Week 149	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	
Week 152	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	

a: Database Cutoff Date: 08AUG2023
b: Number of participants: intention-to-treat population, cisplatin eligible

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set			
d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred			
ITT: Intention-to-Treat			

Tabelle 4G-6: Rücklaufquoten mit Gründen für das Fehlen von Werten im BPI-SF (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Baseline	Expected to Complete Questionnaires	240 (100.0)	242 (100.0)
	Completed ^c	208 (86.7)	189 (78.1)
	Compliance (% in those expected to complete questionnaires) ^d	208 (86.7)	189 (78.1)
	Not completed	32 (13.3)	53 (21.9)
	With visit, no record	32 (13.3)	53 (21.9)
Week 1	Missing by Design	0 (0.0)	0 (0.0)
	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	188 (78.3)	164 (67.8)
	Compliance (% in those expected to complete questionnaires) ^d	188 (78.7)	164 (69.8)
	Not completed	51 (21.3)	71 (29.3)
Week 2	With visit, no record	51 (21.3)	71 (29.3)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
Week 3	Completed ^c	193 (80.4)	153 (63.2)
	Compliance (% in those expected to complete questionnaires) ^d	193 (80.8)	153 (65.1)
	Not completed	46 (19.2)	82 (33.9)
	With visit, no record	46 (19.2)	82 (33.9)
	Missing by Design	1 (0.4)	7 (2.9)
Week 4	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	186 (77.5)	163 (67.4)
	Compliance (% in those expected to complete questionnaires) ^d	186 (77.8)	163 (69.4)
Week 5	Not completed	53 (22.1)	72 (29.8)
	With visit, no record	53 (22.1)	72 (29.8)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	2 (0.8)
Week 6	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	182 (75.8)	157 (64.9)
	Compliance (% in those expected to complete questionnaires) ^d	182 (76.2)	157 (66.8)
	Not completed	57 (23.8)	78 (32.2)
	With visit, no record	57 (23.8)	78 (32.2)
Week 7	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to death	0 (0.0)	1 (0.4)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 5	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	178 (74.2)	157 (64.9)
	Compliance (% in those expected to complete questionnaires) ^d	178 (74.8)	157 (67.4)
	Not completed	60 (25.0)	76 (31.4)
	With visit, no record	60 (25.0)	76 (31.4)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 6	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	173 (72.1)	151 (62.4)
	Compliance (% in those expected to complete questionnaires) ^d	173 (72.7)	151 (64.8)
	Not completed	65 (27.1)	82 (33.9)
	With visit, no record	65 (27.1)	82 (33.9)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 7	Expected to Complete Questionnaires	236 (98.3)	233 (96.3)
	Completed ^c	179 (74.6)	160 (66.1)
	Compliance (% in those expected to complete questionnaires) ^d	179 (75.8)	160 (68.7)
	Not completed	57 (23.8)	73 (30.2)
	With visit, no record	57 (23.8)	73 (30.2)
	Missing by Design	4 (1.7)	9 (3.7)
	Discontinued due to death	2 (0.8)	3 (1.2)
	Discontinued due to withdrawal by participant	1 (0.4)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 8	Expected to Complete Questionnaires	235 (97.9)	230 (95.0)
	Completed ^c	174 (72.5)	146 (60.3)
	Compliance (% in those expected to complete questionnaires) ^d	174 (74.0)	146 (63.5)
	Not completed	61 (25.4)	84 (34.7)
	With visit, no record	61 (25.4)	84 (34.7)
	Missing by Design	5 (2.1)	12 (5.0)
	Discontinued due to death	3 (1.3)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 9	Expected to Complete Questionnaires	234 (97.5)	230 (95.0)
	Completed ^c	183 (76.3)	152 (62.8)
	Compliance (% in those expected to complete questionnaires) ^d	183 (78.2)	152 (66.1)
	Not completed	51 (21.3)	78 (32.2)
	With visit, no record	51 (21.3)	78 (32.2)
	Missing by Design	6 (2.5)	12 (5.0)
	Discontinued due to death	4 (1.7)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 10	Expected to Complete Questionnaires	234 (97.5)	228 (94.2)
	Completed ^c	177 (73.8)	141 (58.3)
	Compliance (% in those expected to complete questionnaires) ^d	177 (75.6)	141 (61.8)
	Not completed	57 (23.8)	87 (36.0)
	With visit, no record	57 (23.8)	87 (36.0)
	Missing by Design	6 (2.5)	14 (5.8)
	Discontinued due to death	4 (1.7)	7 (2.9)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 11	Expected to Complete Questionnaires	233 (97.1)	226 (93.4)
	Completed ^c	179 (74.6)	145 (59.9)
	Compliance (% in those expected to complete questionnaires) ^d	179 (76.8)	145 (64.2)
	Not completed	54 (22.5)	81 (33.5)
	With visit, no record	54 (22.5)	81 (33.5)
	Missing by Design	7 (2.9)	16 (6.6)
	Discontinued due to death	4 (1.7)	9 (3.7)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 12	Expected to Complete Questionnaires	233 (97.1)	223 (92.1)
	Completed ^c	173 (72.1)	140 (57.9)
	Compliance (% in those expected to complete questionnaires) ^d	173 (74.2)	140 (62.8)
	Not completed	60 (25.0)	83 (34.3)
	With visit, no record	60 (25.0)	83 (34.3)
	Missing by Design	7 (2.9)	19 (7.9)
	Discontinued due to death	4 (1.7)	12 (5.0)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 14	Expected to Complete Questionnaires	231 (96.3)	221 (91.3)
	Completed ^c	169 (70.4)	129 (53.3)
	Compliance (% in those expected to complete questionnaires) ^d	169 (73.2)	129 (58.4)
	Not completed	62 (25.8)	92 (38.0)
	With visit, no record	62 (25.8)	92 (38.0)
	Missing by Design	9 (3.8)	21 (8.7)
	Discontinued due to death	6 (2.5)	15 (6.2)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 17	Expected to Complete Questionnaires	227 (94.6)	217 (89.7)
	Completed ^c	164 (68.3)	133 (55.0)
	Compliance (% in those expected to complete questionnaires) ^d	164 (72.2)	133 (61.3)
	Not completed	63 (26.3)	84 (34.7)
	With visit, no record	63 (26.3)	84 (34.7)
	Missing by Design	13 (5.4)	25 (10.3)
	Discontinued due to death	10 (4.2)	18 (7.4)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 20	Expected to Complete Questionnaires	226 (94.2)	211 (87.2)
	Completed ^c	155 (64.6)	111 (45.9)
	Compliance (% in those expected to complete questionnaires) ^d	155 (68.6)	111 (52.6)
	Not completed	71 (29.6)	100 (41.3)
	With visit, no record	71 (29.6)	100 (41.3)
	Missing by Design	14 (5.8)	31 (12.8)
	Discontinued due to death	11 (4.6)	24 (9.9)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 23	Expected to Complete Questionnaires	223 (92.9)	206 (85.1)
	Completed ^c	152 (63.3)	98 (40.5)
	Compliance (% in those expected to complete questionnaires) ^d	152 (68.2)	98 (47.6)
	Not completed	71 (29.6)	108 (44.6)
	With visit, no record	71 (29.6)	108 (44.6)
	Missing by Design	17 (7.1)	36 (14.9)
	Discontinued due to death	14 (5.8)	29 (12.0)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 26	Expected to Complete Questionnaires	220 (91.7)	200 (82.6)
	Completed ^c	145 (60.4)	96 (39.7)
	Compliance (% in those expected to complete questionnaires) ^d	145 (65.9)	96 (48.0)
	Not completed	75 (31.3)	104 (43.0)
	With visit, no record	75 (31.3)	104 (43.0)
	Missing by Design	20 (8.3)	42 (17.4)
	Discontinued due to death	17 (7.1)	35 (14.5)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 29	Expected to Complete Questionnaires	215 (89.6)	198 (81.8)
	Completed ^c	146 (60.8)	87 (36.0)
	Compliance (% in those expected to complete questionnaires) ^d	146 (67.9)	87 (43.9)
	Not completed	69 (28.8)	111 (45.9)
	With visit, no record	69 (28.8)	111 (45.9)
	Missing by Design	25 (10.4)	44 (18.2)
	Discontinued due to death	21 (8.8)	37 (15.3)
	Discontinued due to withdrawal by participant	3 (1.3)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 32	Expected to Complete Questionnaires	214 (89.2)	187 (77.3)
	Completed ^c	125 (52.1)	77 (31.8)
	Compliance (% in those expected to complete questionnaires) ^d	125 (58.4)	77 (41.2)
	Not completed	89 (37.1)	110 (45.5)
	With visit, no record	89 (37.1)	110 (45.5)
	Missing by Design	26 (10.8)	55 (22.7)
	Discontinued due to death	22 (9.2)	47 (19.4)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 35	Expected to Complete Questionnaires	211 (87.9)	180 (74.4)
	Completed ^c	122 (50.8)	70 (28.9)
	Compliance (% in those expected to complete questionnaires) ^d	122 (57.8)	70 (38.9)
	Not completed	89 (37.1)	110 (45.5)
	With visit, no record	89 (37.1)	110 (45.5)
	Missing by Design	29 (12.1)	62 (25.6)
	Discontinued due to death	25 (10.4)	54 (22.3)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 38	Expected to Complete Questionnaires	208 (86.7)	174 (71.9)
	Completed ^c	124 (51.7)	66 (27.3)
	Compliance (% in those expected to complete questionnaires) ^d	124 (59.6)	66 (37.9)
	Not completed	84 (35.0)	108 (44.6)
	With visit, no record	84 (35.0)	108 (44.6)
	Missing by Design	32 (13.3)	68 (28.1)
	Discontinued due to death	27 (11.3)	59 (24.4)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 41	Expected to Complete Questionnaires	202 (84.2)	164 (67.8)
	Completed ^c	119 (49.6)	57 (23.6)
	Compliance (% in those expected to complete questionnaires) ^d	119 (58.9)	57 (34.8)
	Not completed	83 (34.6)	107 (44.2)
	With visit, no record	83 (34.6)	107 (44.2)
	Missing by Design	38 (15.8)	78 (32.2)
	Discontinued due to death	30 (12.5)	65 (26.9)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	4 (1.7)	5 (2.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 44	Expected to Complete Questionnaires	190 (79.2)	148 (61.2)
	Completed ^c	100 (41.7)	54 (22.3)
	Compliance (% in those expected to complete questionnaires) ^d	100 (52.6)	54 (36.5)
	Not completed	90 (37.5)	94 (38.8)
	With visit, no record	90 (37.5)	94 (38.8)
	Missing by Design	50 (20.8)	94 (38.8)
	Discontinued due to death	33 (13.8)	68 (28.1)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	13 (5.4)	18 (7.4)
Week 47	Expected to Complete Questionnaires	172 (71.7)	142 (58.7)
	Completed ^c	94 (39.2)	50 (20.7)
	Compliance (% in those expected to complete questionnaires) ^d	94 (54.7)	50 (35.2)
	Not completed	78 (32.5)	92 (38.0)
	With visit, no record	78 (32.5)	92 (38.0)
	Missing by Design	68 (28.3)	100 (41.3)
	Discontinued due to death	39 (16.3)	71 (29.3)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	25 (10.4)	21 (8.7)
Week 50	Expected to Complete Questionnaires	162 (67.5)	132 (54.5)
	Completed ^c	84 (35.0)	47 (19.4)
	Compliance (% in those expected to complete questionnaires) ^d	84 (51.9)	47 (35.6)
	Not completed	78 (32.5)	85 (35.1)
	With visit, no record	78 (32.5)	85 (35.1)
	Missing by Design	78 (32.5)	110 (45.5)
	Discontinued due to death	41 (17.1)	73 (30.2)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	33 (13.8)	29 (12.0)
Week 53	Expected to Complete Questionnaires	149 (62.1)	122 (50.4)
	Completed ^c	74 (30.8)	42 (17.4)
	Compliance (% in those expected to complete questionnaires) ^d	74 (49.7)	42 (34.4)
	Not completed	75 (31.3)	80 (33.1)
	With visit, no record	75 (31.3)	80 (33.1)
	Missing by Design	91 (37.9)	120 (49.6)
	Discontinued due to death	44 (18.3)	77 (31.8)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	43 (17.9)	35 (14.5)
Week 56	Expected to Complete Questionnaires	140 (58.3)	117 (48.3)
	Completed ^c	76 (31.7)	34 (14.0)
	Compliance (% in those expected to complete questionnaires) ^d	76 (54.3)	34 (29.1)
	Not completed	64 (26.7)	83 (34.3)
	With visit, no record	64 (26.7)	83 (34.3)
	Missing by Design	100 (41.7)	125 (51.7)
	Discontinued due to death	48 (20.0)	79 (32.6)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	48 (20.0)	38 (15.7)
Week 59	Expected to Complete Questionnaires	132 (55.0)	107 (44.2)
	Completed ^c	68 (28.3)	33 (13.6)
	Compliance (% in those expected to complete questionnaires) ^d	68 (51.5)	33 (30.8)
	Not completed	64 (26.7)	74 (30.6)
	With visit, no record	64 (26.7)	74 (30.6)
	Missing by Design	108 (45.0)	135 (55.8)
	Discontinued due to death	49 (20.4)	82 (33.9)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	54 (22.5)	45 (18.6)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 62	Expected to Complete Questionnaires	127 (52.9)	100 (41.3)
	Completed ^c	63 (26.3)	29 (12.0)
	Compliance (% in those expected to complete questionnaires) ^d	63 (49.6)	29 (29.0)
	Not completed	64 (26.7)	71 (29.3)
	With visit, no record	64 (26.7)	71 (29.3)
	Missing by Design	113 (47.1)	142 (58.7)
	Discontinued due to death	50 (20.8)	86 (35.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	58 (24.2)	48 (19.8)
Week 65	Expected to Complete Questionnaires	112 (46.7)	92 (38.0)
	Completed ^c	54 (22.5)	26 (10.7)
	Compliance (% in those expected to complete questionnaires) ^d	54 (48.2)	26 (28.3)
	Not completed	58 (24.2)	66 (27.3)
	With visit, no record	58 (24.2)	66 (27.3)
	Missing by Design	128 (53.3)	150 (62.0)
	Discontinued due to death	53 (22.1)	87 (36.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	70 (29.2)	55 (22.7)
Week 68	Expected to Complete Questionnaires	105 (43.8)	83 (34.3)
	Completed ^c	52 (21.7)	21 (8.7)
	Compliance (% in those expected to complete questionnaires) ^d	52 (49.5)	21 (25.3)
	Not completed	53 (22.1)	62 (25.6)
	With visit, no record	53 (22.1)	62 (25.6)
	Missing by Design	135 (56.3)	159 (65.7)
	Discontinued due to death	55 (22.9)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	75 (31.3)	59 (24.4)
Week 71	Expected to Complete Questionnaires	98 (40.8)	79 (32.6)
	Completed ^c	49 (20.4)	19 (7.9)
	Compliance (% in those expected to complete questionnaires) ^d	49 (50.0)	19 (24.1)
	Not completed	49 (20.4)	60 (24.8)
	With visit, no record	49 (20.4)	60 (24.8)
	Missing by Design	142 (59.2)	163 (67.4)
	Discontinued due to death	56 (23.3)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	81 (33.8)	63 (26.0)
Week 74	Expected to Complete Questionnaires	92 (38.3)	66 (27.3)
	Completed ^c	46 (19.2)	18 (7.4)
	Compliance (% in those expected to complete questionnaires) ^d	46 (50.0)	18 (27.3)
	Not completed	46 (19.2)	48 (19.8)
	With visit, no record	46 (19.2)	48 (19.8)
	Missing by Design	148 (61.7)	176 (72.7)
	Discontinued due to death	57 (23.8)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	86 (35.8)	70 (28.9)
Week 77	Expected to Complete Questionnaires	82 (34.2)	62 (25.6)
	Completed ^c	43 (17.9)	15 (6.2)
	Compliance (% in those expected to complete questionnaires) ^d	43 (52.4)	15 (24.2)
	Not completed	39 (16.3)	47 (19.4)
	With visit, no record	39 (16.3)	47 (19.4)
	Missing by Design	158 (65.8)	180 (74.4)
	Discontinued due to death	58 (24.2)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	95 (39.6)	74 (30.6)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 80	Expected to Complete Questionnaires	73 (30.4)	55 (22.7)
	Completed ^c	38 (15.8)	13 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	38 (52.1)	13 (23.6)
	Not completed	35 (14.6)	42 (17.4)
	With visit, no record	35 (14.6)	42 (17.4)
	Missing by Design	167 (69.6)	187 (77.3)
	Discontinued due to death	59 (24.6)	103 (42.6)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	103 (42.9)	76 (31.4)
Week 83	Expected to Complete Questionnaires	70 (29.2)	49 (20.2)
	Completed ^c	36 (15.0)	12 (5.0)
	Compliance (% in those expected to complete questionnaires) ^d	36 (51.4)	12 (24.5)
	Not completed	34 (14.2)	37 (15.3)
	With visit, no record	34 (14.2)	37 (15.3)
	Missing by Design	170 (70.8)	193 (79.8)
	Discontinued due to death	59 (24.6)	104 (43.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	106 (44.2)	81 (33.5)
Week 86	Expected to Complete Questionnaires	63 (26.3)	40 (16.5)
	Completed ^c	32 (13.3)	11 (4.5)
	Compliance (% in those expected to complete questionnaires) ^d	32 (50.8)	11 (27.5)
	Not completed	31 (12.9)	29 (12.0)
	With visit, no record	31 (12.9)	29 (12.0)
	Missing by Design	177 (73.8)	202 (83.5)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	112 (46.7)	87 (36.0)
Week 89	Expected to Complete Questionnaires	57 (23.8)	38 (15.7)
	Completed ^c	31 (12.9)	10 (4.1)
	Compliance (% in those expected to complete questionnaires) ^d	31 (54.4)	10 (26.3)
	Not completed	26 (10.8)	28 (11.6)
	With visit, no record	26 (10.8)	28 (11.6)
	Missing by Design	183 (76.3)	204 (84.3)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	118 (49.2)	89 (36.8)
Week 92	Expected to Complete Questionnaires	49 (20.4)	33 (13.6)
	Completed ^c	25 (10.4)	8 (3.3)
	Compliance (% in those expected to complete questionnaires) ^d	25 (51.0)	8 (24.2)
	Not completed	24 (10.0)	25 (10.3)
	With visit, no record	24 (10.0)	25 (10.3)
	Missing by Design	191 (79.6)	209 (86.4)
	Discontinued due to death	61 (25.4)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	125 (52.1)	93 (38.4)
Week 95	Expected to Complete Questionnaires	41 (17.1)	30 (12.4)
	Completed ^c	21 (8.8)	9 (3.7)
	Compliance (% in those expected to complete questionnaires) ^d	21 (51.2)	9 (30.0)
	Not completed	20 (8.3)	21 (8.7)
	With visit, no record	20 (8.3)	21 (8.7)
	Missing by Design	199 (82.9)	212 (87.6)
	Discontinued due to death	62 (25.8)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	132 (55.0)	96 (39.7)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 98	Expected to Complete Questionnaires	35 (14.6)	27 (11.2)
	Completed ^c	17 (7.1)	6 (2.5)
	Compliance (% in those expected to complete questionnaires) ^d	17 (48.6)	6 (22.2)
	Not completed	18 (7.5)	21 (8.7)
	With visit, no record	18 (7.5)	21 (8.7)
	Missing by Design	205 (85.4)	215 (88.8)
	Discontinued due to death	63 (26.3)	108 (44.6)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	137 (57.1)	98 (40.5)
Week 101	Expected to Complete Questionnaires	30 (12.5)	25 (10.3)
	Completed ^c	14 (5.8)	5 (2.1)
	Compliance (% in those expected to complete questionnaires) ^d	14 (46.7)	5 (20.0)
	Not completed	16 (6.7)	20 (8.3)
	With visit, no record	16 (6.7)	20 (8.3)
	Missing by Design	210 (87.5)	217 (89.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	140 (58.3)	100 (41.3)
Week 104	Expected to Complete Questionnaires	26 (10.8)	20 (8.3)
	Completed ^c	10 (4.2)	4 (1.7)
	Compliance (% in those expected to complete questionnaires) ^d	10 (38.5)	4 (20.0)
	Not completed	16 (6.7)	16 (6.6)
	With visit, no record	16 (6.7)	16 (6.6)
	Missing by Design	214 (89.2)	222 (91.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	144 (60.0)	105 (43.4)
Week 107	Expected to Complete Questionnaires	24 (10.0)	16 (6.6)
	Completed ^c	8 (3.3)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	8 (33.3)	3 (18.8)
	Not completed	16 (6.7)	13 (5.4)
	With visit, no record	16 (6.7)	13 (5.4)
	Missing by Design	216 (90.0)	226 (93.4)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	146 (60.8)	109 (45.0)
Week 110	Expected to Complete Questionnaires	21 (8.8)	15 (6.2)
	Completed ^c	6 (2.5)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	6 (28.6)	3 (20.0)
	Not completed	15 (6.3)	12 (5.0)
	With visit, no record	15 (6.3)	12 (5.0)
	Missing by Design	219 (91.3)	227 (93.8)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	149 (62.1)	110 (45.5)
Week 113	Expected to Complete Questionnaires	18 (7.5)	15 (6.2)
	Completed ^c	8 (3.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	8 (44.4)	2 (13.3)
	Not completed	10 (4.2)	13 (5.4)
	With visit, no record	10 (4.2)	13 (5.4)
	Missing by Design	222 (92.5)	227 (93.8)
	Discontinued due to death	66 (27.5)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	150 (62.5)	110 (45.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 116	Expected to Complete Questionnaires	15 (6.3)	14 (5.8)
	Completed ^c	5 (2.1)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	5 (33.3)	3 (21.4)
	Not completed	10 (4.2)	11 (4.5)
	With visit, no record	10 (4.2)	11 (4.5)
	Missing by Design	225 (93.8)	228 (94.2)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	152 (63.3)	111 (45.9)	
Week 119	Expected to Complete Questionnaires	11 (4.6)	12 (5.0)
	Completed ^c	5 (2.1)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	5 (45.5)	1 (8.3)
	Not completed	6 (2.5)	11 (4.5)
	With visit, no record	6 (2.5)	11 (4.5)
	Missing by Design	229 (95.4)	230 (95.0)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	156 (65.0)	113 (46.7)	
Week 122	Expected to Complete Questionnaires	9 (3.8)	9 (3.7)
	Completed ^c	4 (1.7)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	4 (44.4)	3 (33.3)
	Not completed	5 (2.1)	6 (2.5)
	With visit, no record	5 (2.1)	6 (2.5)
	Missing by Design	231 (96.3)	233 (96.3)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	158 (65.8)	115 (47.5)	
Week 125	Expected to Complete Questionnaires	8 (3.3)	6 (2.5)
	Completed ^c	3 (1.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	3 (37.5)	2 (33.3)
	Not completed	5 (2.1)	4 (1.7)
	With visit, no record	5 (2.1)	4 (1.7)
	Missing by Design	232 (96.7)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	159 (66.3)	118 (48.8)	
Week 128	Expected to Complete Questionnaires	6 (2.5)	6 (2.5)
	Completed ^c	1 (0.4)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	1 (16.7)	3 (50.0)
	Not completed	5 (2.1)	3 (1.2)
	With visit, no record	5 (2.1)	3 (1.2)
	Missing by Design	234 (97.5)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	161 (67.1)	118 (48.8)	
Week 131	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 134	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	
Week 137	Expected to Complete Questionnaires	2 (0.8)	5 (2.1)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (50.0)	2 (40.0)
	Not completed	1 (0.4)	3 (1.2)
	With visit, no record	1 (0.4)	3 (1.2)
	Missing by Design	238 (99.2)	237 (97.9)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	164 (68.3)	118 (48.8)	
Week 140	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 143	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 146	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	
Week 149	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 152	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	165 (68.8)	121 (50.0)

a: Database Cutoff Date: 08AUG2023
b: Number of participants: intention-to-treat population, cisplatin eligible
c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set
d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred
ITT: Intention-to-Treat

Tabelle 4G-7: Rücklaufquoten mit Gründen für das Fehlen von Werten in der EQ-5D VAS (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Baseline	Expected to Complete Questionnaires	240 (100.0)	242 (100.0)
	Completed ^c	211 (87.9)	190 (78.5)
	Compliance (% in those expected to complete questionnaires) ^d	211 (87.9)	190 (78.5)
	Not completed	29 (12.1)	52 (21.5)
	With visit, no record	29 (12.1)	52 (21.5)
	Missing by Design	0 (0.0)	0 (0.0)
Week 1	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	190 (79.2)	179 (74.0)
	Compliance (% in those expected to complete questionnaires) ^d	190 (79.5)	179 (76.2)
	Not completed	49 (20.4)	56 (23.1)
	With visit, no record	49 (20.4)	56 (23.1)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
Visit not scheduled	1 (0.4)	2 (0.8)	
Week 2	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	204 (85.0)	174 (71.9)
	Compliance (% in those expected to complete questionnaires) ^d	204 (85.4)	174 (74.0)
	Not completed	35 (14.6)	61 (25.2)
	With visit, no record	35 (14.6)	61 (25.2)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
Visit not scheduled	1 (0.4)	2 (0.8)	
Week 3	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	199 (82.9)	186 (76.9)
	Compliance (% in those expected to complete questionnaires) ^d	199 (83.3)	186 (79.1)
	Not completed	40 (16.7)	49 (20.2)
	With visit, no record	40 (16.7)	49 (20.2)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
Visit not scheduled	1 (0.4)	2 (0.8)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 4	Expected to Complete Questionnaires	239 (99.6)	235 (97.1)
	Completed ^c	195 (81.3)	184 (76.0)
	Compliance (% in those expected to complete questionnaires) ^d	195 (81.6)	184 (78.3)
	Not completed	44 (18.3)	51 (21.1)
	With visit, no record	44 (18.3)	51 (21.1)
	Missing by Design	1 (0.4)	7 (2.9)
	Discontinued due to death	0 (0.0)	1 (0.4)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 5	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	193 (80.4)	188 (77.7)
	Compliance (% in those expected to complete questionnaires) ^d	193 (81.1)	188 (80.7)
	Not completed	45 (18.8)	45 (18.6)
	With visit, no record	45 (18.8)	45 (18.6)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 6	Expected to Complete Questionnaires	238 (99.2)	233 (96.3)
	Completed ^c	191 (79.6)	174 (71.9)
	Compliance (% in those expected to complete questionnaires) ^d	191 (80.3)	174 (74.7)
	Not completed	47 (19.6)	59 (24.4)
	With visit, no record	47 (19.6)	59 (24.4)
	Missing by Design	2 (0.8)	9 (3.7)
	Discontinued due to death	1 (0.4)	3 (1.2)
	Discontinued due to withdrawal by participant	0 (0.0)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 7	Expected to Complete Questionnaires	236 (98.3)	233 (96.3)
	Completed ^c	196 (81.7)	188 (77.7)
	Compliance (% in those expected to complete questionnaires) ^d	196 (83.1)	188 (80.7)
	Not completed	40 (16.7)	45 (18.6)
	With visit, no record	40 (16.7)	45 (18.6)
	Missing by Design	4 (1.7)	9 (3.7)
	Discontinued due to death	2 (0.8)	3 (1.2)
	Discontinued due to withdrawal by participant	1 (0.4)	5 (2.1)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 8	Expected to Complete Questionnaires	235 (97.9)	230 (95.0)
	Completed ^c	193 (80.4)	168 (69.4)
	Compliance (% in those expected to complete questionnaires) ^d	193 (82.1)	168 (73.0)
	Not completed	42 (17.5)	62 (25.6)
	With visit, no record	42 (17.5)	62 (25.6)
	Missing by Design	5 (2.1)	12 (5.0)
	Discontinued due to death	3 (1.3)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 9	Expected to Complete Questionnaires	234 (97.5)	230 (95.0)
	Completed ^c	198 (82.5)	178 (73.6)
	Compliance (% in those expected to complete questionnaires) ^d	198 (84.6)	178 (77.4)
	Not completed	36 (15.0)	52 (21.5)
	With visit, no record	36 (15.0)	52 (21.5)
	Missing by Design	6 (2.5)	12 (5.0)
	Discontinued due to death	4 (1.7)	5 (2.1)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 10	Expected to Complete Questionnaires	234 (97.5)	228 (94.2)
	Completed ^c	191 (79.6)	166 (68.6)
	Compliance (% in those expected to complete questionnaires) ^d	191 (81.6)	166 (72.8)
	Not completed	43 (17.9)	62 (25.6)
	With visit, no record	43 (17.9)	62 (25.6)
	Missing by Design	6 (2.5)	14 (5.8)
	Discontinued due to death	4 (1.7)	7 (2.9)
	Discontinued due to withdrawal by participant	1 (0.4)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 11	Expected to Complete Questionnaires	233 (97.1)	226 (93.4)
	Completed ^c	196 (81.7)	168 (69.4)
	Compliance (% in those expected to complete questionnaires) ^d	196 (84.1)	168 (74.3)
	Not completed	37 (15.4)	58 (24.0)
	With visit, no record	37 (15.4)	58 (24.0)
	Missing by Design	7 (2.9)	16 (6.6)
	Discontinued due to death	4 (1.7)	9 (3.7)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 12	Expected to Complete Questionnaires	233 (97.1)	223 (92.1)
	Completed ^c	186 (77.5)	160 (66.1)
	Compliance (% in those expected to complete questionnaires) ^d	186 (79.8)	160 (71.7)
	Not completed	47 (19.6)	63 (26.0)
	With visit, no record	47 (19.6)	63 (26.0)
	Missing by Design	7 (2.9)	19 (7.9)
	Discontinued due to death	4 (1.7)	12 (5.0)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	1 (0.4)
Week 14	Expected to Complete Questionnaires	231 (96.3)	221 (91.3)
	Completed ^c	186 (77.5)	154 (63.6)
	Compliance (% in those expected to complete questionnaires) ^d	186 (80.5)	154 (69.7)
	Not completed	45 (18.8)	67 (27.7)
	With visit, no record	45 (18.8)	67 (27.7)
	Missing by Design	9 (3.8)	21 (8.7)
	Discontinued due to death	6 (2.5)	15 (6.2)
	Discontinued due to withdrawal by participant	2 (0.8)	6 (2.5)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 17	Expected to Complete Questionnaires	227 (94.6)	217 (89.7)
	Completed ^c	178 (74.2)	156 (64.5)
	Compliance (% in those expected to complete questionnaires) ^d	178 (78.4)	156 (71.9)
	Not completed	49 (20.4)	61 (25.2)
	With visit, no record	49 (20.4)	61 (25.2)
	Missing by Design	13 (5.4)	25 (10.3)
	Discontinued due to death	10 (4.2)	18 (7.4)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 20	Expected to Complete Questionnaires	226 (94.2)	211 (87.2)
	Completed ^c	168 (70.0)	127 (52.5)
	Compliance (% in those expected to complete questionnaires) ^d	168 (74.3)	127 (60.2)
	Not completed	58 (24.2)	84 (34.7)
	With visit, no record	58 (24.2)	84 (34.7)
	Missing by Design	14 (5.8)	31 (12.8)
	Discontinued due to death	11 (4.6)	24 (9.9)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 23	Expected to Complete Questionnaires	223 (92.9)	206 (85.1)
	Completed ^c	162 (67.5)	117 (48.3)
	Compliance (% in those expected to complete questionnaires) ^d	162 (72.6)	117 (56.8)
	Not completed	61 (25.4)	89 (36.8)
	With visit, no record	61 (25.4)	89 (36.8)
	Missing by Design	17 (7.1)	36 (14.9)
	Discontinued due to death	14 (5.8)	29 (12.0)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 26	Expected to Complete Questionnaires	220 (91.7)	200 (82.6)
	Completed ^c	157 (65.4)	108 (44.6)
	Compliance (% in those expected to complete questionnaires) ^d	157 (71.4)	108 (54.0)
	Not completed	63 (26.3)	92 (38.0)
	With visit, no record	63 (26.3)	92 (38.0)
	Missing by Design	20 (8.3)	42 (17.4)
	Discontinued due to death	17 (7.1)	35 (14.5)
	Discontinued due to withdrawal by participant	2 (0.8)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 29	Expected to Complete Questionnaires	215 (89.6)	198 (81.8)
	Completed ^c	157 (65.4)	100 (41.3)
	Compliance (% in those expected to complete questionnaires) ^d	157 (73.0)	100 (50.5)
	Not completed	58 (24.2)	98 (40.5)
	With visit, no record	58 (24.2)	98 (40.5)
	Missing by Design	25 (10.4)	44 (18.2)
	Discontinued due to death	21 (8.8)	37 (15.3)
	Discontinued due to withdrawal by participant	3 (1.3)	7 (2.9)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 32	Expected to Complete Questionnaires	214 (89.2)	187 (77.3)
	Completed ^c	135 (56.3)	83 (34.3)
	Compliance (% in those expected to complete questionnaires) ^d	135 (63.1)	83 (44.4)
	Not completed	79 (32.9)	104 (43.0)
	With visit, no record	79 (32.9)	104 (43.0)
	Missing by Design	26 (10.8)	55 (22.7)
	Discontinued due to death	22 (9.2)	47 (19.4)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 35	Expected to Complete Questionnaires	211 (87.9)	180 (74.4)
	Completed ^c	133 (55.4)	76 (31.4)
	Compliance (% in those expected to complete questionnaires) ^d	133 (63.0)	76 (42.2)
	Not completed	78 (32.5)	104 (43.0)
	With visit, no record	78 (32.5)	104 (43.0)
	Missing by Design	29 (12.1)	62 (25.6)
	Discontinued due to death	25 (10.4)	54 (22.3)
	Discontinued due to withdrawal by participant	3 (1.3)	8 (3.3)
	Visit not scheduled	1 (0.4)	0 (0.0)
Week 38	Expected to Complete Questionnaires	208 (86.7)	174 (71.9)
	Completed ^c	133 (55.4)	74 (30.6)
	Compliance (% in those expected to complete questionnaires) ^d	133 (63.9)	74 (42.5)
	Not completed	75 (31.3)	100 (41.3)
	With visit, no record	75 (31.3)	100 (41.3)
	Missing by Design	32 (13.3)	68 (28.1)
	Discontinued due to death	27 (11.3)	59 (24.4)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	1 (0.4)	1 (0.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 41	Expected to Complete Questionnaires	202 (84.2)	164 (67.8)
	Completed ^c	129 (53.8)	65 (26.9)
	Compliance (% in those expected to complete questionnaires) ^d	129 (63.9)	65 (39.6)
	Not completed	73 (30.4)	99 (40.9)
	With visit, no record	73 (30.4)	99 (40.9)
	Missing by Design	38 (15.8)	78 (32.2)
	Discontinued due to death	30 (12.5)	65 (26.9)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	4 (1.7)	5 (2.1)
Week 44	Expected to Complete Questionnaires	190 (79.2)	148 (61.2)
	Completed ^c	108 (45.0)	60 (24.8)
	Compliance (% in those expected to complete questionnaires) ^d	108 (56.8)	60 (40.5)
	Not completed	82 (34.2)	88 (36.4)
	With visit, no record	82 (34.2)	88 (36.4)
	Missing by Design	50 (20.8)	94 (38.8)
	Discontinued due to death	33 (13.8)	68 (28.1)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	13 (5.4)	18 (7.4)
Week 47	Expected to Complete Questionnaires	172 (71.7)	142 (58.7)
	Completed ^c	100 (41.7)	57 (23.6)
	Compliance (% in those expected to complete questionnaires) ^d	100 (58.1)	57 (40.1)
	Not completed	72 (30.0)	85 (35.1)
	With visit, no record	72 (30.0)	85 (35.1)
	Missing by Design	68 (28.3)	100 (41.3)
	Discontinued due to death	39 (16.3)	71 (29.3)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	25 (10.4)	21 (8.7)
Week 50	Expected to Complete Questionnaires	162 (67.5)	132 (54.5)
	Completed ^c	89 (37.1)	51 (21.1)
	Compliance (% in those expected to complete questionnaires) ^d	89 (54.9)	51 (38.6)
	Not completed	73 (30.4)	81 (33.5)
	With visit, no record	73 (30.4)	81 (33.5)
	Missing by Design	78 (32.5)	110 (45.5)
	Discontinued due to death	41 (17.1)	73 (30.2)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	33 (13.8)	29 (12.0)
Week 53	Expected to Complete Questionnaires	149 (62.1)	122 (50.4)
	Completed ^c	79 (32.9)	46 (19.0)
	Compliance (% in those expected to complete questionnaires) ^d	79 (53.0)	46 (37.7)
	Not completed	70 (29.2)	76 (31.4)
	With visit, no record	70 (29.2)	76 (31.4)
	Missing by Design	91 (37.9)	120 (49.6)
	Discontinued due to death	44 (18.3)	77 (31.8)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	43 (17.9)	35 (14.5)
Week 56	Expected to Complete Questionnaires	140 (58.3)	117 (48.3)
	Completed ^c	81 (33.8)	39 (16.1)
	Compliance (% in those expected to complete questionnaires) ^d	81 (57.9)	39 (33.3)
	Not completed	59 (24.6)	78 (32.2)
	With visit, no record	59 (24.6)	78 (32.2)
	Missing by Design	100 (41.7)	125 (51.7)
	Discontinued due to death	48 (20.0)	79 (32.6)
	Discontinued due to withdrawal by participant	4 (1.7)	8 (3.3)
	Visit not scheduled	48 (20.0)	38 (15.7)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 59	Expected to Complete Questionnaires	132 (55.0)	107 (44.2)
	Completed ^c	72 (30.0)	37 (15.3)
	Compliance (% in those expected to complete questionnaires) ^d	72 (54.5)	37 (34.6)
	Not completed	60 (25.0)	70 (28.9)
	With visit, no record	60 (25.0)	70 (28.9)
	Missing by Design	108 (45.0)	135 (55.8)
	Discontinued due to death	49 (20.4)	82 (33.9)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	54 (22.5)	45 (18.6)
Week 62	Expected to Complete Questionnaires	127 (52.9)	100 (41.3)
	Completed ^c	65 (27.1)	32 (13.2)
	Compliance (% in those expected to complete questionnaires) ^d	65 (51.2)	32 (32.0)
	Not completed	62 (25.8)	68 (28.1)
	With visit, no record	62 (25.8)	68 (28.1)
	Missing by Design	113 (47.1)	142 (58.7)
	Discontinued due to death	50 (20.8)	86 (35.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	58 (24.2)	48 (19.8)
Week 65	Expected to Complete Questionnaires	112 (46.7)	92 (38.0)
	Completed ^c	58 (24.2)	30 (12.4)
	Compliance (% in those expected to complete questionnaires) ^d	58 (51.8)	30 (32.6)
	Not completed	54 (22.5)	62 (25.6)
	With visit, no record	54 (22.5)	62 (25.6)
	Missing by Design	128 (53.3)	150 (62.0)
	Discontinued due to death	53 (22.1)	87 (36.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	70 (29.2)	55 (22.7)
Week 68	Expected to Complete Questionnaires	105 (43.8)	83 (34.3)
	Completed ^c	53 (22.1)	25 (10.3)
	Compliance (% in those expected to complete questionnaires) ^d	53 (50.5)	25 (30.1)
	Not completed	52 (21.7)	58 (24.0)
	With visit, no record	52 (21.7)	58 (24.0)
	Missing by Design	135 (56.3)	159 (65.7)
	Discontinued due to death	55 (22.9)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	75 (31.3)	59 (24.4)
Week 71	Expected to Complete Questionnaires	98 (40.8)	79 (32.6)
	Completed ^c	51 (21.3)	22 (9.1)
	Compliance (% in those expected to complete questionnaires) ^d	51 (52.0)	22 (27.8)
	Not completed	47 (19.6)	57 (23.6)
	With visit, no record	47 (19.6)	57 (23.6)
	Missing by Design	142 (59.2)	163 (67.4)
	Discontinued due to death	56 (23.3)	92 (38.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	81 (33.8)	63 (26.0)
Week 74	Expected to Complete Questionnaires	92 (38.3)	66 (27.3)
	Completed ^c	47 (19.6)	21 (8.7)
	Compliance (% in those expected to complete questionnaires) ^d	47 (51.1)	21 (31.8)
	Not completed	45 (18.8)	45 (18.6)
	With visit, no record	45 (18.8)	45 (18.6)
	Missing by Design	148 (61.7)	176 (72.7)
	Discontinued due to death	57 (23.8)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	86 (35.8)	70 (28.9)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 77	Expected to Complete Questionnaires	82 (34.2)	62 (25.6)
	Completed ^c	45 (18.8)	18 (7.4)
	Compliance (% in those expected to complete questionnaires) ^d	45 (54.9)	18 (29.0)
	Not completed	37 (15.4)	44 (18.2)
	With visit, no record	37 (15.4)	44 (18.2)
	Missing by Design	158 (65.8)	180 (74.4)
	Discontinued due to death	58 (24.2)	98 (40.5)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	95 (39.6)	74 (30.6)
Week 80	Expected to Complete Questionnaires	73 (30.4)	55 (22.7)
	Completed ^c	40 (16.7)	14 (5.8)
	Compliance (% in those expected to complete questionnaires) ^d	40 (54.8)	14 (25.5)
	Not completed	33 (13.8)	41 (16.9)
	With visit, no record	33 (13.8)	41 (16.9)
	Missing by Design	167 (69.6)	187 (77.3)
	Discontinued due to death	59 (24.6)	103 (42.6)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	103 (42.9)	76 (31.4)
Week 83	Expected to Complete Questionnaires	70 (29.2)	49 (20.2)
	Completed ^c	37 (15.4)	13 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	37 (52.9)	13 (26.5)
	Not completed	33 (13.8)	36 (14.9)
	With visit, no record	33 (13.8)	36 (14.9)
	Missing by Design	170 (70.8)	193 (79.8)
	Discontinued due to death	59 (24.6)	104 (43.0)
	Discontinued due to withdrawal by participant	5 (2.1)	8 (3.3)
	Visit not scheduled	106 (44.2)	81 (33.5)
Week 86	Expected to Complete Questionnaires	63 (26.3)	40 (16.5)
	Completed ^c	34 (14.2)	12 (5.0)
	Compliance (% in those expected to complete questionnaires) ^d	34 (54.0)	12 (30.0)
	Not completed	29 (12.1)	28 (11.6)
	With visit, no record	29 (12.1)	28 (11.6)
	Missing by Design	177 (73.8)	202 (83.5)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	112 (46.7)	87 (36.0)
Week 89	Expected to Complete Questionnaires	57 (23.8)	38 (15.7)
	Completed ^c	33 (13.8)	11 (4.5)
	Compliance (% in those expected to complete questionnaires) ^d	33 (57.9)	11 (28.9)
	Not completed	24 (10.0)	27 (11.2)
	With visit, no record	24 (10.0)	27 (11.2)
	Missing by Design	183 (76.3)	204 (84.3)
	Discontinued due to death	60 (25.0)	106 (43.8)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	118 (49.2)	89 (36.8)
Week 92	Expected to Complete Questionnaires	49 (20.4)	33 (13.6)
	Completed ^c	27 (11.3)	8 (3.3)
	Compliance (% in those expected to complete questionnaires) ^d	27 (55.1)	8 (24.2)
	Not completed	22 (9.2)	25 (10.3)
	With visit, no record	22 (9.2)	25 (10.3)
	Missing by Design	191 (79.6)	209 (86.4)
	Discontinued due to death	61 (25.4)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	125 (52.1)	93 (38.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 95	Expected to Complete Questionnaires	41 (17.1)	30 (12.4)
	Completed ^c	22 (9.2)	9 (3.7)
	Compliance (% in those expected to complete questionnaires) ^d	22 (53.7)	9 (30.0)
	Not completed	19 (7.9)	21 (8.7)
	With visit, no record	19 (7.9)	21 (8.7)
	Missing by Design	199 (82.9)	212 (87.6)
	Discontinued due to death	62 (25.8)	107 (44.2)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	132 (55.0)	96 (39.7)
Week 98	Expected to Complete Questionnaires	35 (14.6)	27 (11.2)
	Completed ^c	18 (7.5)	6 (2.5)
	Compliance (% in those expected to complete questionnaires) ^d	18 (51.4)	6 (22.2)
	Not completed	17 (7.1)	21 (8.7)
	With visit, no record	17 (7.1)	21 (8.7)
	Missing by Design	205 (85.4)	215 (88.8)
	Discontinued due to death	63 (26.3)	108 (44.6)
	Discontinued due to withdrawal by participant	5 (2.1)	9 (3.7)
	Visit not scheduled	137 (57.1)	98 (40.5)
Week 101	Expected to Complete Questionnaires	30 (12.5)	25 (10.3)
	Completed ^c	14 (5.8)	5 (2.1)
	Compliance (% in those expected to complete questionnaires) ^d	14 (46.7)	5 (20.0)
	Not completed	16 (6.7)	20 (8.3)
	With visit, no record	16 (6.7)	20 (8.3)
	Missing by Design	210 (87.5)	217 (89.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	140 (58.3)	100 (41.3)
Week 104	Expected to Complete Questionnaires	26 (10.8)	20 (8.3)
	Completed ^c	10 (4.2)	4 (1.7)
	Compliance (% in those expected to complete questionnaires) ^d	10 (38.5)	4 (20.0)
	Not completed	16 (6.7)	16 (6.6)
	With visit, no record	16 (6.7)	16 (6.6)
	Missing by Design	214 (89.2)	222 (91.7)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	144 (60.0)	105 (43.4)
Week 107	Expected to Complete Questionnaires	24 (10.0)	16 (6.6)
	Completed ^c	8 (3.3)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	8 (33.3)	3 (18.8)
	Not completed	16 (6.7)	13 (5.4)
	With visit, no record	16 (6.7)	13 (5.4)
	Missing by Design	216 (90.0)	226 (93.4)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	146 (60.8)	109 (45.0)
Week 110	Expected to Complete Questionnaires	21 (8.8)	15 (6.2)
	Completed ^c	6 (2.5)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	6 (28.6)	3 (20.0)
	Not completed	15 (6.3)	12 (5.0)
	With visit, no record	15 (6.3)	12 (5.0)
	Missing by Design	219 (91.3)	227 (93.8)
	Discontinued due to death	64 (26.7)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
	Visit not scheduled	149 (62.1)	110 (45.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 113	Expected to Complete Questionnaires	18 (7.5)	15 (6.2)
	Completed ^c	8 (3.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	8 (44.4)	2 (13.3)
	Not completed	10 (4.2)	13 (5.4)
	With visit, no record	10 (4.2)	13 (5.4)
	Missing by Design	222 (92.5)	227 (93.8)
	Discontinued due to death	66 (27.5)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	150 (62.5)	110 (45.5)	
Week 116	Expected to Complete Questionnaires	15 (6.3)	14 (5.8)
	Completed ^c	5 (2.1)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	5 (33.3)	3 (21.4)
	Not completed	10 (4.2)	11 (4.5)
	With visit, no record	10 (4.2)	11 (4.5)
	Missing by Design	225 (93.8)	228 (94.2)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	152 (63.3)	111 (45.9)	
Week 119	Expected to Complete Questionnaires	11 (4.6)	12 (5.0)
	Completed ^c	5 (2.1)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	5 (45.5)	1 (8.3)
	Not completed	6 (2.5)	11 (4.5)
	With visit, no record	6 (2.5)	11 (4.5)
	Missing by Design	229 (95.4)	230 (95.0)
	Discontinued due to death	67 (27.9)	108 (44.6)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	156 (65.0)	113 (46.7)	
Week 122	Expected to Complete Questionnaires	9 (3.8)	9 (3.7)
	Completed ^c	4 (1.7)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	4 (44.4)	3 (33.3)
	Not completed	5 (2.1)	6 (2.5)
	With visit, no record	5 (2.1)	6 (2.5)
	Missing by Design	231 (96.3)	233 (96.3)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	158 (65.8)	115 (47.5)	
Week 125	Expected to Complete Questionnaires	8 (3.3)	6 (2.5)
	Completed ^c	3 (1.3)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	3 (37.5)	2 (33.3)
	Not completed	5 (2.1)	4 (1.7)
	With visit, no record	5 (2.1)	4 (1.7)
	Missing by Design	232 (96.7)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	159 (66.3)	118 (48.8)	
Week 128	Expected to Complete Questionnaires	6 (2.5)	6 (2.5)
	Completed ^c	1 (0.4)	3 (1.2)
	Compliance (% in those expected to complete questionnaires) ^d	1 (16.7)	3 (50.0)
	Not completed	5 (2.1)	3 (1.2)
	With visit, no record	5 (2.1)	3 (1.2)
	Missing by Design	234 (97.5)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	161 (67.1)	118 (48.8)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 131	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	
Week 134	Expected to Complete Questionnaires	4 (1.7)	6 (2.5)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (25.0)	2 (33.3)
	Not completed	3 (1.3)	4 (1.7)
	With visit, no record	3 (1.3)	4 (1.7)
	Missing by Design	236 (98.3)	236 (97.5)
	Discontinued due to death	67 (27.9)	109 (45.0)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	163 (67.9)	118 (48.8)	
Week 137	Expected to Complete Questionnaires	2 (0.8)	5 (2.1)
	Completed ^c	1 (0.4)	2 (0.8)
	Compliance (% in those expected to complete questionnaires) ^d	1 (50.0)	2 (40.0)
	Not completed	1 (0.4)	3 (1.2)
	With visit, no record	1 (0.4)	3 (1.2)
	Missing by Design	238 (99.2)	237 (97.9)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	164 (68.3)	118 (48.8)	
Week 140	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 143	Expected to Complete Questionnaires	1 (0.4)	3 (1.2)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (33.3)
	Not completed	1 (0.4)	2 (0.8)
	With visit, no record	1 (0.4)	2 (0.8)
	Missing by Design	239 (99.6)	239 (98.8)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	120 (49.6)	
Week 146	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 240 n (%)	N ^b = 242 n (%)
Week 149	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	
Week 152	Expected to Complete Questionnaires	1 (0.4)	2 (0.8)
	Completed ^c	0 (0.0)	1 (0.4)
	Compliance (% in those expected to complete questionnaires) ^d	0 (0.0)	1 (50.0)
	Not completed	1 (0.4)	1 (0.4)
	With visit, no record	1 (0.4)	1 (0.4)
	Missing by Design	239 (99.6)	240 (99.2)
	Discontinued due to death	68 (28.3)	110 (45.5)
	Discontinued due to withdrawal by participant	6 (2.5)	9 (3.7)
Visit not scheduled	165 (68.8)	121 (50.0)	

a: Database Cutoff Date: 08AUG2023
b: Number of participants: intention-to-treat population, cisplatin eligible
c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set
d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred
ITT: Intention-to-Treat

Cisplatin ungeeignet

Tabelle 4G-8: Rücklaufquoten mit Gründen für das Fehlen von Werten im EORTC QLQ-C30 (Cisplatin ungeeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Baseline	Expected to Complete Questionnaires	202 (100.0)	202 (100.0)
	Completed ^c	160 (79.2)	165 (81.7)
	Compliance (% in those expected to complete questionnaires) ^d	160 (79.2)	165 (81.7)
	Not completed	42 (20.8)	37 (18.3)
	With visit, no record	42 (20.8)	37 (18.3)
	Missing by Design	0 (0.0)	0 (0.0)
Week 1	Expected to Complete Questionnaires	201 (99.5)	197 (97.5)
	Completed ^c	141 (69.8)	144 (71.3)
	Compliance (% in those expected to complete questionnaires) ^d	141 (70.1)	144 (73.1)
	Not completed	60 (29.7)	53 (26.2)
	With visit, no record	60 (29.7)	53 (26.2)
	Missing by Design	1 (0.5)	5 (2.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
Visit not scheduled	1 (0.5)	4 (2.0)	
Week 2	Expected to Complete Questionnaires	198 (98.0)	194 (96.0)
	Completed ^c	150 (74.3)	147 (72.8)
	Compliance (% in those expected to complete questionnaires) ^d	150 (75.8)	147 (75.8)
	Not completed	48 (23.8)	47 (23.3)
	With visit, no record	48 (23.8)	47 (23.3)
	Missing by Design	4 (2.0)	8 (4.0)
	Discontinued due to death	3 (1.5)	3 (1.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
Visit not scheduled	1 (0.5)	4 (2.0)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 3	Expected to Complete Questionnaires	196 (97.0)	193 (95.5)
	Completed ^c	139 (68.8)	149 (73.8)
	Compliance (% in those expected to complete questionnaires) ^d	139 (70.9)	149 (77.2)
	Not completed	57 (28.2)	44 (21.8)
	With visit, no record	57 (28.2)	44 (21.8)
	Missing by Design	6 (3.0)	9 (4.5)
	Discontinued due to death	5 (2.5)	4 (2.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 4	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	145 (71.8)	150 (74.3)
	Compliance (% in those expected to complete questionnaires) ^d	145 (75.1)	150 (78.9)
	Not completed	48 (23.8)	40 (19.8)
	With visit, no record	48 (23.8)	40 (19.8)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 5	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	137 (67.8)	153 (75.7)
	Compliance (% in those expected to complete questionnaires) ^d	137 (71.0)	153 (80.5)
	Not completed	56 (27.7)	37 (18.3)
	With visit, no record	56 (27.7)	37 (18.3)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 6	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	146 (72.3)	145 (71.8)
	Compliance (% in those expected to complete questionnaires) ^d	146 (76.4)	145 (76.3)
	Not completed	45 (22.3)	45 (22.3)
	With visit, no record	45 (22.3)	45 (22.3)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 7	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	147 (72.8)	148 (73.3)
	Compliance (% in those expected to complete questionnaires) ^d	147 (77.0)	148 (77.9)
	Not completed	44 (21.8)	42 (20.8)
	With visit, no record	44 (21.8)	42 (20.8)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 8	Expected to Complete Questionnaires	191 (94.6)	189 (93.6)
	Completed ^c	147 (72.8)	145 (71.8)
	Compliance (% in those expected to complete questionnaires) ^d	147 (77.0)	145 (76.7)
	Not completed	44 (21.8)	44 (21.8)
	With visit, no record	44 (21.8)	44 (21.8)
	Missing by Design	11 (5.4)	13 (6.4)
	Discontinued due to death	10 (5.0)	8 (4.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 9	Expected to Complete Questionnaires	190 (94.1)	188 (93.1)
	Completed ^c	142 (70.3)	141 (69.8)
	Compliance (% in those expected to complete questionnaires) ^d	142 (74.7)	141 (75.0)
	Not completed	48 (23.8)	47 (23.3)
	With visit, no record	48 (23.8)	47 (23.3)
	Missing by Design	12 (5.9)	14 (6.9)
	Discontinued due to death	10 (5.0)	10 (5.0)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 10	Expected to Complete Questionnaires	188 (93.1)	187 (92.6)
	Completed ^c	139 (68.8)	142 (70.3)
	Compliance (% in those expected to complete questionnaires) ^d	139 (73.9)	142 (75.9)
	Not completed	49 (24.3)	45 (22.3)
	With visit, no record	49 (24.3)	45 (22.3)
	Missing by Design	14 (6.9)	15 (7.4)
	Discontinued due to death	12 (5.9)	11 (5.4)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 11	Expected to Complete Questionnaires	186 (92.1)	186 (92.1)
	Completed ^c	137 (67.8)	126 (62.4)
	Compliance (% in those expected to complete questionnaires) ^d	137 (73.7)	126 (67.7)
	Not completed	49 (24.3)	60 (29.7)
	With visit, no record	49 (24.3)	60 (29.7)
	Missing by Design	16 (7.9)	16 (7.9)
	Discontinued due to death	13 (6.4)	12 (5.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 12	Expected to Complete Questionnaires	186 (92.1)	185 (91.6)
	Completed ^c	142 (70.3)	130 (64.4)
	Compliance (% in those expected to complete questionnaires) ^d	142 (76.3)	130 (70.3)
	Not completed	44 (21.8)	55 (27.2)
	With visit, no record	44 (21.8)	55 (27.2)
	Missing by Design	16 (7.9)	17 (8.4)
	Discontinued due to death	13 (6.4)	13 (6.4)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 14	Expected to Complete Questionnaires	185 (91.6)	180 (89.1)
	Completed ^c	139 (68.8)	125 (61.9)
	Compliance (% in those expected to complete questionnaires) ^d	139 (75.1)	125 (69.4)
	Not completed	46 (22.8)	55 (27.2)
	With visit, no record	46 (22.8)	55 (27.2)
	Missing by Design	17 (8.4)	22 (10.9)
	Discontinued due to death	14 (6.9)	18 (8.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 17	Expected to Complete Questionnaires	181 (89.6)	174 (86.1)
	Completed ^c	132 (65.3)	120 (59.4)
	Compliance (% in those expected to complete questionnaires) ^d	132 (72.9)	120 (69.0)
	Not completed	49 (24.3)	54 (26.7)
	With visit, no record	49 (24.3)	54 (26.7)
	Missing by Design	21 (10.4)	28 (13.9)
	Discontinued due to death	18 (8.9)	24 (11.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 20	Expected to Complete Questionnaires	180 (89.1)	169 (83.7)
	Completed ^c	120 (59.4)	104 (51.5)
	Compliance (% in those expected to complete questionnaires) ^d	120 (66.7)	104 (61.5)
	Not completed	60 (29.7)	65 (32.2)
	With visit, no record	60 (29.7)	65 (32.2)
	Missing by Design	22 (10.9)	33 (16.3)
	Discontinued due to death	18 (8.9)	29 (14.4)
	Discontinued due to withdrawal by participant	3 (1.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 23	Expected to Complete Questionnaires	177 (87.6)	159 (78.7)
	Completed ^c	117 (57.9)	88 (43.6)
	Compliance (% in those expected to complete questionnaires) ^d	117 (66.1)	88 (55.3)
	Not completed	60 (29.7)	71 (35.1)
	With visit, no record	60 (29.7)	71 (35.1)
	Missing by Design	25 (12.4)	43 (21.3)
	Discontinued due to death	21 (10.4)	38 (18.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 26	Expected to Complete Questionnaires	173 (85.6)	154 (76.2)
	Completed ^c	112 (55.4)	81 (40.1)
	Compliance (% in those expected to complete questionnaires) ^d	112 (64.7)	81 (52.6)
	Not completed	61 (30.2)	73 (36.1)
	With visit, no record	61 (30.2)	73 (36.1)
	Missing by Design	29 (14.4)	48 (23.8)
	Discontinued due to death	25 (12.4)	44 (21.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 29	Expected to Complete Questionnaires	170 (84.2)	150 (74.3)
	Completed ^c	107 (53.0)	77 (38.1)
	Compliance (% in those expected to complete questionnaires) ^d	107 (62.9)	77 (51.3)
	Not completed	63 (31.2)	73 (36.1)
	With visit, no record	63 (31.2)	73 (36.1)
	Missing by Design	32 (15.8)	52 (25.7)
	Discontinued due to death	28 (13.9)	48 (23.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 32	Expected to Complete Questionnaires	165 (81.7)	142 (70.3)
	Completed ^c	102 (50.5)	63 (31.2)
	Compliance (% in those expected to complete questionnaires) ^d	102 (61.8)	63 (44.4)
	Not completed	63 (31.2)	79 (39.1)
	With visit, no record	63 (31.2)	79 (39.1)
	Missing by Design	37 (18.3)	60 (29.7)
	Discontinued due to death	31 (15.3)	55 (27.2)
	Discontinued due to withdrawal by participant	5 (2.5)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 35	Expected to Complete Questionnaires	163 (80.7)	135 (66.8)
	Completed ^c	98 (48.5)	62 (30.7)
	Compliance (% in those expected to complete questionnaires) ^d	98 (60.1)	62 (45.9)
	Not completed	65 (32.2)	73 (36.1)
	With visit, no record	65 (32.2)	73 (36.1)
	Missing by Design	39 (19.3)	67 (33.2)
	Discontinued due to death	32 (15.8)	62 (30.7)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 38	Expected to Complete Questionnaires	157 (77.7)	129 (63.9)
	Completed ^c	97 (48.0)	56 (27.7)
	Compliance (% in those expected to complete questionnaires) ^d	97 (61.8)	56 (43.4)
	Not completed	60 (29.7)	73 (36.1)
	With visit, no record	60 (29.7)	73 (36.1)
	Missing by Design	45 (22.3)	73 (36.1)
	Discontinued due to death	37 (18.3)	67 (33.2)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	2 (1.0)	3 (1.5)
Week 41	Expected to Complete Questionnaires	153 (75.7)	122 (60.4)
	Completed ^c	95 (47.0)	52 (25.7)
	Compliance (% in those expected to complete questionnaires) ^d	95 (62.1)	52 (42.6)
	Not completed	58 (28.7)	70 (34.7)
	With visit, no record	58 (28.7)	70 (34.7)
	Missing by Design	49 (24.3)	80 (39.6)
	Discontinued due to death	39 (19.3)	71 (35.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	4 (2.0)	6 (3.0)
Week 44	Expected to Complete Questionnaires	141 (69.8)	108 (53.5)
	Completed ^c	86 (42.6)	49 (24.3)
	Compliance (% in those expected to complete questionnaires) ^d	86 (61.0)	49 (45.4)
	Not completed	55 (27.2)	59 (29.2)
	With visit, no record	55 (27.2)	59 (29.2)
	Missing by Design	61 (30.2)	94 (46.5)
	Discontinued due to death	42 (20.8)	77 (38.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	13 (6.4)	14 (6.9)
Week 47	Expected to Complete Questionnaires	131 (64.9)	98 (48.5)
	Completed ^c	79 (39.1)	43 (21.3)
	Compliance (% in those expected to complete questionnaires) ^d	79 (60.3)	43 (43.9)
	Not completed	52 (25.7)	55 (27.2)
	With visit, no record	52 (25.7)	55 (27.2)
	Missing by Design	71 (35.1)	104 (51.5)
	Discontinued due to death	45 (22.3)	81 (40.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	20 (9.9)	20 (9.9)
Week 50	Expected to Complete Questionnaires	126 (62.4)	92 (45.5)
	Completed ^c	74 (36.6)	36 (17.8)
	Compliance (% in those expected to complete questionnaires) ^d	74 (58.7)	36 (39.1)
	Not completed	52 (25.7)	56 (27.7)
	With visit, no record	52 (25.7)	56 (27.7)
	Missing by Design	76 (37.6)	110 (54.5)
	Discontinued due to death	45 (22.3)	84 (41.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	25 (12.4)	23 (11.4)
Week 53	Expected to Complete Questionnaires	120 (59.4)	80 (39.6)
	Completed ^c	74 (36.6)	31 (15.3)
	Compliance (% in those expected to complete questionnaires) ^d	74 (61.7)	31 (38.8)
	Not completed	46 (22.8)	49 (24.3)
	With visit, no record	46 (22.8)	49 (24.3)
	Missing by Design	82 (40.6)	122 (60.4)
	Discontinued due to death	48 (23.8)	90 (44.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	28 (13.9)	29 (14.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 56	Expected to Complete Questionnaires	112 (55.4)	73 (36.1)
	Completed ^c	72 (35.6)	30 (14.9)
	Compliance (% in those expected to complete questionnaires) ^d	72 (64.3)	30 (41.1)
	Not completed	40 (19.8)	43 (21.3)
	With visit, no record	40 (19.8)	43 (21.3)
	Missing by Design	90 (44.6)	129 (63.9)
	Discontinued due to death	48 (23.8)	94 (46.5)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	36 (17.8)	32 (15.8)
Week 59	Expected to Complete Questionnaires	106 (52.5)	64 (31.7)
	Completed ^c	69 (34.2)	23 (11.4)
	Compliance (% in those expected to complete questionnaires) ^d	69 (65.1)	23 (35.9)
	Not completed	37 (18.3)	41 (20.3)
	With visit, no record	37 (18.3)	41 (20.3)
	Missing by Design	96 (47.5)	138 (68.3)
	Discontinued due to death	50 (24.8)	98 (48.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	40 (19.8)	36 (17.8)
Week 62	Expected to Complete Questionnaires	94 (46.5)	60 (29.7)
	Completed ^c	62 (30.7)	20 (9.9)
	Compliance (% in those expected to complete questionnaires) ^d	62 (66.0)	20 (33.3)
	Not completed	32 (15.8)	40 (19.8)
	With visit, no record	32 (15.8)	40 (19.8)
	Missing by Design	108 (53.5)	142 (70.3)
	Discontinued due to death	53 (26.2)	100 (49.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	49 (24.3)	37 (18.3)	
Week 65	Expected to Complete Questionnaires	88 (43.6)	52 (25.7)
	Completed ^c	43 (21.3)	17 (8.4)
	Compliance (% in those expected to complete questionnaires) ^d	43 (48.9)	17 (32.7)
	Not completed	45 (22.3)	35 (17.3)
	With visit, no record	45 (22.3)	35 (17.3)
	Missing by Design	114 (56.4)	150 (74.3)
	Discontinued due to death	53 (26.2)	102 (50.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	55 (27.2)	43 (21.3)	
Week 68	Expected to Complete Questionnaires	83 (41.1)	48 (23.8)
	Completed ^c	46 (22.8)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	46 (55.4)	13 (27.1)
	Not completed	37 (18.3)	35 (17.3)
	With visit, no record	37 (18.3)	35 (17.3)
	Missing by Design	119 (58.9)	154 (76.2)
	Discontinued due to death	54 (26.7)	104 (51.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	59 (29.2)	45 (22.3)	
Week 71	Expected to Complete Questionnaires	79 (39.1)	42 (20.8)
	Completed ^c	42 (20.8)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	42 (53.2)	13 (31.0)
	Not completed	37 (18.3)	29 (14.4)
	With visit, no record	37 (18.3)	29 (14.4)
	Missing by Design	123 (60.9)	160 (79.2)
	Discontinued due to death	54 (26.7)	106 (52.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Visit not scheduled	63 (31.2)	49 (24.3)
Week 74	Expected to Complete Questionnaires	71 (35.1)	38 (18.8)
	Completed ^c	38 (18.8)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	38 (53.5)	11 (28.9)
	Not completed	33 (16.3)	27 (13.4)
	With visit, no record	33 (16.3)	27 (13.4)
	Missing by Design	131 (64.9)	164 (81.2)
	Discontinued due to death	55 (27.2)	107 (53.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	70 (34.7)	52 (25.7)
Week 77	Expected to Complete Questionnaires	64 (31.7)	33 (16.3)
	Completed ^c	37 (18.3)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	37 (57.8)	11 (33.3)
	Not completed	27 (13.4)	22 (10.9)
	With visit, no record	27 (13.4)	22 (10.9)
	Missing by Design	138 (68.3)	169 (83.7)
	Discontinued due to death	55 (27.2)	109 (54.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	77 (38.1)	55 (27.2)
Week 80	Expected to Complete Questionnaires	60 (29.7)	30 (14.9)
	Completed ^c	36 (17.8)	8 (4.0)
	Compliance (% in those expected to complete questionnaires) ^d	36 (60.0)	8 (26.7)
	Not completed	24 (11.9)	22 (10.9)
	With visit, no record	24 (11.9)	22 (10.9)
	Missing by Design	142 (70.3)	172 (85.1)
	Discontinued due to death	57 (28.2)	110 (54.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	79 (39.1)	57 (28.2)
Week 83	Expected to Complete Questionnaires	56 (27.7)	26 (12.9)
	Completed ^c	30 (14.9)	9 (4.5)
	Compliance (% in those expected to complete questionnaires) ^d	30 (53.6)	9 (34.6)
	Not completed	26 (12.9)	17 (8.4)
	With visit, no record	26 (12.9)	17 (8.4)
	Missing by Design	146 (72.3)	176 (87.1)
	Discontinued due to death	59 (29.2)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	81 (40.1)	59 (29.2)
Week 86	Expected to Complete Questionnaires	49 (24.3)	20 (9.9)
	Completed ^c	26 (12.9)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	26 (53.1)	6 (30.0)
	Not completed	23 (11.4)	14 (6.9)
	With visit, no record	23 (11.4)	14 (6.9)
	Missing by Design	153 (75.7)	182 (90.1)
	Discontinued due to death	60 (29.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	87 (43.1)	65 (32.2)
Week 89	Expected to Complete Questionnaires	43 (21.3)	17 (8.4)
	Completed ^c	20 (9.9)	7 (3.5)
	Compliance (% in those expected to complete questionnaires) ^d	20 (46.5)	7 (41.2)
	Not completed	23 (11.4)	10 (5.0)
	With visit, no record	23 (11.4)	10 (5.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Missing by Design	159 (78.7)	185 (91.6)
	Discontinued due to death	62 (30.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	91 (45.0)	68 (33.7)
Week 92	Expected to Complete Questionnaires	36 (17.8)	14 (6.9)
	Completed ^c	19 (9.4)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	19 (52.8)	6 (42.9)
	Not completed	17 (8.4)	8 (4.0)
	With visit, no record	17 (8.4)	8 (4.0)
	Missing by Design	166 (82.2)	188 (93.1)
	Discontinued due to death	63 (31.2)	114 (56.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	97 (48.0)	69 (34.2)
Week 95	Expected to Complete Questionnaires	29 (14.4)	11 (5.4)
	Completed ^c	14 (6.9)	4 (2.0)
	Compliance (% in those expected to complete questionnaires) ^d	14 (48.3)	4 (36.4)
	Not completed	15 (7.4)	7 (3.5)
	With visit, no record	15 (7.4)	7 (3.5)
	Missing by Design	173 (85.6)	191 (94.6)
	Discontinued due to death	63 (31.2)	115 (56.9)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	103 (51.0)	71 (35.1)
Week 98	Expected to Complete Questionnaires	23 (11.4)	8 (4.0)
	Completed ^c	10 (5.0)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	10 (43.5)	3 (37.5)
	Not completed	13 (6.4)	5 (2.5)
	With visit, no record	13 (6.4)	5 (2.5)
	Missing by Design	179 (88.6)	194 (96.0)
	Discontinued due to death	63 (31.2)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	109 (54.0)	73 (36.1)
Week 101	Expected to Complete Questionnaires	17 (8.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (41.2)	3 (37.5)
	Not completed	10 (5.0)	5 (2.5)
	With visit, no record	10 (5.0)	5 (2.5)
	Missing by Design	185 (91.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	114 (56.4)	73 (36.1)
Week 104	Expected to Complete Questionnaires	13 (6.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (53.8)	3 (37.5)
	Not completed	6 (3.0)	5 (2.5)
	With visit, no record	6 (3.0)	5 (2.5)
	Missing by Design	189 (93.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	118 (58.4)	73 (36.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 107	Expected to Complete Questionnaires	12 (5.9)	7 (3.5)
	Completed ^c	7 (3.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	7 (58.3)	2 (28.6)
	Not completed	5 (2.5)	5 (2.5)
	With visit, no record	5 (2.5)	5 (2.5)
	Missing by Design	190 (94.1)	195 (96.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	118 (58.4)	74 (36.6)	
Week 110	Expected to Complete Questionnaires	9 (4.5)	5 (2.5)
	Completed ^c	3 (1.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	3 (33.3)	2 (40.0)
	Not completed	6 (3.0)	3 (1.5)
	With visit, no record	6 (3.0)	3 (1.5)
	Missing by Design	193 (95.5)	197 (97.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	121 (59.9)	76 (37.6)	
Week 113	Expected to Complete Questionnaires	5 (2.5)	3 (1.5)
	Completed ^c	4 (2.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	4 (80.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	197 (97.5)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	125 (61.9)	77 (38.1)	
Week 116	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	3 (1.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	3 (75.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	126 (62.4)	77 (38.1)	
Week 119	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	126 (62.4)	77 (38.1)	
Week 122	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
Missing by Design	198 (98.0)	199 (98.5)	
Discontinued due to death	64 (31.7)	116 (57.4)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 125	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (66.7)	1 (50.0)
	Not completed	1 (0.5)	1 (0.5)
	With visit, no record	1 (0.5)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)
Week 128	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	1 (0.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	1 (50.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)
Week 131	Expected to Complete Questionnaires	3 (1.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	0 (0.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	79 (39.1)
Week 134	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	129 (63.9)	79 (39.1)
Week 137	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	129 (63.9)	79 (39.1)
Week 140	Expected to Complete Questionnaires	0 (0.0)	1 (0.5)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Missing by Design	202 (100.0)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	79 (39.1)
Week 143	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 146	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 149	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 152	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)

a: Database Cutoff Date: 08AUG2023
b: Number of participants: intention-to-treat population, cisplatin ineligible
c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set
d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred
ITT: Intention-to-Treat

Tabelle 4G-9: Rücklaufquoten mit Gründen für das Fehlen von Werten im BPI-SF (Cisplatin ungeeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Baseline	Expected to Complete Questionnaires	202 (100.0)	202 (100.0)
	Completed ^c	166 (82.2)	166 (82.2)
	Compliance (% in those expected to complete questionnaires) ^d	166 (82.2)	166 (82.2)
	Not completed	36 (17.8)	36 (17.8)
	With visit, no record	36 (17.8)	36 (17.8)
	Missing by Design	0 (0.0)	0 (0.0)
Week 1	Expected to Complete Questionnaires	201 (99.5)	197 (97.5)
	Completed ^c	134 (66.3)	142 (70.3)
	Compliance (% in those expected to complete questionnaires) ^d	134 (66.7)	142 (72.1)
	Not completed	67 (33.2)	55 (27.2)
	With visit, no record	67 (33.2)	55 (27.2)
	Missing by Design	1 (0.5)	5 (2.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 2	Expected to Complete Questionnaires	198 (98.0)	194 (96.0)
	Completed ^c	141 (69.8)	140 (69.3)
	Compliance (% in those expected to complete questionnaires) ^d	141 (71.2)	140 (72.2)
	Not completed	57 (28.2)	54 (26.7)
	With visit, no record	57 (28.2)	54 (26.7)
	Missing by Design	4 (2.0)	8 (4.0)
	Discontinued due to death	3 (1.5)	3 (1.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 3	Expected to Complete Questionnaires	196 (97.0)	193 (95.5)
	Completed ^c	126 (62.4)	138 (68.3)
	Compliance (% in those expected to complete questionnaires) ^d	126 (64.3)	138 (71.5)
	Not completed	70 (34.7)	55 (27.2)
	With visit, no record	70 (34.7)	55 (27.2)
	Missing by Design	6 (3.0)	9 (4.5)
	Discontinued due to death	5 (2.5)	4 (2.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 4	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	134 (66.3)	137 (67.8)
	Compliance (% in those expected to complete questionnaires) ^d	134 (69.4)	137 (72.1)
	Not completed	59 (29.2)	53 (26.2)
	With visit, no record	59 (29.2)	53 (26.2)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 5	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	126 (62.4)	141 (69.8)
	Compliance (% in those expected to complete questionnaires) ^d	126 (65.3)	141 (74.2)
	Not completed	67 (33.2)	49 (24.3)
	With visit, no record	67 (33.2)	49 (24.3)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 6	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	128 (63.4)	131 (64.9)
	Compliance (% in those expected to complete questionnaires) ^d	128 (67.0)	131 (68.9)
	Not completed	63 (31.2)	59 (29.2)
	With visit, no record	63 (31.2)	59 (29.2)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 7	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	129 (63.9)	136 (67.3)
	Compliance (% in those expected to complete questionnaires) ^d	129 (67.5)	136 (71.6)
	Not completed	62 (30.7)	54 (26.7)
	With visit, no record	62 (30.7)	54 (26.7)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 8	Expected to Complete Questionnaires	191 (94.6)	189 (93.6)
	Completed ^c	129 (63.9)	133 (65.8)
	Compliance (% in those expected to complete questionnaires) ^d	129 (67.5)	133 (70.4)
	Not completed	62 (30.7)	56 (27.7)
	With visit, no record	62 (30.7)	56 (27.7)
	Missing by Design	11 (5.4)	13 (6.4)
	Discontinued due to death	10 (5.0)	8 (4.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 9	Expected to Complete Questionnaires	190 (94.1)	188 (93.1)
	Completed ^c	125 (61.9)	126 (62.4)
	Compliance (% in those expected to complete questionnaires) ^d	125 (65.8)	126 (67.0)
	Not completed	65 (32.2)	62 (30.7)
	With visit, no record	65 (32.2)	62 (30.7)
	Missing by Design	12 (5.9)	14 (6.9)
	Discontinued due to death	10 (5.0)	10 (5.0)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 10	Expected to Complete Questionnaires	188 (93.1)	187 (92.6)
	Completed ^c	122 (60.4)	130 (64.4)
	Compliance (% in those expected to complete questionnaires) ^d	122 (64.9)	130 (69.5)
	Not completed	66 (32.7)	57 (28.2)
	With visit, no record	66 (32.7)	57 (28.2)
	Missing by Design	14 (6.9)	15 (7.4)
	Discontinued due to death	12 (5.9)	11 (5.4)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 11	Expected to Complete Questionnaires	186 (92.1)	186 (92.1)
	Completed ^c	119 (58.9)	115 (56.9)
	Compliance (% in those expected to complete questionnaires) ^d	119 (64.0)	115 (61.8)
	Not completed	67 (33.2)	71 (35.1)
	With visit, no record	67 (33.2)	71 (35.1)
	Missing by Design	16 (7.9)	16 (7.9)
	Discontinued due to death	13 (6.4)	12 (5.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 12	Expected to Complete Questionnaires	186 (92.1)	185 (91.6)
	Completed ^c	123 (60.9)	116 (57.4)
	Compliance (% in those expected to complete questionnaires) ^d	123 (66.1)	116 (62.7)
	Not completed	63 (31.2)	69 (34.2)
	With visit, no record	63 (31.2)	69 (34.2)
	Missing by Design	16 (7.9)	17 (8.4)
	Discontinued due to death	13 (6.4)	13 (6.4)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 14	Expected to Complete Questionnaires	185 (91.6)	180 (89.1)
	Completed ^c	120 (59.4)	110 (54.5)
	Compliance (% in those expected to complete questionnaires) ^d	120 (64.9)	110 (61.1)
	Not completed	65 (32.2)	70 (34.7)
	With visit, no record	65 (32.2)	70 (34.7)
	Missing by Design	17 (8.4)	22 (10.9)
	Discontinued due to death	14 (6.9)	18 (8.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 17	Expected to Complete Questionnaires	181 (89.6)	174 (86.1)
	Completed ^c	114 (56.4)	108 (53.5)
	Compliance (% in those expected to complete questionnaires) ^d	114 (63.0)	108 (62.1)
	Not completed	67 (33.2)	66 (32.7)
	With visit, no record	67 (33.2)	66 (32.7)
	Missing by Design	21 (10.4)	28 (13.9)
	Discontinued due to death	18 (8.9)	24 (11.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 20	Expected to Complete Questionnaires	180 (89.1)	169 (83.7)
	Completed ^c	106 (52.5)	93 (46.0)
	Compliance (% in those expected to complete questionnaires) ^d	106 (58.9)	93 (55.0)
	Not completed	74 (36.6)	76 (37.6)
	With visit, no record	74 (36.6)	76 (37.6)
	Missing by Design	22 (10.9)	33 (16.3)
	Discontinued due to death	18 (8.9)	29 (14.4)
	Discontinued due to withdrawal by participant	3 (1.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 23	Expected to Complete Questionnaires	177 (87.6)	159 (78.7)
	Completed ^c	100 (49.5)	81 (40.1)
	Compliance (% in those expected to complete questionnaires) ^d	100 (56.5)	81 (50.9)
	Not completed	77 (38.1)	78 (38.6)
	With visit, no record	77 (38.1)	78 (38.6)
	Missing by Design	25 (12.4)	43 (21.3)
	Discontinued due to death	21 (10.4)	38 (18.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 26	Expected to Complete Questionnaires	173 (85.6)	154 (76.2)
	Completed ^c	97 (48.0)	76 (37.6)
	Compliance (% in those expected to complete questionnaires) ^d	97 (56.1)	76 (49.4)
	Not completed	76 (37.6)	78 (38.6)
	With visit, no record	76 (37.6)	78 (38.6)
	Missing by Design	29 (14.4)	48 (23.8)
	Discontinued due to death	25 (12.4)	44 (21.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 29	Expected to Complete Questionnaires	170 (84.2)	150 (74.3)
	Completed ^c	95 (47.0)	71 (35.1)
	Compliance (% in those expected to complete questionnaires) ^d	95 (55.9)	71 (47.3)
	Not completed	75 (37.1)	79 (39.1)
	With visit, no record	75 (37.1)	79 (39.1)
	Missing by Design	32 (15.8)	52 (25.7)
	Discontinued due to death	28 (13.9)	48 (23.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 32	Expected to Complete Questionnaires	165 (81.7)	142 (70.3)
	Completed ^c	90 (44.6)	59 (29.2)
	Compliance (% in those expected to complete questionnaires) ^d	90 (54.5)	59 (41.5)
	Not completed	75 (37.1)	83 (41.1)
	With visit, no record	75 (37.1)	83 (41.1)
	Missing by Design	37 (18.3)	60 (29.7)
	Discontinued due to death	31 (15.3)	55 (27.2)
	Discontinued due to withdrawal by participant	5 (2.5)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 35	Expected to Complete Questionnaires	163 (80.7)	135 (66.8)
	Completed ^c	88 (43.6)	57 (28.2)
	Compliance (% in those expected to complete questionnaires) ^d	88 (54.0)	57 (42.2)
	Not completed	75 (37.1)	78 (38.6)
	With visit, no record	75 (37.1)	78 (38.6)
	Missing by Design	39 (19.3)	67 (33.2)
	Discontinued due to death	32 (15.8)	62 (30.7)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 38	Expected to Complete Questionnaires	157 (77.7)	129 (63.9)
	Completed ^c	88 (43.6)	50 (24.8)
	Compliance (% in those expected to complete questionnaires) ^d	88 (56.1)	50 (38.8)
	Not completed	69 (34.2)	79 (39.1)
	With visit, no record	69 (34.2)	79 (39.1)
	Missing by Design	45 (22.3)	73 (36.1)
	Discontinued due to death	37 (18.3)	67 (33.2)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	2 (1.0)	3 (1.5)
Week 41	Expected to Complete Questionnaires	153 (75.7)	122 (60.4)
	Completed ^c	87 (43.1)	47 (23.3)
	Compliance (% in those expected to complete questionnaires) ^d	87 (56.9)	47 (38.5)
	Not completed	66 (32.7)	75 (37.1)
	With visit, no record	66 (32.7)	75 (37.1)
	Missing by Design	49 (24.3)	80 (39.6)
	Discontinued due to death	39 (19.3)	71 (35.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	4 (2.0)	6 (3.0)
Week 44	Expected to Complete Questionnaires	141 (69.8)	108 (53.5)
	Completed ^c	77 (38.1)	44 (21.8)
	Compliance (% in those expected to complete questionnaires) ^d	77 (54.6)	44 (40.7)
	Not completed	64 (31.7)	64 (31.7)
	With visit, no record	64 (31.7)	64 (31.7)
	Missing by Design	61 (30.2)	94 (46.5)
	Discontinued due to death	42 (20.8)	77 (38.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	13 (6.4)	14 (6.9)
Week 47	Expected to Complete Questionnaires	131 (64.9)	98 (48.5)
	Completed ^c	72 (35.6)	39 (19.3)
	Compliance (% in those expected to complete questionnaires) ^d	72 (55.0)	39 (39.8)
	Not completed	59 (29.2)	59 (29.2)
	With visit, no record	59 (29.2)	59 (29.2)
	Missing by Design	71 (35.1)	104 (51.5)
	Discontinued due to death	45 (22.3)	81 (40.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	20 (9.9)	20 (9.9)
Week 50	Expected to Complete Questionnaires	126 (62.4)	92 (45.5)
	Completed ^c	66 (32.7)	31 (15.3)
	Compliance (% in those expected to complete questionnaires) ^d	66 (52.4)	31 (33.7)
	Not completed	60 (29.7)	61 (30.2)
	With visit, no record	60 (29.7)	61 (30.2)
	Missing by Design	76 (37.6)	110 (54.5)
	Discontinued due to death	45 (22.3)	84 (41.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	25 (12.4)	23 (11.4)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 53	Expected to Complete Questionnaires	120 (59.4)	80 (39.6)
	Completed ^c	66 (32.7)	28 (13.9)
	Compliance (% in those expected to complete questionnaires) ^d	66 (55.0)	28 (35.0)
	Not completed	54 (26.7)	52 (25.7)
	With visit, no record	54 (26.7)	52 (25.7)
	Missing by Design	82 (40.6)	122 (60.4)
	Discontinued due to death	48 (23.8)	90 (44.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	28 (13.9)	29 (14.4)
Week 56	Expected to Complete Questionnaires	112 (55.4)	73 (36.1)
	Completed ^c	63 (31.2)	29 (14.4)
	Compliance (% in those expected to complete questionnaires) ^d	63 (56.3)	29 (39.7)
	Not completed	49 (24.3)	44 (21.8)
	With visit, no record	49 (24.3)	44 (21.8)
	Missing by Design	90 (44.6)	129 (63.9)
	Discontinued due to death	48 (23.8)	94 (46.5)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	36 (17.8)	32 (15.8)
Week 59	Expected to Complete Questionnaires	106 (52.5)	64 (31.7)
	Completed ^c	59 (29.2)	21 (10.4)
	Compliance (% in those expected to complete questionnaires) ^d	59 (55.7)	21 (32.8)
	Not completed	47 (23.3)	43 (21.3)
	With visit, no record	47 (23.3)	43 (21.3)
	Missing by Design	96 (47.5)	138 (68.3)
	Discontinued due to death	50 (24.8)	98 (48.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	40 (19.8)	36 (17.8)
Week 62	Expected to Complete Questionnaires	94 (46.5)	60 (29.7)
	Completed ^c	54 (26.7)	20 (9.9)
	Compliance (% in those expected to complete questionnaires) ^d	54 (57.4)	20 (33.3)
	Not completed	40 (19.8)	40 (19.8)
	With visit, no record	40 (19.8)	40 (19.8)
	Missing by Design	108 (53.5)	142 (70.3)
	Discontinued due to death	53 (26.2)	100 (49.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	49 (24.3)	37 (18.3)	
Week 65	Expected to Complete Questionnaires	88 (43.6)	52 (25.7)
	Completed ^c	41 (20.3)	16 (7.9)
	Compliance (% in those expected to complete questionnaires) ^d	41 (46.6)	16 (30.8)
	Not completed	47 (23.3)	36 (17.8)
	With visit, no record	47 (23.3)	36 (17.8)
	Missing by Design	114 (56.4)	150 (74.3)
	Discontinued due to death	53 (26.2)	102 (50.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	55 (27.2)	43 (21.3)	
Week 68	Expected to Complete Questionnaires	83 (41.1)	48 (23.8)
	Completed ^c	43 (21.3)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	43 (51.8)	13 (27.1)
	Not completed	40 (19.8)	35 (17.3)
	With visit, no record	40 (19.8)	35 (17.3)
	Missing by Design	119 (58.9)	154 (76.2)
	Discontinued due to death	54 (26.7)	104 (51.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Visit not scheduled	59 (29.2)	45 (22.3)
Week 71	Expected to Complete Questionnaires	79 (39.1)	42 (20.8)
	Completed ^c	39 (19.3)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	39 (49.4)	13 (31.0)
	Not completed	40 (19.8)	29 (14.4)
	With visit, no record	40 (19.8)	29 (14.4)
	Missing by Design	123 (60.9)	160 (79.2)
	Discontinued due to death	54 (26.7)	106 (52.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	63 (31.2)	49 (24.3)
Week 74	Expected to Complete Questionnaires	71 (35.1)	38 (18.8)
	Completed ^c	36 (17.8)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	36 (50.7)	11 (28.9)
	Not completed	35 (17.3)	27 (13.4)
	With visit, no record	35 (17.3)	27 (13.4)
	Missing by Design	131 (64.9)	164 (81.2)
	Discontinued due to death	55 (27.2)	107 (53.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	70 (34.7)	52 (25.7)
Week 77	Expected to Complete Questionnaires	64 (31.7)	33 (16.3)
	Completed ^c	34 (16.8)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	34 (53.1)	11 (33.3)
	Not completed	30 (14.9)	22 (10.9)
	With visit, no record	30 (14.9)	22 (10.9)
	Missing by Design	138 (68.3)	169 (83.7)
	Discontinued due to death	55 (27.2)	109 (54.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	77 (38.1)	55 (27.2)
Week 80	Expected to Complete Questionnaires	60 (29.7)	30 (14.9)
	Completed ^c	35 (17.3)	8 (4.0)
	Compliance (% in those expected to complete questionnaires) ^d	35 (58.3)	8 (26.7)
	Not completed	25 (12.4)	22 (10.9)
	With visit, no record	25 (12.4)	22 (10.9)
	Missing by Design	142 (70.3)	172 (85.1)
	Discontinued due to death	57 (28.2)	110 (54.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	79 (39.1)	57 (28.2)
Week 83	Expected to Complete Questionnaires	56 (27.7)	26 (12.9)
	Completed ^c	30 (14.9)	8 (4.0)
	Compliance (% in those expected to complete questionnaires) ^d	30 (53.6)	8 (30.8)
	Not completed	26 (12.9)	18 (8.9)
	With visit, no record	26 (12.9)	18 (8.9)
	Missing by Design	146 (72.3)	176 (87.1)
	Discontinued due to death	59 (29.2)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	81 (40.1)	59 (29.2)
Week 86	Expected to Complete Questionnaires	49 (24.3)	20 (9.9)
	Completed ^c	26 (12.9)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	26 (53.1)	6 (30.0)
	Not completed	23 (11.4)	14 (6.9)
	With visit, no record	23 (11.4)	14 (6.9)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Missing by Design	153 (75.7)	182 (90.1)
	Discontinued due to death	60 (29.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	87 (43.1)	65 (32.2)
Week 89	Expected to Complete Questionnaires	43 (21.3)	17 (8.4)
	Completed ^c	20 (9.9)	7 (3.5)
	Compliance (% in those expected to complete questionnaires) ^d	20 (46.5)	7 (41.2)
	Not completed	23 (11.4)	10 (5.0)
	With visit, no record	23 (11.4)	10 (5.0)
	Missing by Design	159 (78.7)	185 (91.6)
	Discontinued due to death	62 (30.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	91 (45.0)	68 (33.7)
Week 92	Expected to Complete Questionnaires	36 (17.8)	14 (6.9)
	Completed ^c	19 (9.4)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	19 (52.8)	6 (42.9)
	Not completed	17 (8.4)	8 (4.0)
	With visit, no record	17 (8.4)	8 (4.0)
	Missing by Design	166 (82.2)	188 (93.1)
	Discontinued due to death	63 (31.2)	114 (56.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	97 (48.0)	69 (34.2)
Week 95	Expected to Complete Questionnaires	29 (14.4)	11 (5.4)
	Completed ^c	14 (6.9)	4 (2.0)
	Compliance (% in those expected to complete questionnaires) ^d	14 (48.3)	4 (36.4)
	Not completed	15 (7.4)	7 (3.5)
	With visit, no record	15 (7.4)	7 (3.5)
	Missing by Design	173 (85.6)	191 (94.6)
	Discontinued due to death	63 (31.2)	115 (56.9)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	103 (51.0)	71 (35.1)
Week 98	Expected to Complete Questionnaires	23 (11.4)	8 (4.0)
	Completed ^c	10 (5.0)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	10 (43.5)	3 (37.5)
	Not completed	13 (6.4)	5 (2.5)
	With visit, no record	13 (6.4)	5 (2.5)
	Missing by Design	179 (88.6)	194 (96.0)
	Discontinued due to death	63 (31.2)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	109 (54.0)	73 (36.1)
Week 101	Expected to Complete Questionnaires	17 (8.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (41.2)	3 (37.5)
	Not completed	10 (5.0)	5 (2.5)
	With visit, no record	10 (5.0)	5 (2.5)
	Missing by Design	185 (91.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	114 (56.4)	73 (36.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 104	Expected to Complete Questionnaires	13 (6.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (53.8)	3 (37.5)
	Not completed	6 (3.0)	5 (2.5)
	With visit, no record	6 (3.0)	5 (2.5)
	Missing by Design	189 (93.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	118 (58.4)	73 (36.1)	
Week 107	Expected to Complete Questionnaires	12 (5.9)	7 (3.5)
	Completed ^c	7 (3.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	7 (58.3)	2 (28.6)
	Not completed	5 (2.5)	5 (2.5)
	With visit, no record	5 (2.5)	5 (2.5)
	Missing by Design	190 (94.1)	195 (96.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	118 (58.4)	74 (36.6)	
Week 110	Expected to Complete Questionnaires	9 (4.5)	5 (2.5)
	Completed ^c	3 (1.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	3 (33.3)	2 (40.0)
	Not completed	6 (3.0)	3 (1.5)
	With visit, no record	6 (3.0)	3 (1.5)
	Missing by Design	193 (95.5)	197 (97.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	121 (59.9)	76 (37.6)	
Week 113	Expected to Complete Questionnaires	5 (2.5)	3 (1.5)
	Completed ^c	4 (2.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	4 (80.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	197 (97.5)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	125 (61.9)	77 (38.1)	
Week 116	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	3 (1.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	3 (75.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	126 (62.4)	77 (38.1)	
Week 119	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
Missing by Design	198 (98.0)	199 (98.5)	
Discontinued due to death	64 (31.7)	116 (57.4)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 122	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 125	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (66.7)	1 (50.0)
	Not completed	1 (0.5)	1 (0.5)
	With visit, no record	1 (0.5)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)
Week 128	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	1 (0.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	1 (50.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)
Week 131	Expected to Complete Questionnaires	3 (1.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	0 (0.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	79 (39.1)
Week 134	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	129 (63.9)	79 (39.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 137	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	129 (63.9)	79 (39.1)	
Week 140	Expected to Complete Questionnaires	0 (0.0)	1 (0.5)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	202 (100.0)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
Visit not scheduled	130 (64.4)	79 (39.1)	
Week 143	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 146	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 149	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 152	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)

a: Database Cutoff Date: 08AUG2023
b: Number of participants: intention-to-treat population, cisplatin ineligible
c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set
d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred
ITT: Intention-to-Treat

Tabelle 4G-10: Rücklaufquoten mit Gründen für das Fehlen von Werten in der EQ-5D VAS (Cisplatin ungeeignet)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Baseline	Expected to Complete Questionnaires	202 (100.0)	202 (100.0)
	Completed ^c	166 (82.2)	168 (83.2)
	Compliance (% in those expected to complete questionnaires) ^d	166 (82.2)	168 (83.2)
	Not completed	36 (17.8)	34 (16.8)
	With visit, no record	36 (17.8)	34 (16.8)
	Missing by Design	0 (0.0)	0 (0.0)
Week 1	Expected to Complete Questionnaires	201 (99.5)	197 (97.5)
	Completed ^c	143 (70.8)	146 (72.3)
	Compliance (% in those expected to complete questionnaires) ^d	143 (71.1)	146 (74.1)
	Not completed	58 (28.7)	51 (25.2)
	With visit, no record	58 (28.7)	51 (25.2)
	Missing by Design	1 (0.5)	5 (2.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 2	Expected to Complete Questionnaires	198 (98.0)	194 (96.0)
	Completed ^c	156 (77.2)	153 (75.7)
	Compliance (% in those expected to complete questionnaires) ^d	156 (78.8)	153 (78.9)
	Not completed	42 (20.8)	41 (20.3)
	With visit, no record	42 (20.8)	41 (20.3)
	Missing by Design	4 (2.0)	8 (4.0)
	Discontinued due to death	3 (1.5)	3 (1.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 3	Expected to Complete Questionnaires	196 (97.0)	193 (95.5)
	Completed ^c	141 (69.8)	150 (74.3)
	Compliance (% in those expected to complete questionnaires) ^d	141 (71.9)	150 (77.7)
	Not completed	55 (27.2)	43 (21.3)
	With visit, no record	55 (27.2)	43 (21.3)
	Missing by Design	6 (3.0)	9 (4.5)
	Discontinued due to death	5 (2.5)	4 (2.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 4	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	147 (72.8)	152 (75.2)
	Compliance (% in those expected to complete questionnaires) ^d	147 (76.2)	152 (80.0)
	Not completed	46 (22.8)	38 (18.8)
	With visit, no record	46 (22.8)	38 (18.8)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 5	Expected to Complete Questionnaires	193 (95.5)	190 (94.1)
	Completed ^c	139 (68.8)	157 (77.7)
	Compliance (% in those expected to complete questionnaires) ^d	139 (72.0)	157 (82.6)
	Not completed	54 (26.7)	33 (16.3)
	With visit, no record	54 (26.7)	33 (16.3)
	Missing by Design	9 (4.5)	12 (5.9)
	Discontinued due to death	8 (4.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 6	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	150 (74.3)	146 (72.3)
	Compliance (% in those expected to complete questionnaires) ^d	150 (78.5)	146 (76.8)
	Not completed	41 (20.3)	44 (21.8)
	With visit, no record	41 (20.3)	44 (21.8)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 7	Expected to Complete Questionnaires	191 (94.6)	190 (94.1)
	Completed ^c	152 (75.2)	150 (74.3)
	Compliance (% in those expected to complete questionnaires) ^d	152 (79.6)	150 (78.9)
	Not completed	39 (19.3)	40 (19.8)
	With visit, no record	39 (19.3)	40 (19.8)
	Missing by Design	11 (5.4)	12 (5.9)
	Discontinued due to death	10 (5.0)	7 (3.5)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 8	Expected to Complete Questionnaires	191 (94.6)	189 (93.6)
	Completed ^c	152 (75.2)	147 (72.8)
	Compliance (% in those expected to complete questionnaires) ^d	152 (79.6)	147 (77.8)
	Not completed	39 (19.3)	42 (20.8)
	With visit, no record	39 (19.3)	42 (20.8)
	Missing by Design	11 (5.4)	13 (6.4)
	Discontinued due to death	10 (5.0)	8 (4.0)
	Discontinued due to withdrawal by participant	0 (0.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	4 (2.0)
Week 9	Expected to Complete Questionnaires	190 (94.1)	188 (93.1)
	Completed ^c	144 (71.3)	142 (70.3)
	Compliance (% in those expected to complete questionnaires) ^d	144 (75.8)	142 (75.5)
	Not completed	46 (22.8)	46 (22.8)
	With visit, no record	46 (22.8)	46 (22.8)
	Missing by Design	12 (5.9)	14 (6.9)
	Discontinued due to death	10 (5.0)	10 (5.0)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 10	Expected to Complete Questionnaires	188 (93.1)	187 (92.6)
	Completed ^c	139 (68.8)	143 (70.8)
	Compliance (% in those expected to complete questionnaires) ^d	139 (73.9)	143 (76.5)
	Not completed	49 (24.3)	44 (21.8)
	With visit, no record	49 (24.3)	44 (21.8)
	Missing by Design	14 (6.9)	15 (7.4)
	Discontinued due to death	12 (5.9)	11 (5.4)
	Discontinued due to withdrawal by participant	1 (0.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 11	Expected to Complete Questionnaires	186 (92.1)	186 (92.1)
	Completed ^c	138 (68.3)	127 (62.9)
	Compliance (% in those expected to complete questionnaires) ^d	138 (74.2)	127 (68.3)
	Not completed	48 (23.8)	59 (29.2)
	With visit, no record	48 (23.8)	59 (29.2)
	Missing by Design	16 (7.9)	16 (7.9)
	Discontinued due to death	13 (6.4)	12 (5.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 12	Expected to Complete Questionnaires	186 (92.1)	185 (91.6)
	Completed ^c	143 (70.8)	130 (64.4)
	Compliance (% in those expected to complete questionnaires) ^d	143 (76.9)	130 (70.3)
	Not completed	43 (21.3)	55 (27.2)
	With visit, no record	43 (21.3)	55 (27.2)
	Missing by Design	16 (7.9)	17 (8.4)
	Discontinued due to death	13 (6.4)	13 (6.4)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 14	Expected to Complete Questionnaires	185 (91.6)	180 (89.1)
	Completed ^c	141 (69.8)	125 (61.9)
	Compliance (% in those expected to complete questionnaires) ^d	141 (76.2)	125 (69.4)
	Not completed	44 (21.8)	55 (27.2)
	With visit, no record	44 (21.8)	55 (27.2)
	Missing by Design	17 (8.4)	22 (10.9)
	Discontinued due to death	14 (6.9)	18 (8.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 17	Expected to Complete Questionnaires	181 (89.6)	174 (86.1)
	Completed ^c	133 (65.8)	120 (59.4)
	Compliance (% in those expected to complete questionnaires) ^d	133 (73.5)	120 (69.0)
	Not completed	48 (23.8)	54 (26.7)
	With visit, no record	48 (23.8)	54 (26.7)
	Missing by Design	21 (10.4)	28 (13.9)
	Discontinued due to death	18 (8.9)	24 (11.9)
	Discontinued due to withdrawal by participant	2 (1.0)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 20	Expected to Complete Questionnaires	180 (89.1)	169 (83.7)
	Completed ^c	120 (59.4)	104 (51.5)
	Compliance (% in those expected to complete questionnaires) ^d	120 (66.7)	104 (61.5)
	Not completed	60 (29.7)	65 (32.2)
	With visit, no record	60 (29.7)	65 (32.2)
	Missing by Design	22 (10.9)	33 (16.3)
	Discontinued due to death	18 (8.9)	29 (14.4)
	Discontinued due to withdrawal by participant	3 (1.5)	1 (0.5)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 23	Expected to Complete Questionnaires	177 (87.6)	159 (78.7)
	Completed ^c	117 (57.9)	89 (44.1)
	Compliance (% in those expected to complete questionnaires) ^d	117 (66.1)	89 (56.0)
	Not completed	60 (29.7)	70 (34.7)
	With visit, no record	60 (29.7)	70 (34.7)
	Missing by Design	25 (12.4)	43 (21.3)
	Discontinued due to death	21 (10.4)	38 (18.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	3 (1.5)
Week 26	Expected to Complete Questionnaires	173 (85.6)	154 (76.2)
	Completed ^c	114 (56.4)	81 (40.1)
	Compliance (% in those expected to complete questionnaires) ^d	114 (65.9)	81 (52.6)
	Not completed	59 (29.2)	73 (36.1)
	With visit, no record	59 (29.2)	73 (36.1)
	Missing by Design	29 (14.4)	48 (23.8)
	Discontinued due to death	25 (12.4)	44 (21.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 29	Expected to Complete Questionnaires	170 (84.2)	150 (74.3)
	Completed ^c	108 (53.5)	77 (38.1)
	Compliance (% in those expected to complete questionnaires) ^d	108 (63.5)	77 (51.3)
	Not completed	62 (30.7)	73 (36.1)
	With visit, no record	62 (30.7)	73 (36.1)
	Missing by Design	32 (15.8)	52 (25.7)
	Discontinued due to death	28 (13.9)	48 (23.8)
	Discontinued due to withdrawal by participant	3 (1.5)	2 (1.0)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 32	Expected to Complete Questionnaires	165 (81.7)	142 (70.3)
	Completed ^c	104 (51.5)	64 (31.7)
	Compliance (% in those expected to complete questionnaires) ^d	104 (63.0)	64 (45.1)
	Not completed	61 (30.2)	78 (38.6)
	With visit, no record	61 (30.2)	78 (38.6)
	Missing by Design	37 (18.3)	60 (29.7)
	Discontinued due to death	31 (15.3)	55 (27.2)
	Discontinued due to withdrawal by participant	5 (2.5)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 35	Expected to Complete Questionnaires	163 (80.7)	135 (66.8)
	Completed ^c	98 (48.5)	62 (30.7)
	Compliance (% in those expected to complete questionnaires) ^d	98 (60.1)	62 (45.9)
	Not completed	65 (32.2)	73 (36.1)
	With visit, no record	65 (32.2)	73 (36.1)
	Missing by Design	39 (19.3)	67 (33.2)
	Discontinued due to death	32 (15.8)	62 (30.7)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	1 (0.5)	2 (1.0)
Week 38	Expected to Complete Questionnaires	157 (77.7)	129 (63.9)
	Completed ^c	97 (48.0)	56 (27.7)
	Compliance (% in those expected to complete questionnaires) ^d	97 (61.8)	56 (43.4)
	Not completed	60 (29.7)	73 (36.1)
	With visit, no record	60 (29.7)	73 (36.1)
	Missing by Design	45 (22.3)	73 (36.1)
	Discontinued due to death	37 (18.3)	67 (33.2)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	2 (1.0)	3 (1.5)
Week 41	Expected to Complete Questionnaires	153 (75.7)	122 (60.4)
	Completed ^c	96 (47.5)	52 (25.7)
	Compliance (% in those expected to complete questionnaires) ^d	96 (62.7)	52 (42.6)
	Not completed	57 (28.2)	70 (34.7)
	With visit, no record	57 (28.2)	70 (34.7)
	Missing by Design	49 (24.3)	80 (39.6)
	Discontinued due to death	39 (19.3)	71 (35.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	4 (2.0)	6 (3.0)
Week 44	Expected to Complete Questionnaires	141 (69.8)	108 (53.5)
	Completed ^c	86 (42.6)	49 (24.3)
	Compliance (% in those expected to complete questionnaires) ^d	86 (61.0)	49 (45.4)
	Not completed	55 (27.2)	59 (29.2)
	With visit, no record	55 (27.2)	59 (29.2)
	Missing by Design	61 (30.2)	94 (46.5)
	Discontinued due to death	42 (20.8)	77 (38.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	13 (6.4)	14 (6.9)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 47	Expected to Complete Questionnaires	131 (64.9)	98 (48.5)
	Completed ^c	79 (39.1)	43 (21.3)
	Compliance (% in those expected to complete questionnaires) ^d	79 (60.3)	43 (43.9)
	Not completed	52 (25.7)	55 (27.2)
	With visit, no record	52 (25.7)	55 (27.2)
	Missing by Design	71 (35.1)	104 (51.5)
	Discontinued due to death	45 (22.3)	81 (40.1)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	20 (9.9)	20 (9.9)
Week 50	Expected to Complete Questionnaires	126 (62.4)	92 (45.5)
	Completed ^c	75 (37.1)	36 (17.8)
	Compliance (% in those expected to complete questionnaires) ^d	75 (59.5)	36 (39.1)
	Not completed	51 (25.2)	56 (27.7)
	With visit, no record	51 (25.2)	56 (27.7)
	Missing by Design	76 (37.6)	110 (54.5)
	Discontinued due to death	45 (22.3)	84 (41.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	25 (12.4)	23 (11.4)
Week 53	Expected to Complete Questionnaires	120 (59.4)	80 (39.6)
	Completed ^c	76 (37.6)	31 (15.3)
	Compliance (% in those expected to complete questionnaires) ^d	76 (63.3)	31 (38.8)
	Not completed	44 (21.8)	49 (24.3)
	With visit, no record	44 (21.8)	49 (24.3)
	Missing by Design	82 (40.6)	122 (60.4)
	Discontinued due to death	48 (23.8)	90 (44.6)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	28 (13.9)	29 (14.4)
Week 56	Expected to Complete Questionnaires	112 (55.4)	73 (36.1)
	Completed ^c	73 (36.1)	30 (14.9)
	Compliance (% in those expected to complete questionnaires) ^d	73 (65.2)	30 (41.1)
	Not completed	39 (19.3)	43 (21.3)
	With visit, no record	39 (19.3)	43 (21.3)
	Missing by Design	90 (44.6)	129 (63.9)
	Discontinued due to death	48 (23.8)	94 (46.5)
	Discontinued due to withdrawal by participant	6 (3.0)	3 (1.5)
	Visit not scheduled	36 (17.8)	32 (15.8)
Week 59	Expected to Complete Questionnaires	106 (52.5)	64 (31.7)
	Completed ^c	69 (34.2)	23 (11.4)
	Compliance (% in those expected to complete questionnaires) ^d	69 (65.1)	23 (35.9)
	Not completed	37 (18.3)	41 (20.3)
	With visit, no record	37 (18.3)	41 (20.3)
	Missing by Design	96 (47.5)	138 (68.3)
	Discontinued due to death	50 (24.8)	98 (48.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	40 (19.8)	36 (17.8)
Week 62	Expected to Complete Questionnaires	94 (46.5)	60 (29.7)
	Completed ^c	62 (30.7)	20 (9.9)
	Compliance (% in those expected to complete questionnaires) ^d	62 (66.0)	20 (33.3)
	Not completed	32 (15.8)	40 (19.8)
	With visit, no record	32 (15.8)	40 (19.8)
	Missing by Design	108 (53.5)	142 (70.3)
	Discontinued due to death	53 (26.2)	100 (49.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	49 (24.3)	37 (18.3)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 65	Expected to Complete Questionnaires	88 (43.6)	52 (25.7)
	Completed ^c	43 (21.3)	17 (8.4)
	Compliance (% in those expected to complete questionnaires) ^d	43 (48.9)	17 (32.7)
	Not completed	45 (22.3)	35 (17.3)
	With visit, no record	45 (22.3)	35 (17.3)
	Missing by Design	114 (56.4)	150 (74.3)
	Discontinued due to death	53 (26.2)	102 (50.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	55 (27.2)	43 (21.3)
Week 68	Expected to Complete Questionnaires	83 (41.1)	48 (23.8)
	Completed ^c	46 (22.8)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	46 (55.4)	13 (27.1)
	Not completed	37 (18.3)	35 (17.3)
	With visit, no record	37 (18.3)	35 (17.3)
	Missing by Design	119 (58.9)	154 (76.2)
	Discontinued due to death	54 (26.7)	104 (51.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	59 (29.2)	45 (22.3)
Week 71	Expected to Complete Questionnaires	79 (39.1)	42 (20.8)
	Completed ^c	43 (21.3)	13 (6.4)
	Compliance (% in those expected to complete questionnaires) ^d	43 (54.4)	13 (31.0)
	Not completed	36 (17.8)	29 (14.4)
	With visit, no record	36 (17.8)	29 (14.4)
	Missing by Design	123 (60.9)	160 (79.2)
	Discontinued due to death	54 (26.7)	106 (52.5)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	63 (31.2)	49 (24.3)
Week 74	Expected to Complete Questionnaires	71 (35.1)	38 (18.8)
	Completed ^c	38 (18.8)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	38 (53.5)	11 (28.9)
	Not completed	33 (16.3)	27 (13.4)
	With visit, no record	33 (16.3)	27 (13.4)
	Missing by Design	131 (64.9)	164 (81.2)
	Discontinued due to death	55 (27.2)	107 (53.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	70 (34.7)	52 (25.7)
Week 77	Expected to Complete Questionnaires	64 (31.7)	33 (16.3)
	Completed ^c	37 (18.3)	11 (5.4)
	Compliance (% in those expected to complete questionnaires) ^d	37 (57.8)	11 (33.3)
	Not completed	27 (13.4)	22 (10.9)
	With visit, no record	27 (13.4)	22 (10.9)
	Missing by Design	138 (68.3)	169 (83.7)
	Discontinued due to death	55 (27.2)	109 (54.0)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	77 (38.1)	55 (27.2)
Week 80	Expected to Complete Questionnaires	60 (29.7)	30 (14.9)
	Completed ^c	36 (17.8)	8 (4.0)
	Compliance (% in those expected to complete questionnaires) ^d	36 (60.0)	8 (26.7)
	Not completed	24 (11.9)	22 (10.9)
	With visit, no record	24 (11.9)	22 (10.9)
	Missing by Design	142 (70.3)	172 (85.1)
Discontinued due to death	57 (28.2)	110 (54.5)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	79 (39.1)	57 (28.2)
Week 83	Expected to Complete Questionnaires	56 (27.7)	26 (12.9)
	Completed ^c	30 (14.9)	9 (4.5)
	Compliance (% in those expected to complete questionnaires) ^d	30 (53.6)	9 (34.6)
	Not completed	26 (12.9)	17 (8.4)
	With visit, no record	26 (12.9)	17 (8.4)
	Missing by Design	146 (72.3)	176 (87.1)
	Discontinued due to death	59 (29.2)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	81 (40.1)	59 (29.2)
Week 86	Expected to Complete Questionnaires	49 (24.3)	20 (9.9)
	Completed ^c	26 (12.9)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	26 (53.1)	6 (30.0)
	Not completed	23 (11.4)	14 (6.9)
	With visit, no record	23 (11.4)	14 (6.9)
	Missing by Design	153 (75.7)	182 (90.1)
	Discontinued due to death	60 (29.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	87 (43.1)	65 (32.2)
Week 89	Expected to Complete Questionnaires	43 (21.3)	17 (8.4)
	Completed ^c	20 (9.9)	7 (3.5)
	Compliance (% in those expected to complete questionnaires) ^d	20 (46.5)	7 (41.2)
	Not completed	23 (11.4)	10 (5.0)
	With visit, no record	23 (11.4)	10 (5.0)
	Missing by Design	159 (78.7)	185 (91.6)
	Discontinued due to death	62 (30.7)	112 (55.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	91 (45.0)	68 (33.7)
Week 92	Expected to Complete Questionnaires	36 (17.8)	14 (6.9)
	Completed ^c	19 (9.4)	6 (3.0)
	Compliance (% in those expected to complete questionnaires) ^d	19 (52.8)	6 (42.9)
	Not completed	17 (8.4)	8 (4.0)
	With visit, no record	17 (8.4)	8 (4.0)
	Missing by Design	166 (82.2)	188 (93.1)
	Discontinued due to death	63 (31.2)	114 (56.4)
	Discontinued due to lost to follow-up	0 (0.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	97 (48.0)	69 (34.2)
Week 95	Expected to Complete Questionnaires	29 (14.4)	11 (5.4)
	Completed ^c	14 (6.9)	4 (2.0)
	Compliance (% in those expected to complete questionnaires) ^d	14 (48.3)	4 (36.4)
	Not completed	15 (7.4)	7 (3.5)
	With visit, no record	15 (7.4)	7 (3.5)
	Missing by Design	173 (85.6)	191 (94.6)
	Discontinued due to death	63 (31.2)	115 (56.9)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
	Visit not scheduled	103 (51.0)	71 (35.1)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 98	Expected to Complete Questionnaires	23 (11.4)	8 (4.0)
	Completed ^c	10 (5.0)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	10 (43.5)	3 (37.5)
	Not completed	13 (6.4)	5 (2.5)
	With visit, no record	13 (6.4)	5 (2.5)
	Missing by Design	179 (88.6)	194 (96.0)
	Discontinued due to death	63 (31.2)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	109 (54.0)	73 (36.1)	
Week 101	Expected to Complete Questionnaires	17 (8.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (41.2)	3 (37.5)
	Not completed	10 (5.0)	5 (2.5)
	With visit, no record	10 (5.0)	5 (2.5)
	Missing by Design	185 (91.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	114 (56.4)	73 (36.1)	
Week 104	Expected to Complete Questionnaires	13 (6.4)	8 (4.0)
	Completed ^c	7 (3.5)	3 (1.5)
	Compliance (% in those expected to complete questionnaires) ^d	7 (53.8)	3 (37.5)
	Not completed	6 (3.0)	5 (2.5)
	With visit, no record	6 (3.0)	5 (2.5)
	Missing by Design	189 (93.6)	194 (96.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	1 (0.5)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	118 (58.4)	73 (36.1)	
Week 107	Expected to Complete Questionnaires	12 (5.9)	7 (3.5)
	Completed ^c	7 (3.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	7 (58.3)	2 (28.6)
	Not completed	5 (2.5)	5 (2.5)
	With visit, no record	5 (2.5)	5 (2.5)
	Missing by Design	190 (94.1)	195 (96.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	118 (58.4)	74 (36.6)	
Week 110	Expected to Complete Questionnaires	9 (4.5)	5 (2.5)
	Completed ^c	3 (1.5)	2 (1.0)
	Compliance (% in those expected to complete questionnaires) ^d	3 (33.3)	2 (40.0)
	Not completed	6 (3.0)	3 (1.5)
	With visit, no record	6 (3.0)	3 (1.5)
	Missing by Design	193 (95.5)	197 (97.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	4 (2.0)
Visit not scheduled	121 (59.9)	76 (37.6)	
Week 113	Expected to Complete Questionnaires	5 (2.5)	3 (1.5)
	Completed ^c	4 (2.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	4 (80.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	197 (97.5)	199 (98.5)
Discontinued due to death	64 (31.7)	116 (57.4)	

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	125 (61.9)	77 (38.1)
Week 116	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	3 (1.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	3 (75.0)	1 (33.3)
	Not completed	1 (0.5)	2 (1.0)
	With visit, no record	1 (0.5)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 119	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 122	Expected to Complete Questionnaires	4 (2.0)	3 (1.5)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (50.0)	1 (33.3)
	Not completed	2 (1.0)	2 (1.0)
	With visit, no record	2 (1.0)	2 (1.0)
	Missing by Design	198 (98.0)	199 (98.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	126 (62.4)	77 (38.1)
Week 125	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	2 (1.0)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	2 (66.7)	1 (50.0)
	Not completed	1 (0.5)	1 (0.5)
	With visit, no record	1 (0.5)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)
Week 128	Expected to Complete Questionnaires	3 (1.5)	2 (1.0)
	Completed ^c	1 (0.5)	1 (0.5)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	1 (50.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	200 (99.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	78 (38.6)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 131	Expected to Complete Questionnaires	3 (1.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (33.3)	0 (0.0)
	Not completed	2 (1.0)	1 (0.5)
	With visit, no record	2 (1.0)	1 (0.5)
	Missing by Design	199 (98.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	127 (62.9)	79 (39.1)
Week 134	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	129 (63.9)	79 (39.1)
Week 137	Expected to Complete Questionnaires	1 (0.5)	1 (0.5)
	Completed ^c	1 (0.5)	0 (0.0)
	Compliance (% in those expected to complete questionnaires) ^d	1 (100.0)	0 (0.0)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	201 (99.5)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	129 (63.9)	79 (39.1)
Week 140	Expected to Complete Questionnaires	0 (0.0)	1 (0.5)
	Not completed	0 (0.0)	1 (0.5)
	With visit, no record	0 (0.0)	1 (0.5)
	Missing by Design	202 (100.0)	201 (99.5)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	79 (39.1)
Week 143	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 146	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
Week 149	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)

Study: KEYNOTE-A39 ^a		EV+Pembro	Plat+Gem
Visit	Category	N ^b = 202 n (%)	N ^b = 202 n (%)
Week 152	Missing by Design	202 (100.0)	202 (100.0)
	Discontinued due to death	64 (31.7)	116 (57.4)
	Discontinued due to lost to follow-up	2 (1.0)	1 (0.5)
	Discontinued due to withdrawal by participant	6 (3.0)	5 (2.5)
	Visit not scheduled	130 (64.4)	80 (39.6)
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: intention-to-treat population, cisplatin ineligible</p> <p>c: Completion rate is defined as the proportion of subjects who completed the instrument among the ITT analysis set</p> <p>d: Compliance rate is defined as the proportion of subjects who completed the instrument among those expected to complete at each visit. Subjects are expected to complete the instrument if the scheduled visit occurred</p> <p>ITT: Intention-to-Treat</p>			

Anhang 4-G3: Ergebnisse der Auswertungen über den Studienverlauf für die Endpunkte Krankheitssymptomatik und Gesundheitszustand anhand von EORTC QLQ-C30 und EQ-5D VAS KEYNOTE A39

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Auswertungen über den Studienverlauf des EORTC QLQ-C30, der EQ-5D VAS und des BPI-SF dargestellt.

Cisplatin geeignet

EORTC QLQ-C30

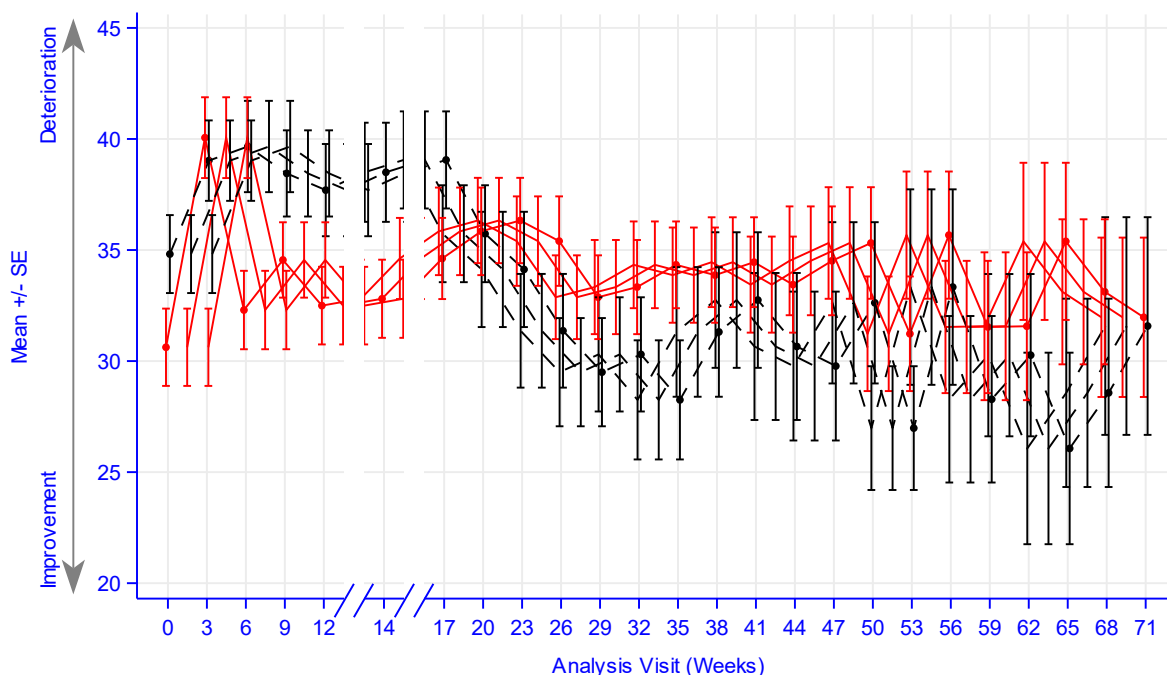
Tabelle 4G-11: Auswertung über den Studienverlauf der Symptomskala Erschöpfung des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	30,6 (24,9)	34,8 (24,0)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	34,0 (24,5)	40,6 (23,7)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	37,5 (25,1)	43,9 (26,0)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (33,3; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	40,1 (24,7)	39,0 (23,0)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	35,5 (23,4)	40,0 (22,8)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	34,0 (23,4)	42,8 (22,9)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	32,3 (23,2)	39,7 (25,3)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 7		
N ^c	178	159
Mittelwert (SD)	33,6 (22,0)	38,4 (23,0)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	33,3 (22,9)	41,1 (23,4)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	182	152
Mittelwert (SD)	34,6 (22,9)	38,4 (23,9)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	32,6 (20,6)	39,2 (24,1)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 88,9	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	33,0 (23,6)	38,9 (24,5)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	32,5 (23,0)	37,7 (24,6)
Median (Q1; Q3)	33,3 (22,2; 33,3)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	32,8 (22,9)	38,5 (25,3)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	34,6 (23,4)	39,1 (25,1)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 61,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	35,8 (24,5)	35,7 (23,0)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	36,3 (23,7)	34,1 (25,7)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (11,1; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 26		
N ^c	145	96
Mittelwert (SD)	35,4 (24,3)	31,4 (25,1)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	32,9 (22,8)	29,5 (22,7)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	33,3 (23,7)	30,3 (22,6)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	34,3 (21,6)	28,3 (22,4)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	33,9 (23,9)	31,3 (23,7)
Median (Q1; Q3)	33,3 (16,7; 44,4)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	34,5 (22,1)	32,7 (23,0)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	33,4 (21,6)	30,7 (24,3)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 88,9	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	34,5 (23,8)	29,8 (23,7)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	35,3 (23,0)	32,6 (24,9)
Median (Q1; Q3)	33,3 (22,2; 50,0)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	31,2 (22,2)	27,0 (18,1)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 56		
N ^c	76	34
Mittelwert (SD)	35,7 (25,0)	33,3 (25,7)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	31,5 (24,6)	28,3 (21,5)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	31,6 (26,4)	30,3 (19,7)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 77,8
Woche 65		
N ^c	54	26
Mittelwert (SD)	35,4 (26,0)	26,1 (22,0)
Median (Q1; Q3)	33,3 (11,1; 55,6)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	33,1 (23,5)	28,6 (19,4)
Median (Q1; Q3)	33,3 (22,2; 38,9)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 71		
N ^c	49	19
Mittelwert (SD)	32,0 (25,1)	31,6 (21,4)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

EV+Pembro	205	185	172	182	173	169	164	155	152	145	146	125	122	124	119	100	94	84	74	76	68	63	54	52	49
Plat+Gem	187	162	151	152	140	129	132	111	98	96	87	77	70	66	57	54	50	47	42	34	33	29	26	21	19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Fatigue

Abbildung 4G-1: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Erschöpfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

Tabelle 4G-12: Auswertung über den Studienverlauf der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	5,9 (14,3)	5,7 (10,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 1		
N ^c	188	159
Mittelwert (SD)	8,4 (17,5)	16,7 (20,2)
Median (Q1; Q3)	0,0 (0,0; 16,7)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0

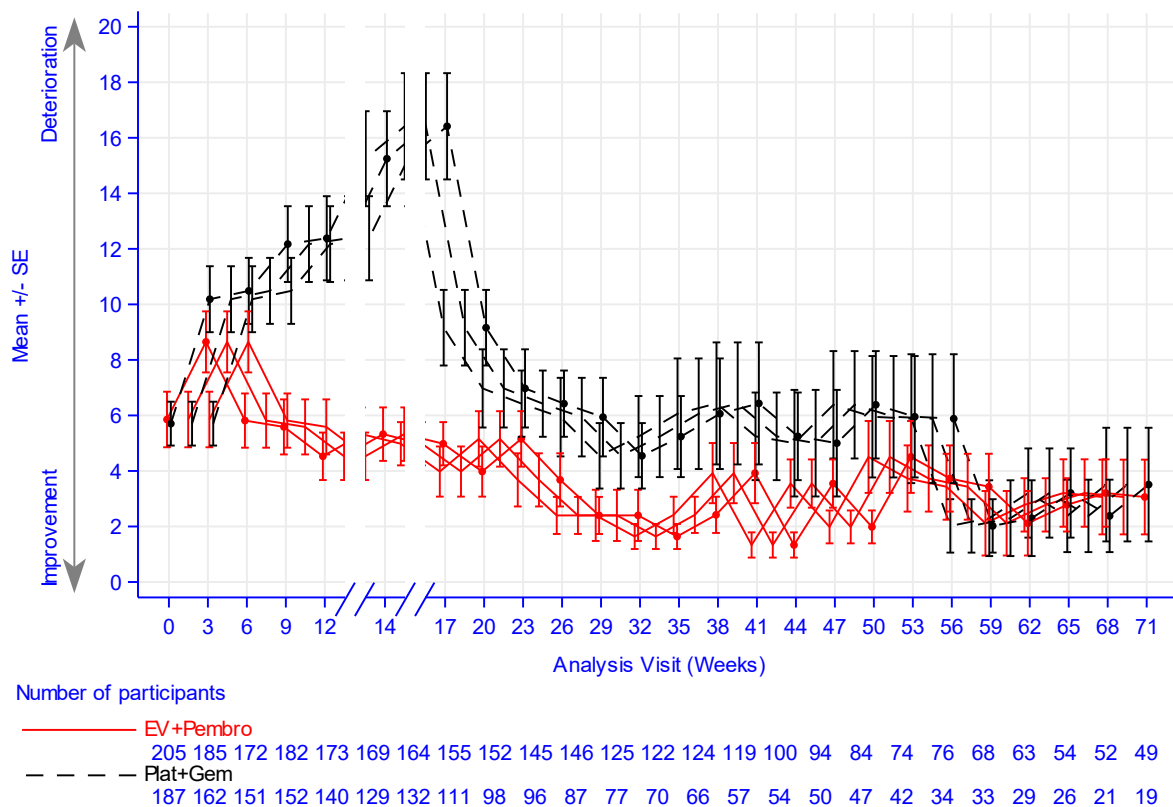
EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	9,5 (17,5)	14,7 (19,3)
Median (Q1; Q3)	0,0 (0,0; 16,7)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	8,6 (15,0)	10,2 (15,1)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 4		
N ^c	181	157
Mittelwert (SD)	5,4 (10,4)	13,7 (17,8)
Median (Q1; Q3)	0,0 (0,0; 16,7)	16,7 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 83,3
Woche 5		
N ^c	175	157
Mittelwert (SD)	6,3 (11,9)	13,9 (16,9)
Median (Q1; Q3)	0,0 (0,0; 16,7)	16,7 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 83,3
Woche 6		
N ^c	172	151
Mittelwert (SD)	5,8 (12,8)	10,5 (14,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	5,6 (12,4)	13,3 (17,0)
Median (Q1; Q3)	0,0 (0,0; 16,7)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 8		
N ^c	173	146
Mittelwert (SD)	5,1 (9,7)	14,3 (17,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 83,3
Woche 9		
N ^c	182	152
Mittelwert (SD)	5,6 (13,4)	12,2 (16,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 10		
N ^c	177	141
Mittelwert (SD)	4,0 (10,1)	14,8 (19,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	4,0 (9,3)	17,1 (20,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Min, Max	0,0; 50,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	4,5 (11,2)	12,4 (17,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	5,3 (12,5)	15,2 (19,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 17		
N ^c	164	132
Mittelwert (SD)	5,0 (10,0)	16,4 (22,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	4,0 (11,3)	9,2 (14,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 23		
N ^c	152	98
Mittelwert (SD)	5,2 (12,3)	7,0 (13,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 26		
N ^c	145	96
Mittelwert (SD)	3,7 (11,5)	6,4 (11,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 50,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	2,4 (8,1)	5,9 (13,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 32		
N ^c	125	77
Mittelwert (SD)	2,4 (10,3)	4,5 (10,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 50,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	1,6 (5,0)	5,2 (12,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 16,7	0,0; 66,7
Woche 38		
N ^c	124	66
Mittelwert (SD)	2,4 (7,3)	6,1 (16,2)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 83,3
Woche 41		
N ^c	119	57
Mittelwert (SD)	3,9 (11,8)	6,4 (16,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	1,3 (4,5)	5,2 (11,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 16,7	0,0; 50,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	3,5 (8,4)	5,0 (13,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 50		
N ^c	84	47
Mittelwert (SD)	2,0 (5,4)	6,4 (13,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 16,7	0,0; 66,7
Woche 53		
N ^c	74	42
Mittelwert (SD)	4,5 (11,1)	6,0 (14,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 56		
N ^c	76	34
Mittelwert (SD)	3,7 (10,4)	5,9 (13,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 59		
N ^c	68	33
Mittelwert (SD)	3,4 (9,8)	2,0 (5,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 16,7
Woche 62		
N ^c	63	29
Mittelwert (SD)	2,1 (9,2)	2,3 (7,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 65		
N ^c	54	26
Mittelwert (SD)	2,8 (7,1)	3,2 (8,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 68		
N ^c	52	21
Mittelwert (SD)	3,2 (8,8)	2,4 (6,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 71		
N ^c	49	19
Mittelwert (SD)	3,1 (9,4)	3,5 (8,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 33,3

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Nausea and Vomiting

Abbildung 4G-2: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Übelkeit und Erbrechen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

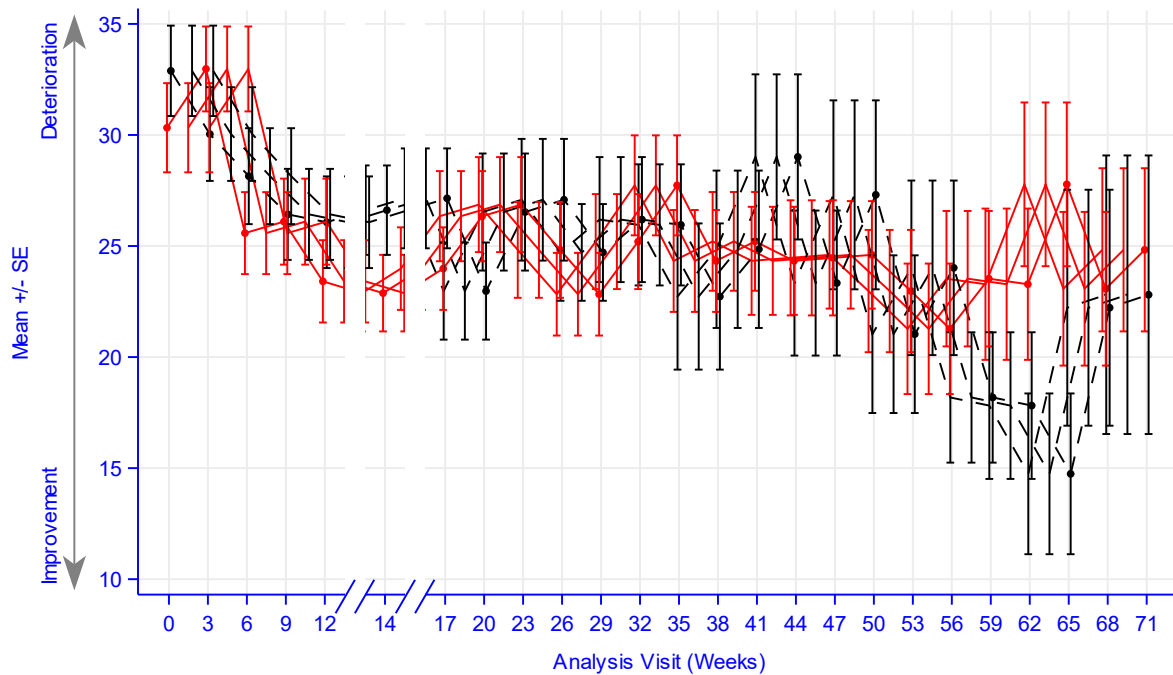
Tabelle 4G-13: Auswertung über den Studienverlauf der Symptomskala Schmerzen des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	30,3 (28,7)	32,9 (27,8)
Median (Q1; Q3)	33,3 (0,0; 50,0)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	31,9 (27,4)	32,3 (26,6)
Median (Q1; Q3)	33,3 (0,0; 50,0)	33,3 (16,7; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	32,2 (26,3)	33,7 (27,4)
Median (Q1; Q3)	33,3 (16,7; 50,0)	33,3 (16,7; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	33,0 (26,0)	30,0 (26,8)
Median (Q1; Q3)	33,3 (16,7; 50,0)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	24,1 (22,7)	27,8 (26,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	23,1 (24,2)	29,1 (26,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	25,6 (24,2)	28,1 (26,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	24,9 (26,0)	26,6 (24,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	23,9 (25,1)	29,5 (25,2)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	182	152
Mittelwert (SD)	26,1 (26,1)	26,4 (25,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	24,8 (22,8)	25,1 (24,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	23,2 (23,4)	25,7 (23,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	23,4 (24,4)	26,1 (24,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	22,9 (22,4)	26,6 (22,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	24,0 (23,8)	27,1 (25,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 41,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	26,3 (25,3)	23,0 (23,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	26,9 (26,4)	26,5 (26,1)
Median (Q1; Q3)	33,3 (0,0; 41,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	24,8 (26,0)	27,1 (26,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	25,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	22,8 (22,5)	24,7 (20,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	25,2 (23,9)	26,2 (24,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	27,7 (24,9)	26,0 (22,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	24,3 (25,5)	22,7 (26,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	25,2 (24,2)	24,9 (26,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	24,3 (24,3)	29,0 (27,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	24,5 (25,1)	23,3 (23,1)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 50		
N ^c	84	47
Mittelwert (SD)	24,6 (22,2)	27,3 (29,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	23,0 (23,7)	21,0 (23,0)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 56		
N ^c	76	34
Mittelwert (SD)	21,3 (25,6)	24,0 (22,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 59		
N ^c	68	33
Mittelwert (SD)	23,5 (25,1)	18,2 (16,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	23,3 (27,0)	17,8 (17,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 65		
N ^c	54	26
Mittelwert (SD)	27,8 (27,1)	14,7 (18,5)
Median (Q1; Q3)	33,3 (0,0; 50,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 50,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	23,1 (25,0)	22,2 (24,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 71		
N ^c	49	19
Mittelwert (SD)	24,8 (25,7)	22,8 (27,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

—	EV+Pembro	205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
---	Plat+Gem	187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Pain

Abbildung 4G-3: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerzen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

Tabelle 4G-14: Auswertung über den Studienverlauf der Symptomskala Dyspnoe des EORTC QLQ-C30 (Cisplatin geeignet)

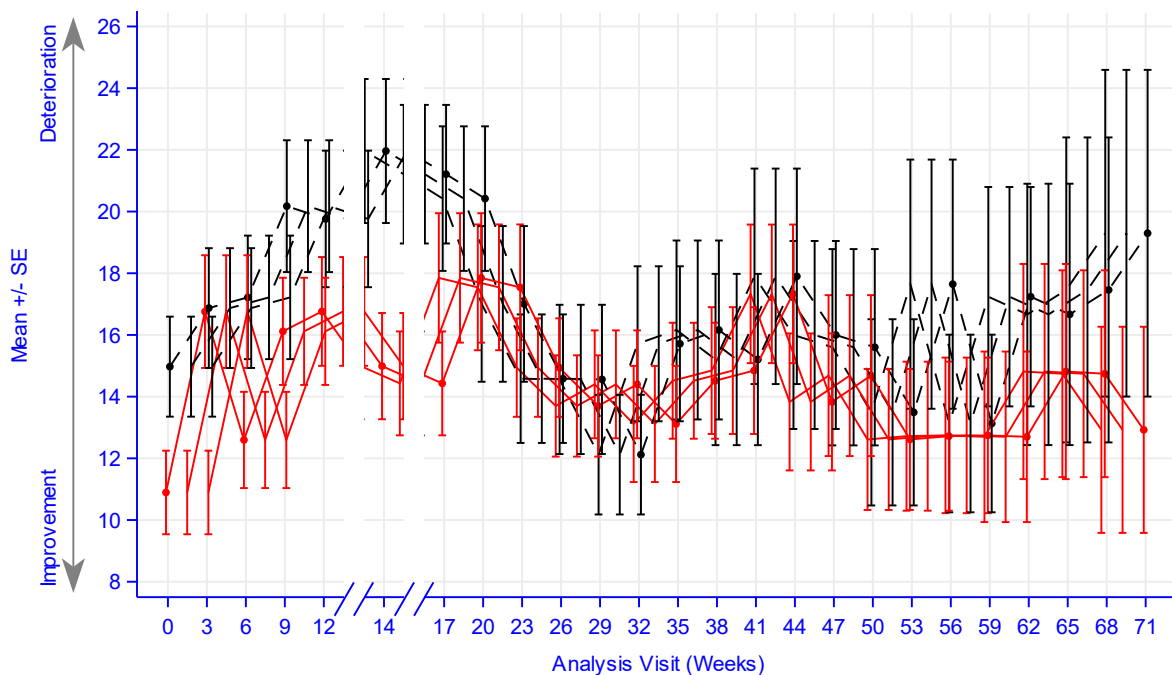
EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	10,9 (19,4)	15,0 (22,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	12,4 (21,0)	13,6 (22,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	13,9 (21,9)	15,9 (24,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	16,8 (24,8)	16,9 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	14,0 (23,1)	16,3 (23,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	14,3 (24,1)	18,3 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	12,6 (20,5)	17,2 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	14,6 (21,5)	17,0 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	13,9 (21,6)	20,5 (27,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	182	152
Mittelwert (SD)	16,1 (23,4)	20,2 (26,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	13,4 (20,5)	21,5 (26,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	15,6 (21,9)	21,4 (28,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 12		
N ^c	173	140
Mittelwert (SD)	16,8 (23,2)	19,8 (26,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	15,0 (22,4)	22,0 (26,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	14,4 (21,6)	21,2 (25,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	17,8 (26,1)	20,4 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	17,5 (25,1)	17,0 (25,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	14,9 (19,2)	14,6 (20,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 29		
N ^c	146	87
Mittelwert (SD)	13,7 (19,8)	14,6 (22,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	14,4 (19,6)	12,1 (17,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 35		
N ^c	122	70
Mittelwert (SD)	13,1 (20,8)	15,7 (21,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 38		
N ^c	124	66
Mittelwert (SD)	14,5 (20,9)	16,2 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 41		
N ^c	119	57
Mittelwert (SD)	14,8 (22,4)	15,2 (21,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	17,3 (22,5)	17,9 (25,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	13,8 (21,5)	16,0 (21,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	14,7 (23,9)	15,6 (21,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	12,6 (19,7)	13,5 (19,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 56		
N ^c	76	34
Mittelwert (SD)	12,7 (21,1)	17,6 (23,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	12,7 (20,8)	13,1 (16,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 62		
N ^c	63	29
Mittelwert (SD)	12,7 (21,9)	17,2 (19,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 65		
N ^c	54	26
Mittelwert (SD)	14,8 (25,6)	16,7 (21,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 68		
N ^c	52	21
Mittelwert (SD)	14,7 (24,2)	17,5 (22,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 71		
N ^c	49	19
Mittelwert (SD)	12,9 (23,4)	19,3 (23,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome – Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro

205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49

- - - Plat+Gem

187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Dyspnoea

Abbildung 4G-4: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Dyspnoe zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

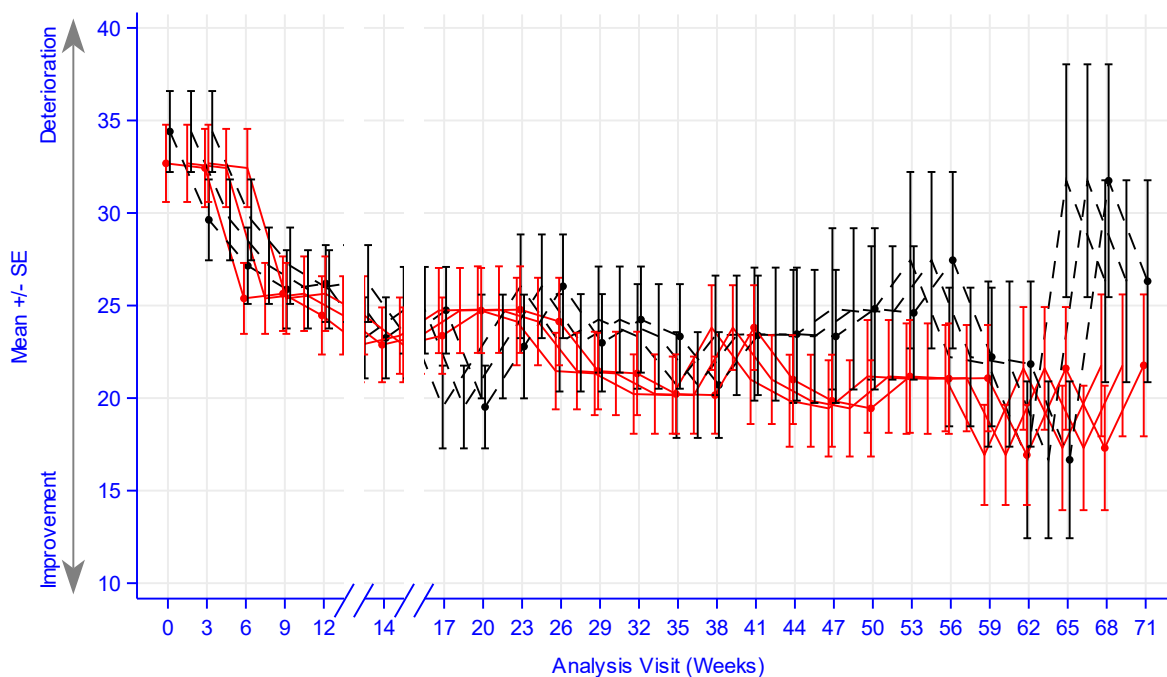
Tabelle 4G-15: Auswertung über den Studienverlauf der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	32,7 (29,9)	34,4 (29,9)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	32,4 (28,3)	33,1 (28,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	31,1 (27,7)	38,6 (28,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (33,3; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	32,4 (28,7)	29,6 (27,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	25,4 (24,7)	28,0 (24,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	25,5 (27,1)	30,1 (24,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	25,4 (25,1)	27,2 (25,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	25,8 (27,1)	27,5 (25,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	24,9 (27,0)	26,7 (26,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	182	152
Mittelwert (SD)	25,6 (27,2)	25,9 (26,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	25,0 (25,5)	27,9 (23,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	25,8 (27,4)	28,0 (26,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	24,5 (27,8)	26,2 (24,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	22,9 (26,3)	23,3 (24,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	23,4 (26,4)	24,7 (26,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	24,7 (28,6)	19,5 (23,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 23		
N ^c	152	98
Mittelwert (SD)	24,8 (28,8)	22,8 (27,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	24,1 (28,5)	26,0 (27,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	21,5 (25,0)	23,0 (24,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	21,3 (25,2)	24,2 (25,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	20,2 (23,7)	23,3 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	20,2 (23,2)	20,7 (23,2)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	23,8 (25,0)	23,4 (24,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	21,0 (24,0)	23,5 (26,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	19,9 (24,1)	23,3 (25,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	19,4 (23,8)	24,8 (29,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	21,2 (26,2)	24,6 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	21,1 (26,0)	27,5 (27,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	21,1 (23,7)	22,2 (21,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	16,9 (21,5)	21,8 (24,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 65		
N ^c	54	26
Mittelwert (SD)	21,6 (24,4)	16,7 (21,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 68		
N ^c	52	21
Mittelwert (SD)	17,3 (24,2)	31,7 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	21,8 (26,8)	26,3 (23,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

Group	0	3	6	9	12	14	17	20	23	26	29	32	35	38	41	44	47	50	53	56	59	62	65	68	71
EV+Pembro	205	185	172	182	173	169	164	155	152	145	146	125	122	124	119	100	94	84	74	76	68	63	54	52	49
Plat+Gem	187	162	151	152	140	129	132	111	98	96	87	77	70	66	57	54	50	47	42	34	33	29	26	21	19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Insomnia

Abbildung 4G-5: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schlaflosigkeit zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

Tabelle 4G-16: Auswertung über den Studienverlauf der Symptomskala Appetitverlust des EORTC QLQ-C30 (Cisplatin geeignet)

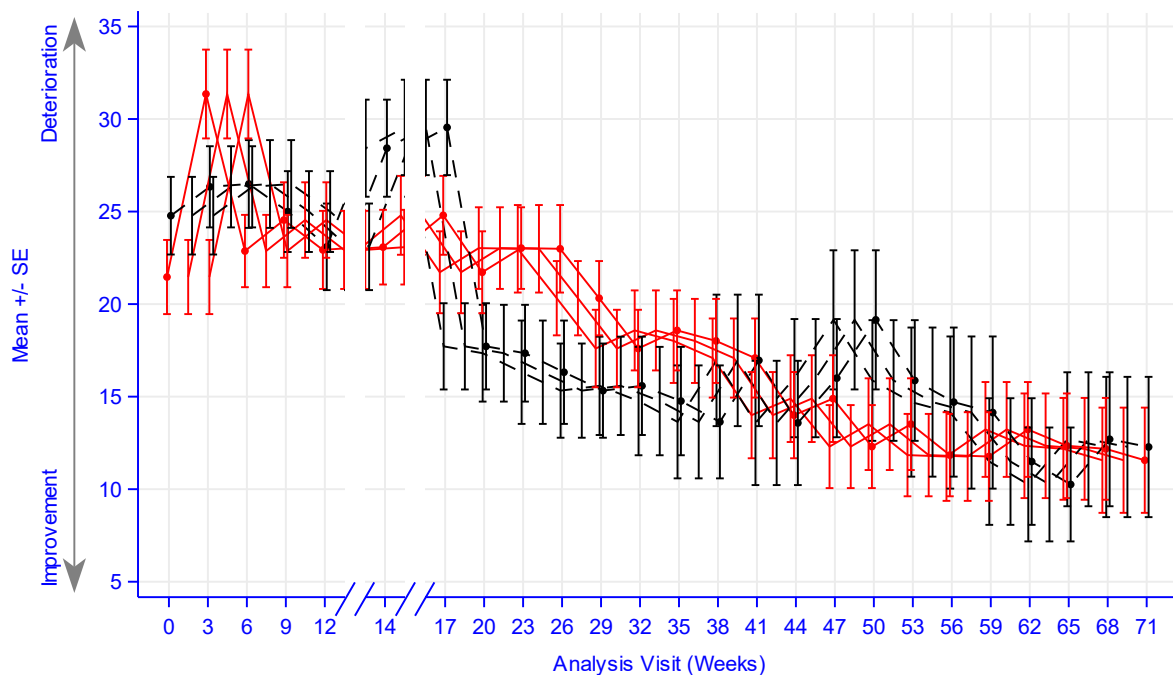
EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	21,5 (28,7)	24,8 (28,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	23,9 (27,6)	33,8 (30,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	30,0 (30,6)	34,4 (32,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	31,4 (32,6)	26,3 (27,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	26,3 (28,1)	29,7 (28,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	24,8 (29,2)	29,9 (28,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	22,9 (25,6)	26,5 (29,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	23,4 (26,4)	28,7 (27,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	22,9 (26,6)	28,1 (27,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	182	152
Mittelwert (SD)	24,5 (27,5)	25,0 (26,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	21,3 (24,0)	26,7 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	22,4 (26,2)	29,2 (30,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 12		
N ^c	173	140
Mittelwert (SD)	22,9 (27,7)	23,1 (27,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	23,1 (26,2)	28,4 (29,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	24,8 (27,3)	29,5 (29,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	21,7 (27,5)	17,7 (24,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	23,0 (27,2)	17,3 (25,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	23,0 (28,5)	16,3 (27,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	20,3 (24,3)	15,3 (23,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	17,6 (23,4)	15,6 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	18,6 (23,9)	14,8 (24,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	18,0 (25,3)	13,6 (24,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 41		
N ^c	119	57
Mittelwert (SD)	17,1 (23,3)	17,0 (26,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	14,0 (23,3)	13,6 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	14,9 (22,7)	16,0 (22,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 50		
N ^c	84	47
Mittelwert (SD)	12,3 (20,6)	19,1 (25,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	13,5 (21,3)	15,9 (21,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 56		
N ^c	76	34
Mittelwert (SD)	11,8 (19,4)	14,7 (23,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 59		
N ^c	68	33
Mittelwert (SD)	11,8 (19,8)	14,1 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	13,2 (20,3)	11,5 (18,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 65		
N ^c	54	26
Mittelwert (SD)	12,3 (20,8)	10,3 (15,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 68		
N ^c	52	21
Mittelwert (SD)	12,2 (19,8)	12,7 (16,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 71		
N ^c	49	19
Mittelwert (SD)	11,6 (19,9)	12,3 (16,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
- - - Plat+Gem	187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Appetite Loss

Abbildung 4G-6: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Appetitverlust zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

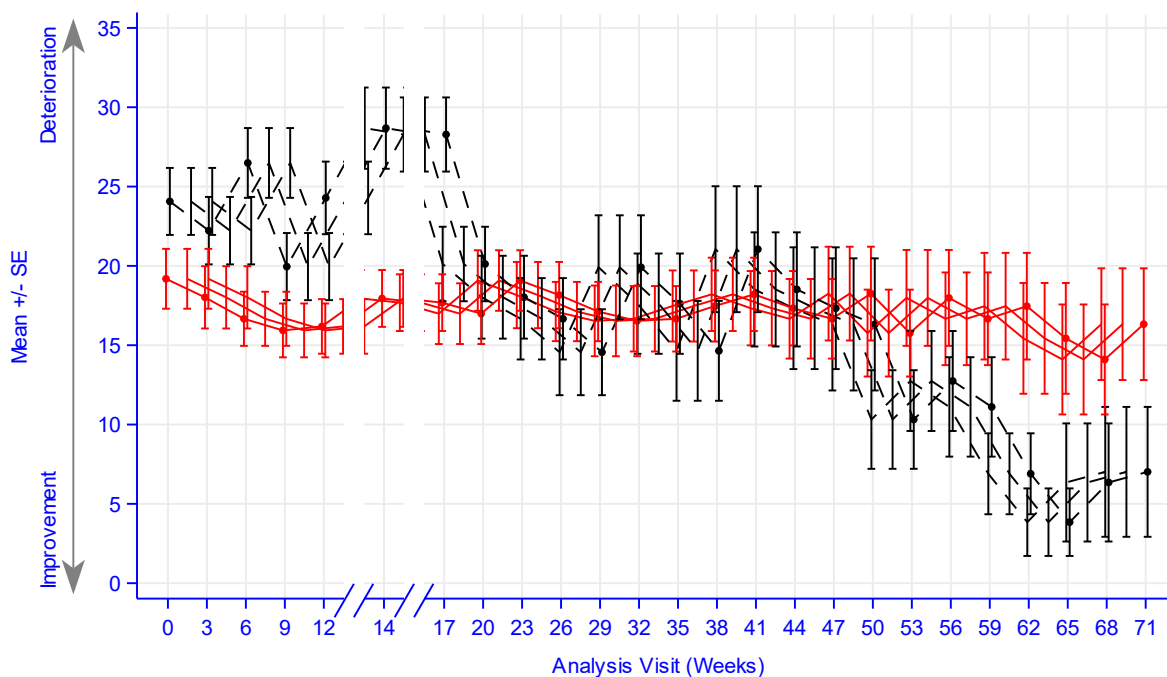
Tabelle 4G-17: Auswertung über den Studienverlauf der Symptomskala Verstopfung des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	19,2 (27,0)	24,1 (28,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	22,5 (30,4)	34,6 (31,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	18,1 (25,9)	31,1 (31,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	18,0 (26,7)	22,2 (27,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	18,0 (23,2)	26,5 (27,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	16,4 (22,3)	27,8 (28,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	16,7 (22,4)	26,5 (27,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	18,7 (24,8)	26,0 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	16,6 (23,7)	28,1 (27,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	182	152
Mittelwert (SD)	15,9 (22,9)	20,0 (26,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	15,6 (23,0)	26,2 (28,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	16,4 (22,2)	25,3 (28,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	16,2 (22,6)	24,3 (27,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	17,9 (23,3)	28,7 (29,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	17,7 (22,9)	28,3 (26,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	17,0 (23,8)	20,1 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	19,1 (23,5)	18,0 (25,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	18,2 (25,1)	16,7 (25,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	17,1 (22,6)	14,6 (25,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	16,5 (24,9)	19,9 (28,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	16,7 (22,8)	17,6 (26,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	17,5 (25,0)	14,6 (25,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	18,2 (25,2)	21,1 (30,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	17,3 (23,4)	18,5 (26,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	16,7 (24,3)	17,3 (27,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	18,3 (27,1)	16,3 (28,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	15,8 (23,6)	10,3 (20,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	18,0 (26,4)	12,7 (18,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 59		
N ^c	68	33
Mittelwert (SD)	16,7 (24,1)	11,1 (18,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	17,5 (26,7)	6,9 (13,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 65		
N ^c	54	26
Mittelwert (SD)	15,4 (25,7)	3,8 (10,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 68		
N ^c	52	21
Mittelwert (SD)	14,1 (25,0)	6,3 (17,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 71		
N ^c	49	19
Mittelwert (SD)	16,3 (24,6)	7,0 (17,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro

205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49

- - - Plat+Gem

187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Constipation

Abbildung 4G-7: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Verstopfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

Tabelle 4G-18: Auswertung über den Studienverlauf der Symptomskala Diarrhö des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	6,5 (15,2)	5,2 (14,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 1		
N ^c	188	159
Mittelwert (SD)	7,8 (18,2)	6,3 (16,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0

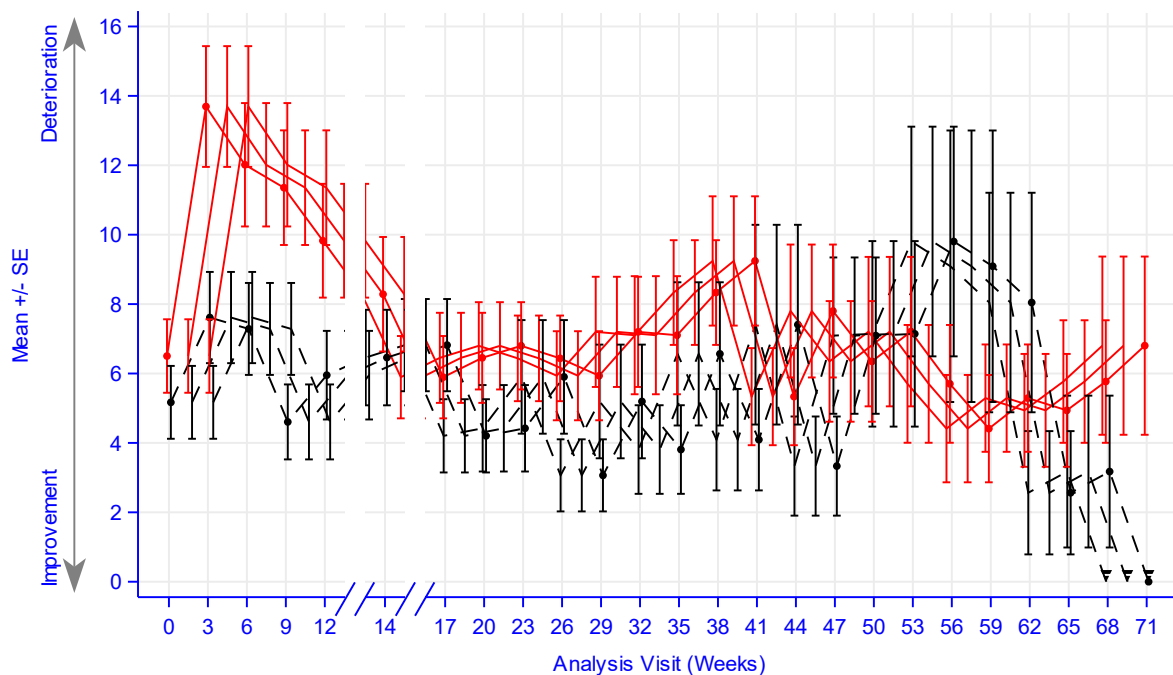
EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	12,2 (23,7)	11,5 (21,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	13,7 (23,7)	7,6 (16,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	9,9 (19,5)	4,9 (15,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	9,1 (21,6)	4,9 (13,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 6		
N ^c	172	151
Mittelwert (SD)	12,0 (23,3)	7,3 (16,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 7		
N ^c	178	159
Mittelwert (SD)	10,1 (22,1)	4,4 (13,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 8		
N ^c	173	146
Mittelwert (SD)	9,1 (19,7)	3,7 (11,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 9		
N ^c	182	152
Mittelwert (SD)	11,4 (22,3)	4,6 (13,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 10		
N ^c	177	141
Mittelwert (SD)	8,1 (19,9)	5,2 (14,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 11		
N ^c	177	145
Mittelwert (SD)	7,9 (19,8)	5,1 (14,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 12		
N ^c	173	140
Mittelwert (SD)	9,8 (21,6)	6,0 (15,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	8,3 (21,4)	6,5 (15,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 17		
N ^c	164	132
Mittelwert (SD)	5,9 (15,2)	6,8 (15,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 20		
N ^c	155	111
Mittelwert (SD)	6,5 (16,2)	4,2 (11,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 23		
N ^c	152	98
Mittelwert (SD)	6,8 (15,5)	4,4 (12,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 26		
N ^c	145	96
Mittelwert (SD)	6,4 (14,9)	5,9 (16,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	5,9 (15,5)	3,1 (9,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 32		
N ^c	125	77
Mittelwert (SD)	7,2 (17,8)	5,2 (14,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 35		
N ^c	122	70
Mittelwert (SD)	7,1 (18,8)	3,8 (10,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 38		
N ^c	124	66
Mittelwert (SD)	8,3 (16,8)	6,6 (16,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 41		
N ^c	119	57
Mittelwert (SD)	9,2 (20,3)	4,1 (11,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 44		
N ^c	100	54
Mittelwert (SD)	5,3 (14,0)	7,4 (21,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	7,8 (18,6)	3,3 (10,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 50		
N ^c	84	47
Mittelwert (SD)	6,3 (15,9)	7,1 (15,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 53		
N ^c	74	42
Mittelwert (SD)	7,2 (18,5)	7,1 (17,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 56		
N ^c	76	34
Mittelwert (SD)	5,7 (14,8)	9,8 (19,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 59		
N ^c	68	33
Mittelwert (SD)	4,4 (12,8)	9,1 (22,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	5,3 (12,3)	8,0 (17,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 65		
N ^c	54	26
Mittelwert (SD)	4,9 (12,0)	2,6 (9,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 68		
N ^c	52	21
Mittelwert (SD)	5,8 (12,7)	3,2 (10,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 71		
N ^c	49	19
Mittelwert (SD)	6,8 (18,0)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 0,0

a: Datenschnitt: 08. August 2023
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet
c: Anzahl der Beobachtungen zu jedem Zeitpunkt
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Number of participants

— EV+Pembro	205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
- - - Plat+Gem	187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Diarrhoea

Abbildung 4G-8: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Diarrhö zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39

EQ-5D-VAS

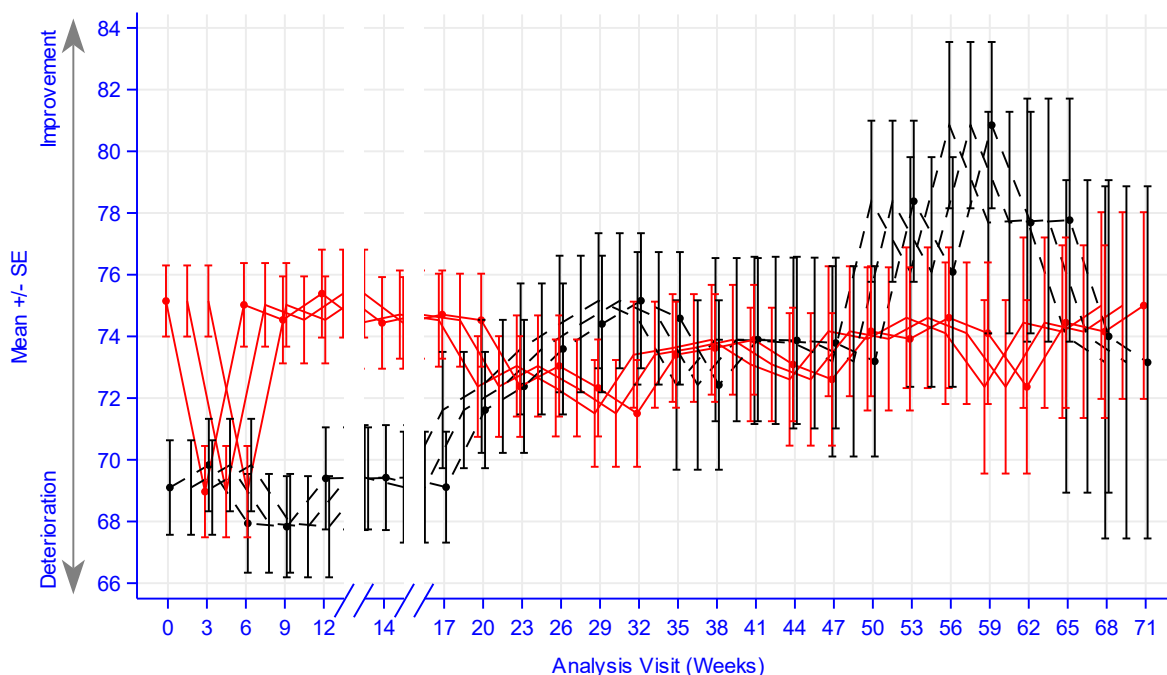
Tabelle 4G-19: Auswertung über den Studienverlauf der EQ-5D-VAS (Cisplatin geeignet)

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	210	189
Mittelwert (SD)	75,1 (16,7)	69,1 (21,1)
Median (Q1; Q3)	79,0 (68,0; 88,0)	71,0 (55,0; 88,0)
Min, Max	15,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	164
Mittelwert (SD)	71,2 (18,8)	66,5 (20,3)
Median (Q1; Q3)	74,5 (60,0; 87,0)	70,0 (51,0; 80,0)
Min, Max	18,0; 100,0	0,0; 100,0
Woche 2		
N ^c	193	154
Mittelwert (SD)	69,9 (19,6)	67,5 (20,0)
Median (Q1; Q3)	73,0 (57,0; 85,0)	70,0 (52,0; 83,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	186	164
Mittelwert (SD)	69,0 (20,2)	69,8 (19,2)
Median (Q1; Q3)	72,0 (57,0; 85,0)	72,5 (56,0; 85,0)
Min, Max	17,0; 100,0	7,0; 100,0
Woche 4		
N ^c	182	158
Mittelwert (SD)	74,5 (18,0)	70,1 (18,3)
Median (Q1; Q3)	80,0 (62,0; 89,0)	72,0 (58,0; 85,0)
Min, Max	20,0; 100,0	10,0; 100,0
Woche 5		
N ^c	178	158
Mittelwert (SD)	74,0 (18,4)	69,1 (19,1)
Median (Q1; Q3)	79,0 (60,0; 89,0)	71,0 (56,0; 84,0)
Min, Max	25,0; 100,0	8,0; 100,0
Woche 6		
N ^c	175	151
Mittelwert (SD)	75,0 (17,9)	67,9 (19,7)
Median (Q1; Q3)	79,0 (63,0; 90,0)	71,0 (52,0; 82,0)
Min, Max	11,0; 100,0	11,0; 100,0
Woche 7		
N ^c	179	161
Mittelwert (SD)	74,8 (19,2)	68,3 (19,1)
Median (Q1; Q3)	80,0 (66,0; 90,0)	70,0 (54,0; 83,0)
Min, Max	0,0; 100,0	1,0; 100,0
Woche 8		
N ^c	175	147
Mittelwert (SD)	74,5 (18,9)	67,6 (20,3)
Median (Q1; Q3)	80,0 (67,0; 90,0)	70,0 (55,0; 84,0)
Min, Max	5,0; 100,0	0,0; 100,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	183	153
Mittelwert (SD)	74,5 (19,1)	67,8 (20,3)
Median (Q1; Q3)	80,0 (65,0; 90,0)	70,0 (52,0; 84,0)
Min, Max	19,0; 100,0	10,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	75,7 (16,9)	67,3 (20,5)
Median (Q1; Q3)	80,0 (65,0; 90,0)	70,0 (50,0; 84,0)
Min, Max	28,0; 100,0	9,0; 100,0
Woche 11		
N ^c	179	145
Mittelwert (SD)	75,8 (17,5)	69,0 (18,8)
Median (Q1; Q3)	80,0 (66,0; 90,0)	70,0 (55,0; 86,0)
Min, Max	11,0; 100,0	9,0; 100,0
Woche 12		
N ^c	173	141
Mittelwert (SD)	75,4 (18,7)	69,4 (19,6)
Median (Q1; Q3)	80,0 (68,0; 90,0)	71,0 (57,0; 85,0)
Min, Max	10,0; 100,0	1,0; 100,0
Woche 14		
N ^c	169	130
Mittelwert (SD)	74,4 (19,3)	69,4 (19,4)
Median (Q1; Q3)	80,0 (65,0; 90,0)	70,0 (51,0; 86,0)
Min, Max	6,0; 100,0	10,0; 100,0
Woche 17		
N ^c	164	133
Mittelwert (SD)	74,7 (18,3)	69,1 (20,7)
Median (Q1; Q3)	80,0 (63,5; 90,0)	70,0 (51,0; 88,0)
Min, Max	20,0; 100,0	8,0; 100,0
Woche 20		
N ^c	156	111
Mittelwert (SD)	74,5 (18,8)	71,6 (19,9)
Median (Q1; Q3)	80,0 (65,0; 90,0)	76,0 (54,0; 88,0)
Min, Max	10,0; 100,0	10,0; 100,0
Woche 23		
N ^c	152	100
Mittelwert (SD)	72,4 (20,1)	72,4 (21,6)
Median (Q1; Q3)	79,5 (60,0; 90,0)	78,5 (55,0; 90,5)
Min, Max	1,0; 100,0	2,0; 100,0
Woche 26		
N ^c	146	96
Mittelwert (SD)	73,0 (19,8)	73,6 (20,8)
Median (Q1; Q3)	78,0 (58,0; 90,0)	80,0 (58,0; 90,0)
Min, Max	23,0; 100,0	8,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	72,3 (19,0)	74,4 (20,6)
Median (Q1; Q3)	78,0 (60,0; 88,0)	79,0 (63,0; 90,0)
Min, Max	13,0; 100,0	3,0; 100,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	71,5 (19,4)	75,2 (19,2)
Median (Q1; Q3)	75,0 (60,0; 88,0)	80,0 (61,0; 90,0)
Min, Max	19,0; 100,0	12,0; 100,0
Woche 35		
N ^c	123	70
Mittelwert (SD)	73,4 (19,1)	74,6 (18,0)
Median (Q1; Q3)	79,0 (60,0; 90,0)	80,0 (62,0; 87,0)
Min, Max	19,0; 100,0	20,0; 100,0
Woche 38		
N ^c	125	66
Mittelwert (SD)	73,6 (19,5)	72,4 (22,3)
Median (Q1; Q3)	76,0 (61,0; 90,0)	80,0 (51,0; 91,0)
Min, Max	13,0; 100,0	20,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	73,9 (19,4)	73,9 (20,0)
Median (Q1; Q3)	79,0 (64,0; 90,0)	80,0 (59,0; 90,0)
Min, Max	17,0; 100,0	27,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	73,1 (18,4)	73,9 (19,9)
Median (Q1; Q3)	76,5 (61,5; 88,5)	80,0 (61,0; 90,0)
Min, Max	13,0; 100,0	11,0; 100,0
Woche 47		
N ^c	94	51
Mittelwert (SD)	72,6 (20,8)	73,8 (19,8)
Median (Q1; Q3)	79,5 (60,0; 90,0)	79,0 (61,0; 91,0)
Min, Max	20,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	74,2 (19,3)	73,2 (21,1)
Median (Q1; Q3)	80,0 (62,5; 88,0)	79,0 (61,0; 90,0)
Min, Max	29,0; 100,0	1,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	73,9 (20,0)	78,4 (16,9)
Median (Q1; Q3)	79,0 (60,0; 90,0)	84,5 (67,0; 91,0)
Min, Max	20,0; 100,0	32,0; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	74,6 (19,9)	76,1 (21,7)
Median (Q1; Q3)	80,0 (60,0; 89,5)	82,5 (71,0; 91,0)
Min, Max	14,0; 100,0	20,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	74,1 (18,9)	80,8 (15,5)
Median (Q1; Q3)	77,5 (64,0; 88,0)	86,0 (75,0; 91,0)
Min, Max	20,0; 99,0	23,0; 100,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	72,4 (22,3)	77,7 (19,3)
Median (Q1; Q3)	79,0 (59,0; 91,0)	79,0 (70,0; 93,0)
Min, Max	15,0; 100,0	11,0; 100,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	74,4 (20,3)	77,8 (20,1)
Median (Q1; Q3)	79,5 (64,0; 90,0)	82,5 (70,0; 92,0)
Min, Max	23,0; 100,0	9,0; 100,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	74,2 (20,2)	74,0 (23,2)
Median (Q1; Q3)	77,0 (65,0; 90,0)	85,0 (66,0; 89,0)
Min, Max	13,0; 99,0	13,0; 100,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	75,0 (21,2)	73,2 (24,9)
Median (Q1; Q3)	80,0 (62,0; 91,0)	81,0 (62,0; 94,0)
Min, Max	15,0; 100,0	16,0; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EQ-5D: European Quality of Life 5 Dimensions; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung; VAS: Visuelle Analogskala		



Number of participants

— EV+Pembro

210 186 175 183 173 169 164 156 152 146 146 125 123 125 119 100 94 84 74 76 68 63 54 52 49

- - - Plat+Gem

189 164 151 153 141 130 133 111 100 96 87 77 70 66 57 54 51 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EQ-5D VAS Score

Abbildung 4G-9: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der EQ-5D VAS zu den verschiedenen Erhebungszeitpunkten der Studie KEYNOTE A39

BPI-SF

Tabelle 4G-20: Auswertung über den Studienverlauf der Symptomskala Stärkster Schmerz der vergangenen 24 Stunden des BPI-SF (Cisplatin geeignet)

BPI-SF Stärkster Schmerz in den letzten 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	208	189
Mittelwert (SD)	3,0 (2,8)	3,3 (2,9)
Median (Q1; Q3)	3,0 (0,0; 5,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 1		
N ^c	188	164
Mittelwert (SD)	3,2 (2,8)	3,1 (2,6)
Median (Q1; Q3)	3,0 (0,0; 6,0)	3,0 (1,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0

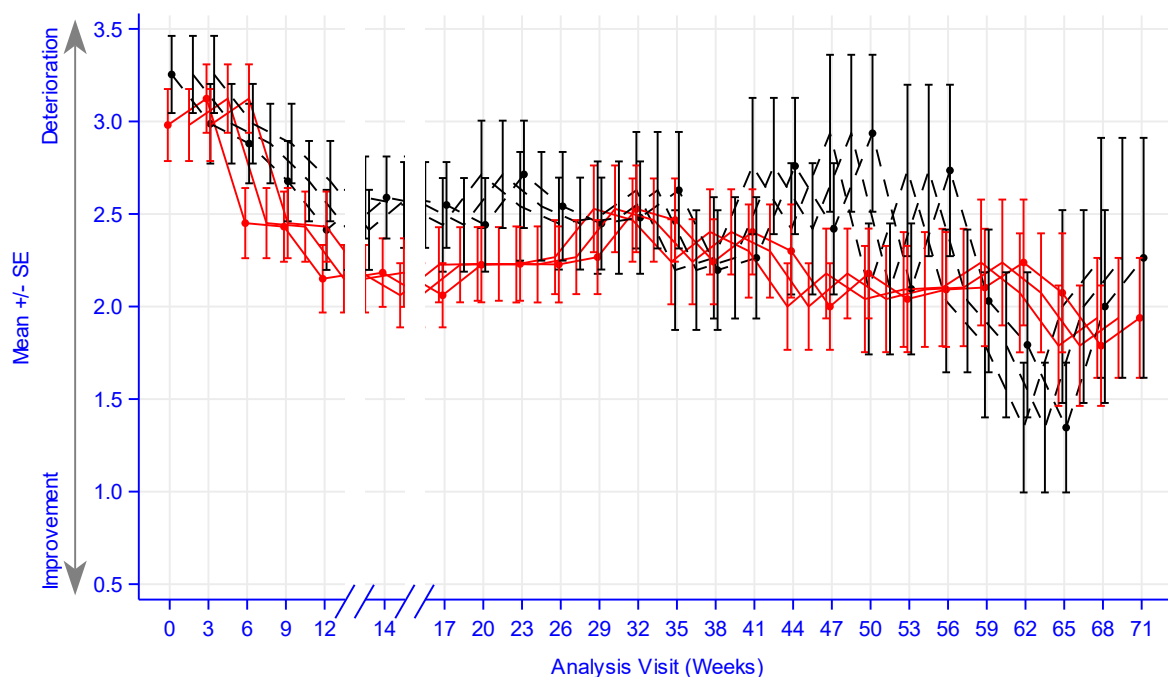
BPI-SF Stärkster Schmerz in den letzten 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	193	153
Mittelwert (SD)	3,2 (2,7)	3,1 (2,6)
Median (Q1; Q3)	3,0 (1,0; 5,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 3		
N ^c	186	163
Mittelwert (SD)	3,1 (2,5)	3,0 (2,7)
Median (Q1; Q3)	3,0 (1,0; 5,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 4		
N ^c	182	157
Mittelwert (SD)	2,3 (2,4)	2,7 (2,6)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 10,0	0,0; 9,0
Woche 5		
N ^c	178	157
Mittelwert (SD)	2,3 (2,4)	3,0 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 6		
N ^c	173	151
Mittelwert (SD)	2,5 (2,5)	2,9 (2,6)
Median (Q1; Q3)	2,0 (0,0; 4,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 7		
N ^c	179	160
Mittelwert (SD)	2,3 (2,5)	2,4 (2,4)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 8		
N ^c	174	146
Mittelwert (SD)	2,1 (2,4)	2,8 (2,7)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 9		
N ^c	183	152
Mittelwert (SD)	2,4 (2,6)	2,7 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	2,2 (2,3)	2,6 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 9,0
Woche 11		
N ^c	179	145
Mittelwert (SD)	1,9 (2,2)	2,2 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)

BPI-SF Stärkster Schmerz in den letzten 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Min, Max	0,0; 10,0	0,0; 9,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	2,2 (2,4)	2,4 (2,6)
Median (Q1; Q3)	1,0 (0,0; 3,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 10,0	0,0; 9,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	2,2 (2,4)	2,6 (2,5)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 9,0
Woche 17		
N ^c	164	133
Mittelwert (SD)	2,1 (2,2)	2,5 (2,7)
Median (Q1; Q3)	2,0 (0,0; 3,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 9,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	2,2 (2,5)	2,4 (2,7)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	2,2 (2,5)	2,7 (2,9)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	2,2 (2,5)	2,5 (2,9)
Median (Q1; Q3)	1,0 (0,0; 4,0)	1,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	2,3 (2,4)	2,4 (2,3)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 8,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	2,5 (2,6)	2,5 (2,7)
Median (Q1; Q3)	2,0 (0,0; 5,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	2,5 (2,5)	2,6 (2,6)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 10,0

BPI-SF Stärkster Schmerz in den letzten 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 38		
N ^c	124	66
Mittelwert (SD)	2,2 (2,6)	2,2 (2,6)
Median (Q1; Q3)	1,0 (0,0; 4,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 8,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	2,4 (2,5)	2,3 (2,5)
Median (Q1; Q3)	2,0 (0,0; 4,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 8,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	2,3 (2,5)	2,8 (2,7)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 8,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	2,0 (2,3)	2,4 (2,5)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 7,0	0,0; 9,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	2,2 (2,2)	2,9 (2,9)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	2,0 (2,5)	2,1 (2,3)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 9,0	0,0; 7,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	2,1 (2,7)	2,7 (2,7)
Median (Q1; Q3)	0,0 (0,0; 4,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 8,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	2,1 (2,6)	2,0 (2,2)
Median (Q1; Q3)	1,0 (0,0; 4,0)	1,0 (0,0; 3,0)
Min, Max	0,0; 9,0	0,0; 8,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	2,2 (2,7)	1,8 (2,1)
Median (Q1; Q3)	1,0 (0,0; 5,0)	1,0 (0,0; 3,0)
Min, Max	0,0; 9,0	0,0; 7,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	2,1 (2,4)	1,3 (1,8)
Median (Q1; Q3)	1,0 (0,0; 3,0)	0,0 (0,0; 3,0)

BPI-SF Stärkster Schmerz in den letzten 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro	Plat+Gem
	N ^b = 210	N ^b = 189
Min, Max	0,0; 8,0	0,0; 6,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	1,8 (2,3)	2,0 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 8,0	0,0; 6,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	1,9 (2,3)	2,3 (2,8)
Median (Q1; Q3)	1,0 (0,0; 3,0)	2,0 (0,0; 4,0)
Min, Max	0,0; 8,0	0,0; 9,0

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 BPI-SF: Brief Pain Inventory - Short Form; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Number of participants

— EV+Pembro	208 186 173 183 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
- - - Plat+Gem	189 163 151 152 140 129 133 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 BPI-SF Pain at its Worst in Last 24 Hours

Abbildung 4G-10: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden zu den verschiedenen Erhebungszeitpunkten des BPI-SF der Studie KEYNOTE A39

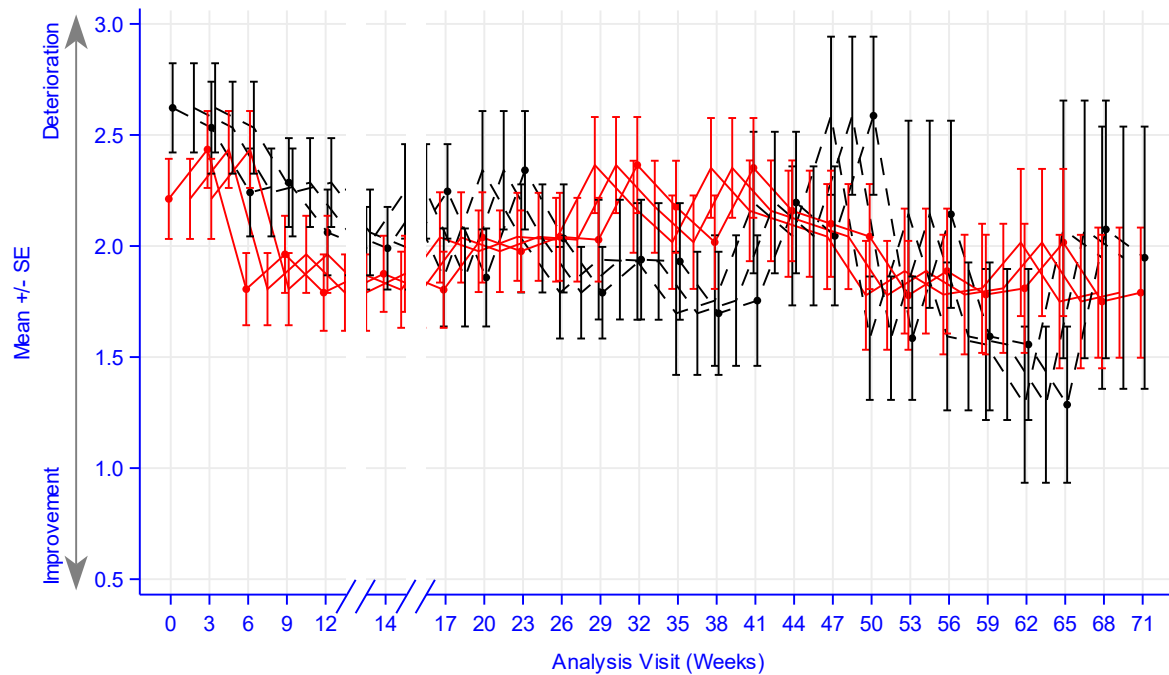
Tabelle 4G-21: Auswertung über den Studienverlauf der Symptomskala Schmerzbeeinträchtigung des BPI-SF (Cisplatin geeignet)

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	208	189
Mittelwert (SD)	2,2 (2,6)	2,6 (2,8)
Median (Q1; Q3)	1,0 (0,0; 3,8)	1,6 (0,0; 4,4)
Min, Max	0,0; 9,6	0,0; 10,0
Woche 1		
N ^c	188	164
Mittelwert (SD)	2,4 (2,5)	2,7 (2,6)
Median (Q1; Q3)	1,7 (0,1; 4,4)	2,4 (0,3; 4,5)
Min, Max	0,0; 9,6	0,0; 10,0
Woche 2		
N ^c	193	153
Mittelwert (SD)	2,6 (2,5)	2,7 (2,6)
Median (Q1; Q3)	1,9 (0,3; 4,3)	2,3 (0,0; 4,7)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 3		
N ^c	186	163
Mittelwert (SD)	2,4 (2,4)	2,5 (2,6)
Median (Q1; Q3)	1,9 (0,4; 4,0)	1,6 (0,0; 4,7)
Min, Max	0,0; 9,3	0,0; 9,0
Woche 4		
N ^c	182	157
Mittelwert (SD)	1,9 (2,1)	2,3 (2,4)
Median (Q1; Q3)	1,1 (0,0; 3,1)	1,7 (0,0; 3,9)
Min, Max	0,0; 8,3	0,0; 9,1
Woche 5		
N ^c	178	157
Mittelwert (SD)	1,9 (2,2)	2,4 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,3)	1,9 (0,0; 4,1)
Min, Max	0,0; 8,4	0,0; 9,3
Woche 6		
N ^c	173	151
Mittelwert (SD)	1,8 (2,1)	2,2 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,4 (0,0; 3,7)
Min, Max	0,0; 9,6	0,0; 9,3
Woche 7		
N ^c	179	160
Mittelwert (SD)	1,9 (2,3)	2,1 (2,3)
Median (Q1; Q3)	1,0 (0,0; 2,7)	1,3 (0,0; 3,5)
Min, Max	0,0; 10,0	0,0; 8,3
Woche 8		
N ^c	174	146
Mittelwert (SD)	1,8 (2,3)	2,3 (2,5)
Median (Q1; Q3)	0,7 (0,0; 2,6)	1,3 (0,0; 3,7)
Min, Max	0,0; 10,0	0,0; 10,0

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	183	152
Mittelwert (SD)	2,0 (2,3)	2,3 (2,5)
Median (Q1; Q3)	1,0 (0,0; 3,4)	1,4 (0,0; 3,8)
Min, Max	0,0; 9,7	0,0; 9,4
Woche 10		
N ^c	177	141
Mittelwert (SD)	1,7 (2,2)	2,1 (2,4)
Median (Q1; Q3)	1,0 (0,0; 2,9)	1,1 (0,0; 3,6)
Min, Max	0,0; 8,4	0,0; 8,9
Woche 11		
N ^c	179	145
Mittelwert (SD)	1,6 (2,1)	1,9 (2,2)
Median (Q1; Q3)	0,9 (0,0; 2,6)	1,0 (0,0; 3,6)
Min, Max	0,0; 9,7	0,0; 8,9
Woche 12		
N ^c	173	140
Mittelwert (SD)	1,8 (2,3)	2,1 (2,3)
Median (Q1; Q3)	0,7 (0,0; 2,9)	1,4 (0,0; 3,3)
Min, Max	0,0; 10,0	0,0; 9,4
Woche 14		
N ^c	169	129
Mittelwert (SD)	1,9 (2,2)	2,0 (2,1)
Median (Q1; Q3)	1,0 (0,0; 3,3)	1,1 (0,0; 3,1)
Min, Max	0,0; 9,0	0,0; 7,7
Woche 17		
N ^c	164	133
Mittelwert (SD)	1,8 (2,2)	2,2 (2,5)
Median (Q1; Q3)	0,9 (0,0; 3,0)	1,3 (0,0; 4,0)
Min, Max	0,0; 9,4	0,0; 8,7
Woche 20		
N ^c	155	111
Mittelwert (SD)	2,0 (2,5)	1,9 (2,3)
Median (Q1; Q3)	1,0 (0,0; 3,1)	1,0 (0,0; 3,1)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	2,0 (2,3)	2,3 (2,6)
Median (Q1; Q3)	1,1 (0,0; 3,4)	1,4 (0,0; 3,9)
Min, Max	0,0; 9,4	0,0; 9,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	2,0 (2,4)	2,0 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,7)	1,0 (0,0; 3,9)
Min, Max	0,0; 9,3	0,0; 9,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	2,0 (2,3)	1,8 (1,9)
Median (Q1; Q3)	1,1 (0,0; 3,6)	1,1 (0,0; 3,6)
Min, Max	0,0; 9,7	0,0; 6,3

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	2,4 (2,4)	1,9 (2,4)
Median (Q1; Q3)	1,9 (0,0; 4,4)	1,0 (0,0; 3,0)
Min, Max	0,0; 8,9	0,0; 8,4
Woche 35		
N ^c	122	70
Mittelwert (SD)	2,2 (2,3)	1,9 (2,2)
Median (Q1; Q3)	1,4 (0,0; 3,7)	1,1 (0,0; 3,0)
Min, Max	0,0; 9,3	0,0; 9,4
Woche 38		
N ^c	124	66
Mittelwert (SD)	2,0 (2,3)	1,7 (2,3)
Median (Q1; Q3)	1,0 (0,0; 3,6)	0,9 (0,0; 3,0)
Min, Max	0,0; 9,7	0,0; 8,1
Woche 41		
N ^c	119	57
Mittelwert (SD)	2,4 (2,5)	1,8 (2,2)
Median (Q1; Q3)	1,4 (0,0; 4,6)	0,9 (0,0; 3,0)
Min, Max	0,0; 10,0	0,0; 8,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	2,2 (2,3)	2,2 (2,3)
Median (Q1; Q3)	1,4 (0,0; 3,9)	1,4 (0,0; 4,0)
Min, Max	0,0; 8,4	0,0; 7,3
Woche 47		
N ^c	94	50
Mittelwert (SD)	2,1 (2,3)	2,0 (2,2)
Median (Q1; Q3)	1,7 (0,0; 3,3)	1,1 (0,0; 3,9)
Min, Max	0,0; 9,4	0,0; 7,6
Woche 50		
N ^c	84	47
Mittelwert (SD)	2,0 (2,2)	2,6 (2,4)
Median (Q1; Q3)	1,3 (0,0; 3,6)	2,1 (0,0; 4,4)
Min, Max	0,0; 7,3	0,0; 8,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	1,8 (2,1)	1,6 (1,8)
Median (Q1; Q3)	1,0 (0,0; 3,6)	0,8 (0,0; 3,0)
Min, Max	0,0; 8,0	0,0; 5,9
Woche 56		
N ^c	76	34
Mittelwert (SD)	1,9 (2,5)	2,1 (2,5)
Median (Q1; Q3)	0,5 (0,0; 3,3)	1,4 (0,0; 3,6)
Min, Max	0,0; 9,9	0,0; 7,3
Woche 59		
N ^c	68	33
Mittelwert (SD)	1,8 (2,2)	1,6 (1,9)
Median (Q1; Q3)	0,9 (0,0; 3,4)	1,0 (0,0; 3,0)
Min, Max	0,0; 9,1	0,0; 8,0

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	1,8 (2,3)	1,6 (1,8)
Median (Q1; Q3)	0,6 (0,0; 3,9)	1,0 (0,0; 2,7)
Min, Max	0,0; 8,9	0,0; 6,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	2,0 (2,4)	1,3 (1,8)
Median (Q1; Q3)	0,8 (0,0; 3,3)	0,1 (0,0; 2,4)
Min, Max	0,0; 7,9	0,0; 6,6
Woche 68		
N ^c	52	21
Mittelwert (SD)	1,8 (2,2)	2,1 (2,7)
Median (Q1; Q3)	0,9 (0,0; 3,3)	1,0 (0,0; 3,0)
Min, Max	0,0; 7,4	0,0; 7,6
Woche 71		
N ^c	49	19
Mittelwert (SD)	1,8 (2,1)	1,9 (2,6)
Median (Q1; Q3)	1,0 (0,0; 3,4)	1,1 (0,0; 2,4)
Min, Max	0,0; 7,0	0,0; 8,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
BPI-SF: Brief Pain Inventory - Short Form; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	208 186 173 183 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
- - - Plat+Gem	189 163 151 152 140 129 133 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
BPI-SF Pain Interference

Abbildung 4G-11: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerzbeeinträchtigung zu den verschiedenen Erhebungszeitpunkten des BPI-SF der Studie KEYNOTE A39

Cisplatin ungeeignet

EORTC QLQ-C30

Tabelle 4G-22: Auswertung über den Studienverlauf der Symptomskala Erschöpfung des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39*	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	36,2 (24,7)	36,3 (28,4)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (11,1; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	38,9 (25,4)	39,2 (25,3)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0

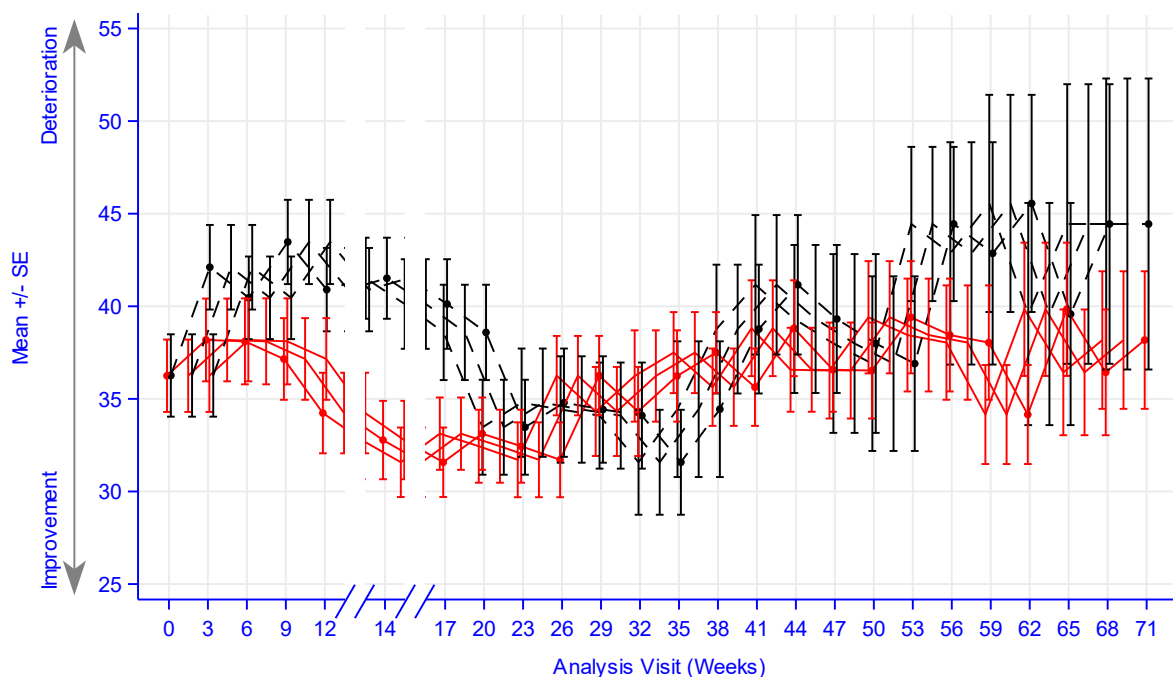
EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	40,4 (24,8)	43,1 (24,5)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	38,2 (25,1)	42,1 (26,8)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	37,1 (24,2)	39,3 (23,7)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	35,9 (25,9)	42,4 (25,6)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	38,1 (26,3)	40,5 (25,5)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	35,6 (23,1)	41,1 (26,9)
Median (Q1; Q3)	33,3 (22,2; 50,0)	33,3 (22,2; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	37,0 (26,1)	43,7 (26,1)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	37,2 (24,6)	43,5 (25,5)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	36,9 (25,5)	40,0 (25,0)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	33,8 (22,8)	40,6 (23,7)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	34,2 (24,1)	40,9 (24,2)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	32,8 (23,2)	41,5 (23,0)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	31,6 (20,0)	40,1 (25,1)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	33,1 (20,1)	38,6 (24,8)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	32,4 (19,7)	33,5 (23,1)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	31,7 (19,8)	34,8 (25,5)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	36,3 (20,9)	34,4 (24,2)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 88,9	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	34,3 (22,8)	34,1 (21,8)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	36,2 (23,1)	31,6 (21,4)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	37,5 (20,5)	34,4 (25,9)
Median (Q1; Q3)	33,3 (27,8; 55,6)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	35,6 (19,5)	38,8 (23,8)
Median (Q1; Q3)	33,3 (22,2; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	38,8 (22,7)	41,2 (25,0)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 61,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	36,6 (19,2)	39,3 (25,0)
Median (Q1; Q3)	33,3 (27,8; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	36,5 (21,1)	38,0 (26,9)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	39,4 (24,2)	36,9 (24,9)
Median (Q1; Q3)	33,3 (27,8; 55,6)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	38,4 (24,2)	44,4 (22,4)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (33,3; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	38,0 (23,7)	42,9 (27,5)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 66,7)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 62		
N ^c	54	20
Mittelwert (SD)	34,2 (19,6)	45,6 (26,2)
Median (Q1; Q3)	33,3 (22,2; 44,4)	38,9 (33,3; 61,1)
Min, Max	0,0; 66,7	0,0; 88,9
Woche 65		
N ^c	41	16
Mittelwert (SD)	39,8 (23,0)	39,6 (24,0)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (22,2; 50,0)
Min, Max	0,0; 88,9	11,1; 88,9
Woche 68		
N ^c	43	13
Mittelwert (SD)	36,4 (22,3)	44,4 (27,2)
Median (Q1; Q3)	33,3 (22,2; 55,6)	33,3 (33,3; 66,7)
Min, Max	0,0; 88,9	0,0; 88,9

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	39	13
Mittelwert (SD)	38,2 (23,2)	44,4 (28,3)
Median (Q1; Q3)	33,3 (22,2; 66,7)	33,3 (33,3; 55,6)
Min, Max	0,0; 88,9	0,0; 100,0

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Number of participants

— EV+Pembro	160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
- - - Plat+Gem	163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Fatigue

Abbildung 4G-12: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Erschöpfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

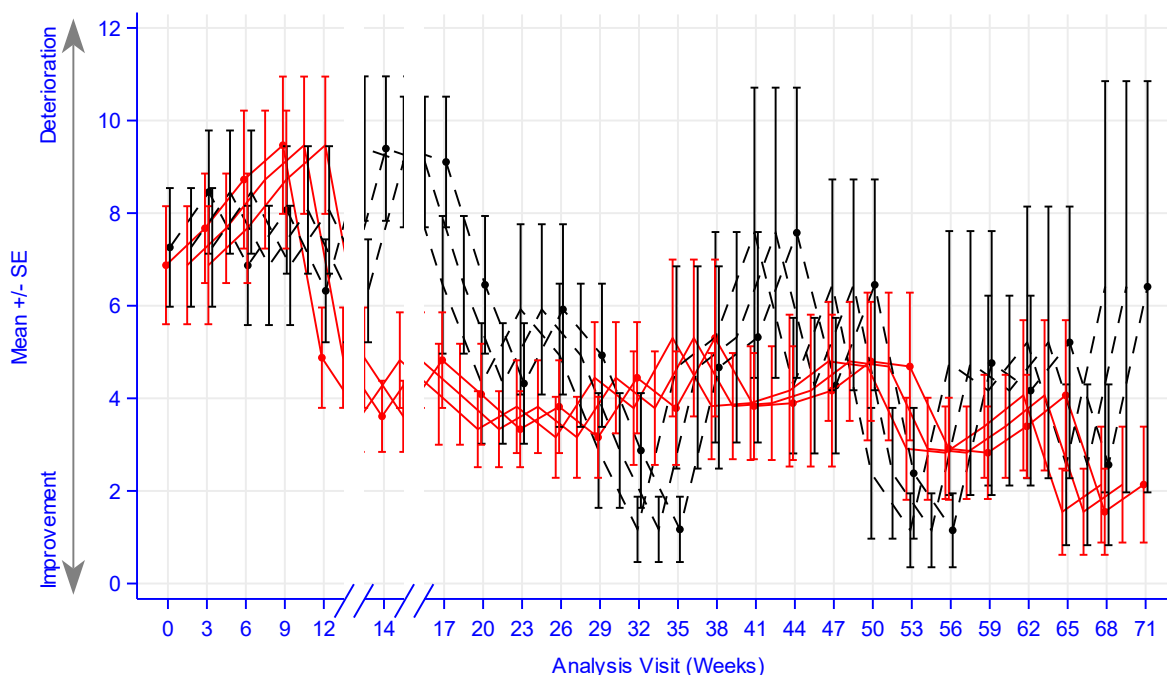
Tabelle 4G-23: Auswertung über den Studienverlauf der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	6,9 (16,1)	7,3 (16,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	9,8 (19,8)	13,2 (21,5)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	138	137
Mittelwert (SD)	11,6 (20,2)	12,9 (19,1)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 3		
N ^c	126	138
Mittelwert (SD)	7,7 (13,3)	8,5 (15,6)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	7,0 (12,2)	7,4 (13,5)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 5		
N ^c	125	139
Mittelwert (SD)	7,2 (16,3)	8,5 (14,9)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 6		
N ^c	128	131
Mittelwert (SD)	8,7 (16,9)	6,9 (14,7)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 7		
N ^c	128	135
Mittelwert (SD)	8,1 (16,1)	10,1 (16,6)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	8,5 (15,4)	10,2 (17,7)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	9,5 (16,6)	8,1 (15,5)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	8,9 (19,1)	9,5 (18,2)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	6,6 (13,6)	8,6 (16,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 12		
N ^c	123	116
Mittelwert (SD)	4,9 (12,0)	6,3 (12,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 50,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	3,6 (8,4)	9,4 (16,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 33,3	0,0; 83,3
Woche 17		
N ^c	114	108
Mittelwert (SD)	4,8 (11,0)	9,1 (14,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 66,7
Woche 20		
N ^c	106	93
Mittelwert (SD)	4,1 (11,2)	6,5 (14,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 23		
N ^c	100	81
Mittelwert (SD)	3,3 (8,2)	4,3 (11,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 26		
N ^c	96	76
Mittelwert (SD)	3,8 (9,8)	5,9 (16,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	3,2 (8,5)	4,9 (13,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro	Plat+Gem
	N ^b = 166	N ^b = 166
Min, Max	0,0; 33,3	0,0; 66,7
Woche 32		
N ^c	90	58
Mittelwert (SD)	4,4 (11,4)	2,9 (9,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 50,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	3,8 (11,5)	1,2 (5,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 38		
N ^c	88	50
Mittelwert (SD)	5,3 (15,9)	4,7 (15,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	3,8 (10,7)	5,3 (15,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 44		
N ^c	77	44
Mittelwert (SD)	3,9 (10,8)	7,6 (20,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	4,2 (13,9)	4,3 (9,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 50		
N ^c	66	31
Mittelwert (SD)	4,8 (10,4)	6,5 (12,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 53		
N ^c	64	28
Mittelwert (SD)	4,7 (12,8)	2,4 (7,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 56		
N ^c	63	29
Mittelwert (SD)	2,9 (8,7)	1,1 (4,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 59		
N ^c	59	21
Mittelwert (SD)	2,8 (7,7)	4,8 (13,1)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE A39 ^a	
	EV+Pembro	Plat+Gem
	N ^b = 166	N ^b = 166
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 50,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	3,4 (8,2)	4,2 (9,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 65		
N ^c	41	16
Mittelwert (SD)	4,1 (10,4)	5,2 (11,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 68		
N ^c	43	13
Mittelwert (SD)	1,6 (6,1)	2,6 (6,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 16,7
Woche 71		
N ^c	39	13
Mittelwert (SD)	2,1 (7,8)	6,4 (16,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 50,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro

160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39

- - - Plat+Gem

163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Nausea and Vomiting

Abbildung 4G-13: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Übelkeit und Erbrechen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-24: Auswertung über den Studienverlauf der Symptomskala Schmerzen des EORTC QLQ-C30 (Cisplatin ungeeignet)

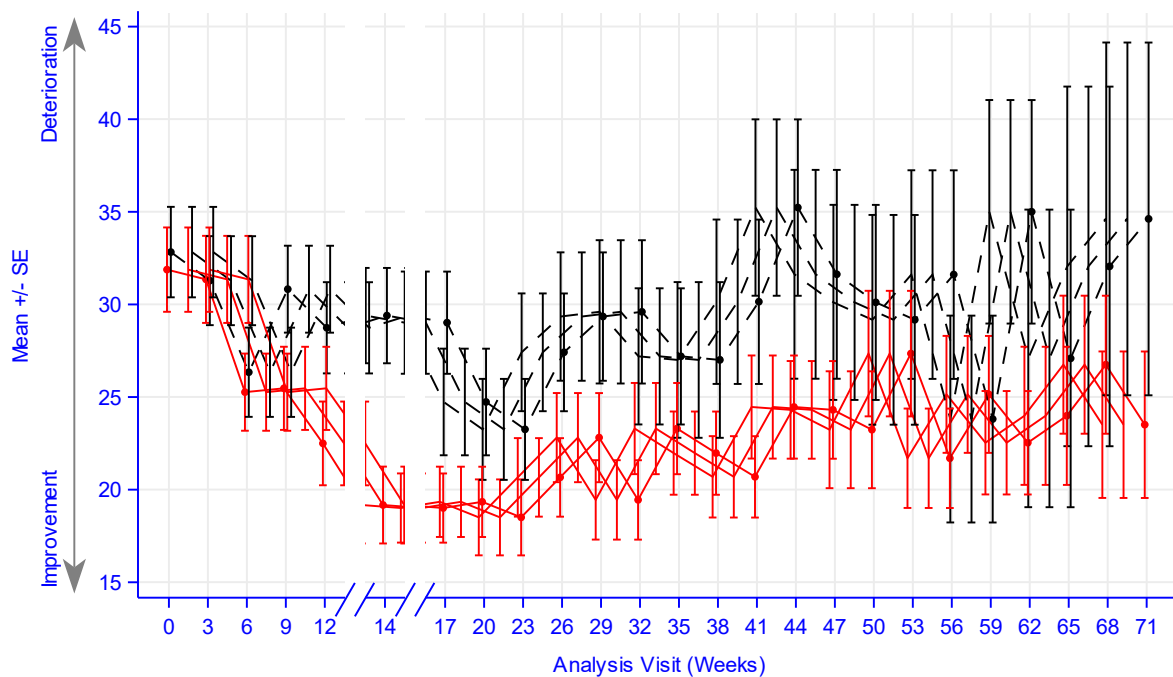
EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	31,9 (28,8)	32,8 (31,2)
Median (Q1; Q3)	33,3 (0,0; 50,0)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	31,1 (28,0)	34,5 (30,3)
Median (Q1; Q3)	33,3 (0,0; 50,0)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	35,6 (28,6)	34,5 (26,6)
Median (Q1; Q3)	33,3 (16,7; 50,0)	33,3 (16,7; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	31,3 (26,4)	31,3 (28,2)
Median (Q1; Q3)	33,3 (0,0; 50,0)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	24,9 (24,5)	29,2 (26,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	22,9 (23,3)	29,3 (26,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	25,3 (23,6)	26,3 (27,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	23,3 (22,8)	29,9 (28,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	23,2 (23,3)	31,6 (28,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	25,5 (25,1)	30,8 (26,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	23,4 (25,8)	28,7 (27,2)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	20,9 (23,0)	31,3 (28,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	22,5 (25,1)	28,7 (26,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	19,2 (22,7)	29,4 (27,0)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	19,0 (19,9)	29,0 (28,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	19,3 (19,5)	24,7 (27,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	18,5 (20,5)	23,3 (24,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 26		
N ^c	96	76
Mittelwert (SD)	20,7 (20,8)	27,4 (27,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	22,8 (23,5)	29,3 (29,2)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	19,4 (20,3)	29,6 (29,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	23,3 (23,1)	27,2 (27,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	22,0 (21,1)	27,0 (29,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 50,0)
Min, Max	0,0; 66,7	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	20,7 (20,5)	30,1 (30,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 50,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	24,5 (24,4)	35,2 (31,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	24,3 (22,4)	31,6 (35,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 66,7)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	23,2 (25,6)	30,1 (29,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	27,3 (27,1)	29,2 (30,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 41,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	21,7 (21,3)	31,6 (30,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	25,1 (24,2)	23,8 (25,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 62		
N ^c	54	20
Mittelwert (SD)	22,5 (20,5)	35,0 (27,0)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (8,3; 66,7)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 65		
N ^c	41	16
Mittelwert (SD)	24,0 (23,9)	27,1 (32,1)
Median (Q1; Q3)	16,7 (0,0; 33,3)	8,3 (0,0; 66,7)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 68		
N ^c	43	13
Mittelwert (SD)	26,7 (24,4)	32,1 (35,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	39	13
Mittelwert (SD)	23,5 (24,7)	34,6 (34,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 83,3	0,0; 100,0
a: Datenschnitt: 08. August 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
- - - Plat+Gem	163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Pain

Abbildung 4G-14: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerzen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

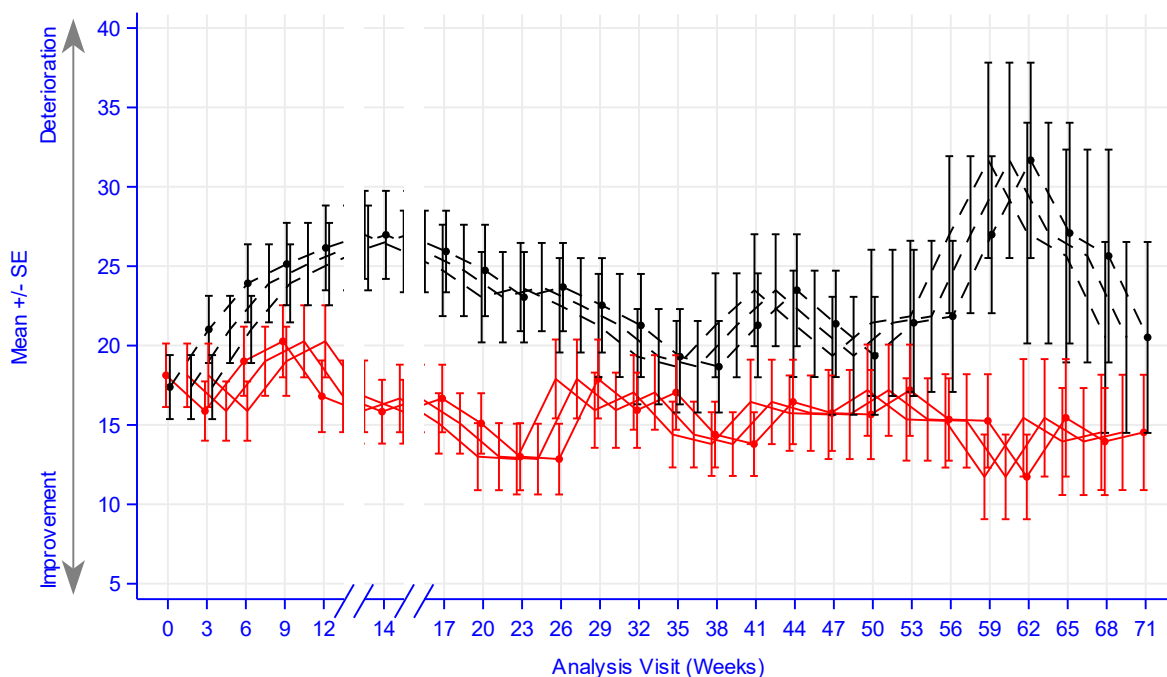
Tabelle 4G-25: Auswertung über den Studienverlauf der Symptomskala Dyspnoe des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	18,1 (25,3)	17,4 (25,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	17,5 (24,8)	19,4 (26,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	138	137
Mittelwert (SD)	18,4 (23,2)	19,2 (25,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	15,9 (21,0)	21,0 (24,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	17,5 (23,4)	20,9 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	18,1 (23,8)	23,3 (26,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	19,0 (24,6)	23,9 (28,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	17,7 (25,1)	22,5 (27,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	20,1 (26,2)	24,3 (28,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	20,3 (25,4)	25,1 (29,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	18,9 (25,0)	21,3 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	17,1 (21,6)	25,8 (29,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	123	116
Mittelwert (SD)	16,8 (25,0)	26,1 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	15,8 (22,0)	27,0 (29,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	16,7 (22,7)	25,9 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	15,1 (19,6)	24,7 (27,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	13,0 (21,1)	23,0 (25,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	12,8 (21,8)	23,7 (24,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	17,9 (24,2)	22,5 (25,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 32		
N ^c	90	58
Mittelwert (SD)	15,9 (22,5)	21,3 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	17,0 (22,0)	19,3 (22,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	14,4 (19,4)	18,7 (20,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 41		
N ^c	87	47
Mittelwert (SD)	13,8 (18,7)	21,3 (22,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 44		
N ^c	77	44
Mittelwert (SD)	16,4 (23,3)	23,5 (23,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 47		
N ^c	72	39
Mittelwert (SD)	15,7 (20,1)	21,4 (20,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 50		
N ^c	66	31
Mittelwert (SD)	15,7 (22,8)	19,4 (20,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 53		
N ^c	64	28
Mittelwert (SD)	17,2 (23,0)	21,4 (24,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	15,3 (20,6)	21,8 (25,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	15,3 (22,6)	27,0 (22,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62		
N ^c	54	20
Mittelwert (SD)	11,7 (19,6)	31,7 (27,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	15,4 (23,7)	27,1 (27,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 68		
N ^c	43	13
Mittelwert (SD)	14,0 (22,1)	25,6 (24,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 71		
N ^c	39	13
Mittelwert (SD)	14,5 (22,7)	20,5 (21,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

EV+Pembro	160	126	128	125	123	120	114	106	100	96	95	90	88	88	87	77	72	66	64	63	59	54	41	43	39
Plat+Gem	163	138	131	126	116	110	108	93	81	76	71	58	57	50	47	44	39	31	28	29	21	20	16	13	13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Dyspnoea

Abbildung 4G-15: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Dyspnoe zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-26: Auswertung über den Studienverlauf der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	34,2 (30,8)	31,1 (34,8)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	31,6 (28,5)	31,2 (31,2)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

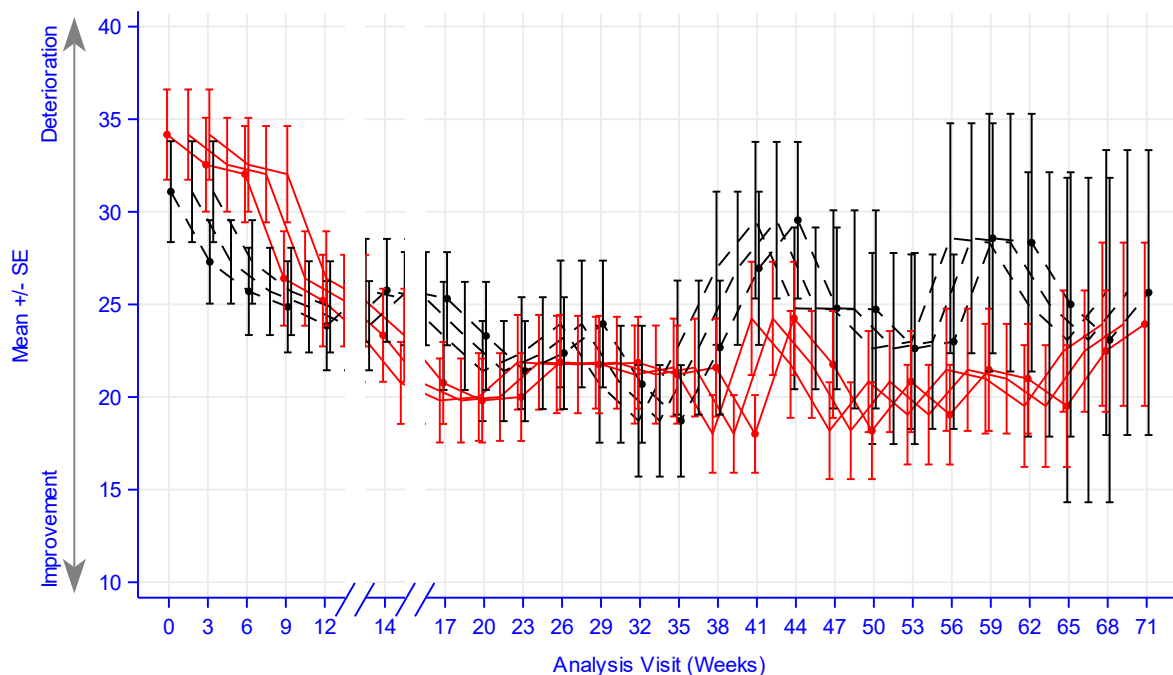
EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	33,6 (30,0)	30,2 (29,4)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	32,5 (28,4)	27,3 (26,5)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	28,8 (26,5)	26,5 (26,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	29,9 (27,7)	27,6 (27,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	32,0 (29,4)	25,7 (27,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	30,7 (30,1)	25,4 (25,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	24,5 (26,9)	27,1 (28,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	26,4 (28,5)	24,9 (27,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	27,0 (28,5)	23,6 (26,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	24,1 (25,3)	24,6 (24,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	25,2 (27,4)	23,8 (25,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	23,3 (27,5)	25,8 (29,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	20,8 (23,6)	25,3 (26,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	19,8 (23,4)	23,3 (28,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	20,0 (23,7)	21,4 (24,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	21,9 (25,1)	22,4 (26,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	21,8 (25,6)	23,9 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	21,9 (23,5)	20,7 (24,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 35		
N ^c	88	57
Mittelwert (SD)	21,2 (24,9)	18,7 (22,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 38		
N ^c	88	50
Mittelwert (SD)	21,6 (24,8)	22,7 (25,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	18,0 (19,6)	27,0 (28,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	24,2 (26,8)	29,5 (28,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	21,8 (24,5)	24,8 (27,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	18,2 (21,2)	24,7 (29,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	20,8 (21,8)	22,6 (27,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	19,0 (21,3)	23,0 (25,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	21,5 (25,3)	28,6 (28,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	21,0 (21,8)	28,3 (31,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	19,5 (21,0)	25,0 (28,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	22,5 (21,5)	23,1 (31,6)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	39	13
Mittelwert (SD)	23,9 (27,5)	25,6 (27,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Number of participants

— EV+Pembro	160	126	128	125	123	120	114	106	100	96	95	90	88	88	87	77	72	66	64	63	59	54	41	43	39
- - - Plat+Gem	163	138	131	126	116	110	108	93	81	76	71	58	57	50	47	44	39	31	28	29	21	20	16	13	13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Insomnia

Abbildung 4G-16: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schlaflosigkeit zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

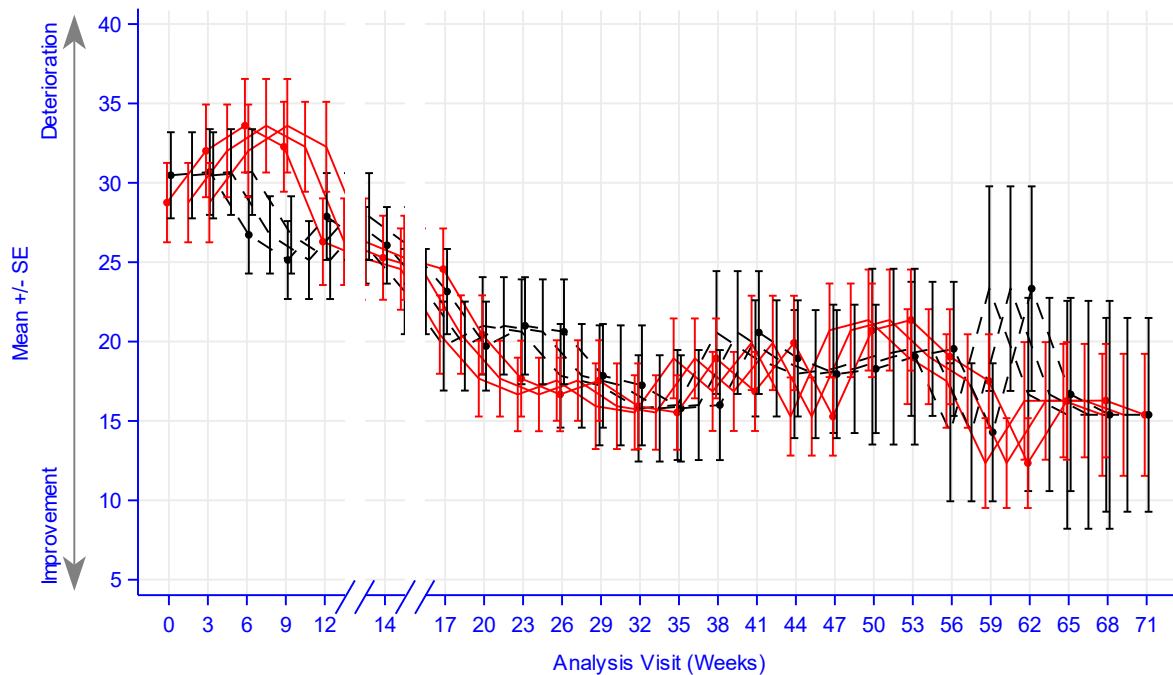
Tabelle 4G-27: Auswertung über den Studienverlauf der Symptomskala Appetitverlust des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	28,7 (31,6)	30,5 (34,6)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	29,6 (32,0)	33,8 (33,3)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	138	137
Mittelwert (SD)	35,0 (31,8)	32,4 (34,5)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	32,0 (32,8)	30,7 (31,7)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	26,6 (28,9)	27,0 (29,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	27,7 (27,7)	30,5 (29,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	33,6 (33,3)	26,7 (27,9)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	29,2 (31,6)	26,9 (29,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	29,9 (29,2)	27,6 (29,2)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	32,3 (31,7)	25,1 (27,5)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	29,0 (30,9)	23,3 (26,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	28,0 (30,1)	24,9 (27,2)
Median (Q1; Q3)	33,3 (0,0; 66,7)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	123	116
Mittelwert (SD)	26,3 (30,3)	27,9 (29,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	25,3 (29,0)	26,1 (25,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	24,6 (27,4)	23,1 (27,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	20,4 (25,4)	19,7 (27,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	17,7 (23,9)	21,0 (27,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	16,7 (22,7)	20,6 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	17,5 (24,7)	17,8 (27,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 32		
N ^c	90	58
Mittelwert (SD)	15,9 (25,6)	17,2 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	15,5 (22,0)	15,8 (25,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	18,9 (23,6)	16,0 (24,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	16,9 (23,2)	20,6 (26,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	19,9 (26,1)	18,9 (24,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	15,3 (20,9)	17,9 (25,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	20,7 (23,9)	18,3 (22,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 53		
N ^c	64	28
Mittelwert (SD)	21,4 (25,5)	19,0 (29,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	19,0 (23,7)	19,5 (22,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	17,5 (22,6)	14,3 (19,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62		
N ^c	54	20
Mittelwert (SD)	12,3 (20,8)	23,3 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	16,3 (23,7)	16,7 (24,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 68		
N ^c	43	13
Mittelwert (SD)	16,3 (23,4)	15,4 (25,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 71		
N ^c	39	13
Mittelwert (SD)	15,4 (24,0)	15,4 (22,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro
 160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
 - - - Plat+Gem
 163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Appetite Loss

Abbildung 4G-17: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Appetitverlust zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-28: Auswertung über den Studienverlauf der Symptomskala Verstopfung des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	21,5 (28,6)	31,5 (34,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	22,3 (28,0)	38,8 (33,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0

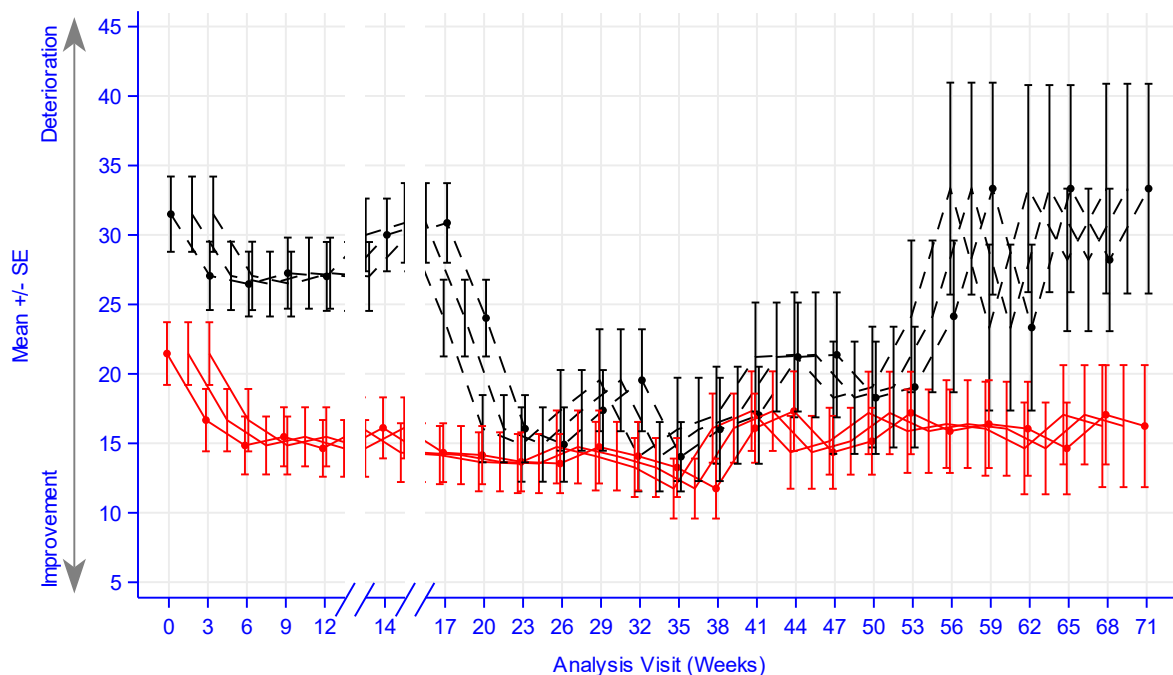
EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	20,5 (27,4)	36,3 (31,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	16,7 (25,2)	27,1 (28,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	20,8 (27,7)	30,7 (28,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	17,6 (25,2)	27,3 (25,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	14,8 (23,6)	26,5 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	19,5 (27,3)	25,2 (27,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	16,9 (26,8)	32,1 (28,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	15,5 (23,8)	27,2 (28,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	17,2 (24,3)	26,7 (27,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	18,5 (24,0)	28,4 (28,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	14,6 (22,6)	27,0 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	16,1 (24,1)	30,0 (27,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	14,3 (22,6)	30,9 (29,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	14,2 (21,6)	24,0 (26,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	13,7 (21,2)	16,0 (21,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	13,5 (20,8)	14,9 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	14,7 (25,6)	17,4 (24,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	14,1 (23,4)	19,5 (27,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	13,3 (19,9)	14,0 (18,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 38		
N ^c	88	50
Mittelwert (SD)	11,7 (20,2)	16,0 (26,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	16,1 (23,2)	17,0 (23,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 44		
N ^c	77	44
Mittelwert (SD)	17,3 (25,1)	21,2 (26,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	14,4 (22,3)	21,4 (28,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	15,2 (19,6)	18,3 (22,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 53		
N ^c	64	28
Mittelwert (SD)	17,2 (23,8)	19,0 (23,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 56		
N ^c	63	29
Mittelwert (SD)	15,9 (23,8)	24,1 (29,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	16,4 (24,3)	33,3 (35,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	16,0 (24,9)	23,3 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	14,6 (21,1)	33,3 (29,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 68		
N ^c	43	13
Mittelwert (SD)	17,1 (23,4)	28,2 (18,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (33,3; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	39	13
Mittelwert (SD)	16,2 (27,4)	33,3 (27,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Number of participants

— EV+Pembro	160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
- - - Plat+Gem	163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Constipation

Abbildung 4G-18: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Verstopfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

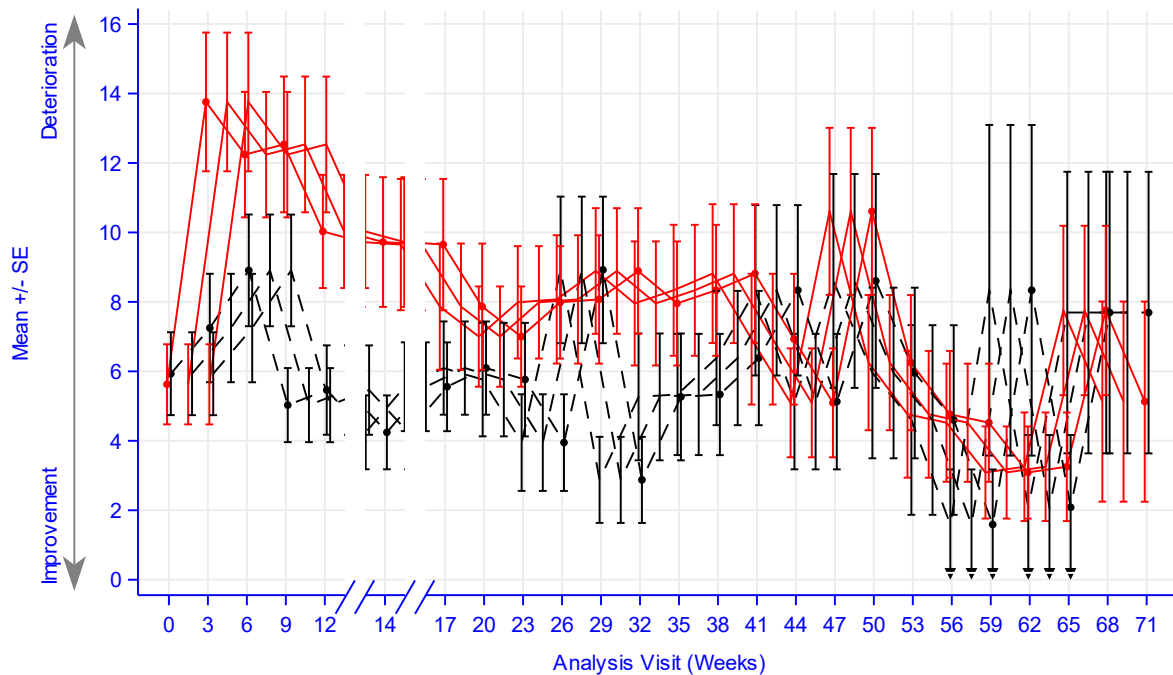
Tabelle 4G-29: Auswertung über den Studienverlauf der Symptomskala Diarrhö des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	5,6 (14,6)	5,9 (15,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 1		
N ^c	133	141
Mittelwert (SD)	6,8 (17,3)	6,1 (17,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	138	137
Mittelwert (SD)	11,6 (22,3)	9,0 (20,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	13,8 (22,4)	7,2 (18,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	8,3 (19,0)	5,8 (13,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 5		
N ^c	125	139
Mittelwert (SD)	7,7 (16,5)	7,4 (16,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 6		
N ^c	128	131
Mittelwert (SD)	12,2 (20,4)	8,9 (18,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	10,2 (21,1)	4,7 (14,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	10,7 (20,5)	5,3 (13,5)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	12,5 (21,9)	5,0 (12,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 10		
N ^c	122	130
Mittelwert (SD)	9,0 (18,2)	4,1 (14,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	8,1 (17,3)	4,3 (12,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 12		
N ^c	123	116
Mittelwert (SD)	10,0 (18,1)	5,5 (13,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 14		
N ^c	120	110
Mittelwert (SD)	9,7 (20,5)	4,2 (11,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 17		
N ^c	114	108
Mittelwert (SD)	9,6 (20,2)	5,6 (13,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 20		
N ^c	106	93
Mittelwert (SD)	7,9 (18,7)	6,1 (13,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 23		
N ^c	100	81
Mittelwert (SD)	7,0 (14,4)	5,8 (14,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 26		
N ^c	96	76
Mittelwert (SD)	8,0 (15,9)	3,9 (12,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 29		
N ^c	95	71
Mittelwert (SD)	8,1 (18,0)	8,9 (17,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 32		
N ^c	90	58
Mittelwert (SD)	8,9 (17,2)	2,9 (9,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 35		
N ^c	88	57
Mittelwert (SD)	8,0 (16,8)	5,3 (13,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 38		
N ^c	88	50
Mittelwert (SD)	8,3 (17,7)	5,3 (12,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 41		
N ^c	87	47
Mittelwert (SD)	8,8 (18,6)	6,4 (13,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 44		
N ^c	77	44
Mittelwert (SD)	6,9 (16,5)	8,3 (16,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 47		
N ^c	72	39
Mittelwert (SD)	5,1 (13,3)	5,1 (12,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 50		
N ^c	66	31
Mittelwert (SD)	10,6 (19,5)	8,6 (17,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 53		
N ^c	64	28
Mittelwert (SD)	6,2 (15,6)	6,0 (13,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 56		
N ^c	63	29
Mittelwert (SD)	4,8 (14,5)	4,6 (14,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 59		
N ^c	59	21
Mittelwert (SD)	4,5 (13,1)	1,6 (7,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3

EORTC QLQ-C30 Diarrhö	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62		
N ^c	54	20
Mittelwert (SD)	3,1 (9,8)	8,3 (21,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 65		
N ^c	41	16
Mittelwert (SD)	3,3 (10,0)	2,1 (8,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 68		
N ^c	43	13
Mittelwert (SD)	7,8 (16,0)	7,7 (14,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 71		
N ^c	39	13
Mittelwert (SD)	5,1 (18,0)	7,7 (14,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
- - - Plat+Gem	163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Diarrhoea

Abbildung 4G-19: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Diarrhö zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

EQ-5D-VAS

Tabelle 4G-30: Auswertung über den Studienverlauf der EQ-5D-VAS (Cisplatin ungeeignet)

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	166	166
Mittelwert (SD)	69,8 (17,8)	70,4 (20,4)
Median (Q1; Q3)	70,0 (60,0; 81,0)	73,0 (59,0; 89,0)
Min, Max	10,0; 100,0	5,0; 100,0
Woche 1		
N ^c	135	142
Mittelwert (SD)	67,8 (18,5)	66,6 (21,6)
Median (Q1; Q3)	70,0 (55,0; 81,0)	70,0 (51,0; 85,0)
Min, Max	3,0; 100,0	3,0; 100,0

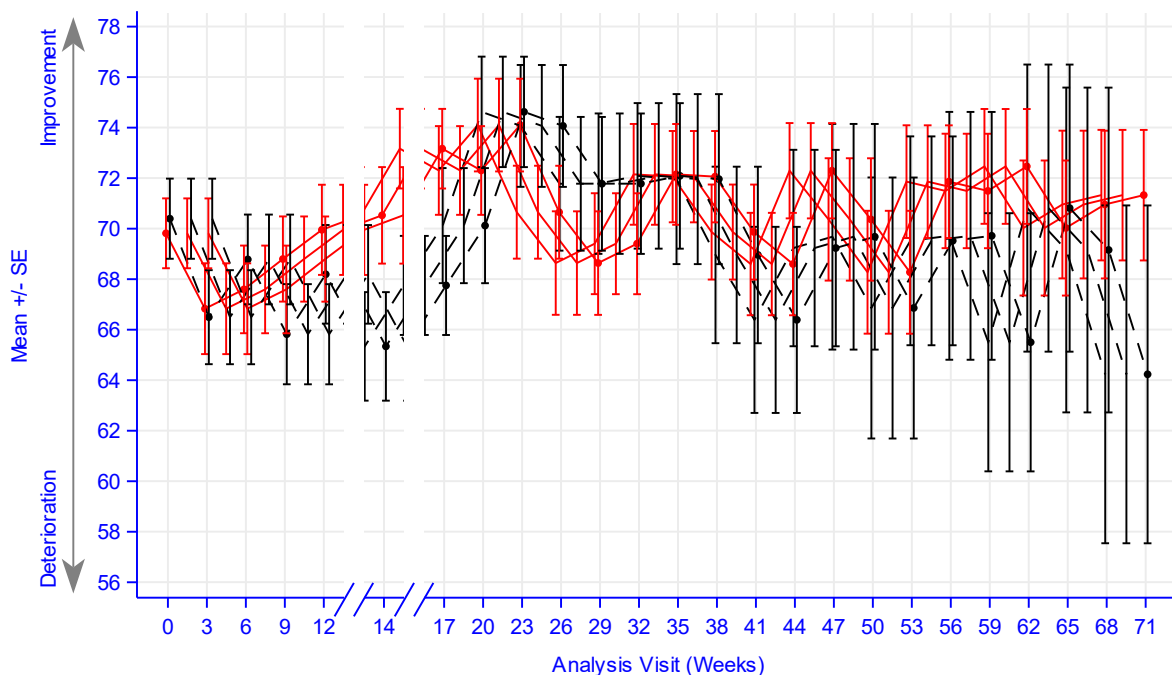
EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	143	141
Mittelwert (SD)	65,2 (18,8)	66,2 (20,1)
Median (Q1; Q3)	65,0 (51,0; 80,0)	70,0 (50,0; 81,0)
Min, Max	4,0; 100,0	3,0; 100,0
Woche 3		
N ^c	128	138
Mittelwert (SD)	66,8 (20,3)	66,5 (21,9)
Median (Q1; Q3)	70,0 (51,0; 83,5)	70,0 (50,0; 85,0)
Min, Max	10,0; 100,0	2,0; 100,0
Woche 4		
N ^c	134	138
Mittelwert (SD)	69,5 (19,1)	69,3 (19,5)
Median (Q1; Q3)	71,5 (58,0; 84,0)	72,0 (58,0; 84,0)
Min, Max	10,0; 100,0	1,0; 100,0
Woche 5		
N ^c	126	141
Mittelwert (SD)	69,2 (18,8)	67,7 (20,2)
Median (Q1; Q3)	71,0 (59,0; 84,0)	70,0 (52,0; 85,0)
Min, Max	11,0; 100,0	10,0; 100,0
Woche 6		
N ^c	130	131
Mittelwert (SD)	67,6 (19,8)	68,8 (20,3)
Median (Q1; Q3)	70,0 (54,0; 82,0)	70,0 (57,0; 85,0)
Min, Max	11,0; 100,0	2,0; 100,0
Woche 7		
N ^c	130	137
Mittelwert (SD)	69,5 (18,6)	67,4 (21,4)
Median (Q1; Q3)	71,0 (58,0; 86,0)	70,0 (51,0; 85,0)
Min, Max	17,0; 100,0	6,0; 100,0
Woche 8		
N ^c	130	134
Mittelwert (SD)	68,7 (19,5)	67,2 (20,5)
Median (Q1; Q3)	70,0 (54,0; 85,0)	70,0 (52,0; 83,0)
Min, Max	11,0; 100,0	5,0; 100,0
Woche 9		
N ^c	127	127
Mittelwert (SD)	68,8 (19,0)	65,8 (22,3)
Median (Q1; Q3)	70,0 (53,0; 85,0)	70,0 (51,0; 81,0)
Min, Max	19,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	70,2 (18,3)	67,9 (21,4)
Median (Q1; Q3)	72,5 (58,0; 84,0)	70,0 (55,0; 85,0)
Min, Max	10,0; 100,0	2,0; 100,0
Woche 11		
N ^c	119	116
Mittelwert (SD)	72,0 (19,7)	66,8 (20,8)
Median (Q1; Q3)	78,0 (59,0; 88,0)	68,0 (52,5; 82,5)
Min, Max	11,0; 100,0	1,0; 100,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	70,0 (19,8)	68,2 (21,0)
Median (Q1; Q3)	75,0 (59,0; 85,0)	70,0 (54,0; 84,0)
Min, Max	12,0; 100,0	2,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	70,5 (20,9)	65,3 (22,5)
Median (Q1; Q3)	77,5 (59,5; 86,0)	68,5 (50,0; 84,0)
Min, Max	7,0; 100,0	1,0; 100,0
Woche 17		
N ^c	115	108
Mittelwert (SD)	73,2 (16,9)	67,8 (20,4)
Median (Q1; Q3)	76,0 (63,0; 85,0)	70,5 (51,0; 85,0)
Min, Max	30,0; 100,0	19,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	72,3 (18,1)	70,1 (22,0)
Median (Q1; Q3)	74,5 (62,0; 85,0)	75,0 (55,0; 89,0)
Min, Max	23,0; 100,0	10,0; 100,0
Woche 23		
N ^c	100	82
Mittelwert (SD)	74,1 (18,4)	74,6 (19,8)
Median (Q1; Q3)	80,0 (63,0; 88,5)	80,0 (65,0; 90,0)
Min, Max	28,0; 100,0	23,0; 100,0
Woche 26		
N ^c	97	76
Mittelwert (SD)	70,6 (18,1)	74,1 (21,0)
Median (Q1; Q3)	75,0 (60,0; 84,0)	78,5 (65,0; 90,0)
Min, Max	21,0; 100,0	6,0; 100,0
Woche 29		
N ^c	96	71
Mittelwert (SD)	68,6 (20,1)	71,8 (22,3)
Median (Q1; Q3)	71,5 (59,0; 80,5)	79,0 (56,0; 90,0)
Min, Max	2,0; 100,0	8,0; 100,0
Woche 32		
N ^c	92	59
Mittelwert (SD)	69,4 (19,2)	71,8 (21,4)
Median (Q1; Q3)	71,5 (59,5; 81,0)	77,0 (60,0; 88,0)
Min, Max	7,0; 100,0	13,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	72,1 (18,7)	72,1 (21,8)
Median (Q1; Q3)	76,5 (64,5; 84,0)	77,0 (59,0; 90,0)
Min, Max	5,0; 100,0	10,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	72,1 (17,0)	72,0 (23,8)
Median (Q1; Q3)	75,5 (63,5; 84,0)	80,0 (51,0; 89,0)
Min, Max	29,0; 100,0	10,0; 100,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	88	47
Mittelwert (SD)	69,9 (17,6)	69,0 (24,0)
Median (Q1; Q3)	70,0 (59,5; 81,5)	70,0 (52,0; 88,0)
Min, Max	7,0; 100,0	7,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	68,6 (17,8)	66,4 (24,4)
Median (Q1; Q3)	71,0 (60,0; 80,0)	74,0 (51,5; 85,0)
Min, Max	4,0; 99,0	11,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	72,3 (16,0)	69,2 (24,3)
Median (Q1; Q3)	74,5 (64,5; 82,0)	76,0 (57,0; 88,0)
Min, Max	31,0; 100,0	11,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	70,4 (19,7)	69,7 (24,9)
Median (Q1; Q3)	74,5 (56,0; 84,0)	75,0 (53,0; 90,0)
Min, Max	5,0; 100,0	10,0; 98,0
Woche 53		
N ^c	66	28
Mittelwert (SD)	68,3 (19,8)	66,9 (27,3)
Median (Q1; Q3)	70,0 (56,0; 85,0)	70,0 (51,0; 91,5)
Min, Max	6,0; 100,0	10,0; 100,0
Woche 56		
N ^c	64	29
Mittelwert (SD)	71,9 (17,8)	69,5 (22,3)
Median (Q1; Q3)	71,5 (60,0; 86,0)	71,0 (61,0; 89,0)
Min, Max	30,0; 100,0	9,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	71,5 (17,4)	69,7 (22,5)
Median (Q1; Q3)	71,0 (59,0; 85,0)	74,0 (57,0; 88,0)
Min, Max	33,0; 99,0	20,0; 97,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	72,5 (16,7)	65,5 (22,9)
Median (Q1; Q3)	70,5 (63,0; 85,0)	71,5 (46,0; 84,0)
Min, Max	36,0; 100,0	22,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	70,0 (17,1)	70,8 (22,7)
Median (Q1; Q3)	70,0 (57,0; 82,0)	75,0 (48,0; 89,5)
Min, Max	33,0; 100,0	30,0; 100,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	71,0 (19,2)	69,2 (23,2)
Median (Q1; Q3)	72,0 (58,0; 86,0)	75,0 (59,0; 85,0)
Min, Max	10,0; 100,0	21,0; 95,0

EQ-5D VAS Score	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	40	13
Mittelwert (SD)	71,3 (16,3)	64,2 (24,1)
Median (Q1; Q3)	70,0 (61,0; 81,5)	75,0 (39,0; 80,0)
Min, Max	41,0; 99,0	30,0; 95,0

a: Datenschnitt: 08. August 2023
 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet
 c: Anzahl der Beobachtungen zu jedem Zeitpunkt
 EQ-5D: European Quality of Life 5 Dimensions; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung; VAS: Visuelle Analogskala



Number of participants

— EV+Pembro	166 128 130 127 123 120 115 106 100 97 96 92 88 88 88 77 72 66 66 64 59 54 41 43 40
- - - Plat+Gem	166 138 131 127 116 110 108 93 82 76 71 59 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EQ-5D VAS Score

Abbildung 4G-20: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der EQ-5D VAS zu den verschiedenen Erhebungszeitpunkten der Studie KEYNOTE A39 (Cisplatin ungeeignet)

BPI-SF

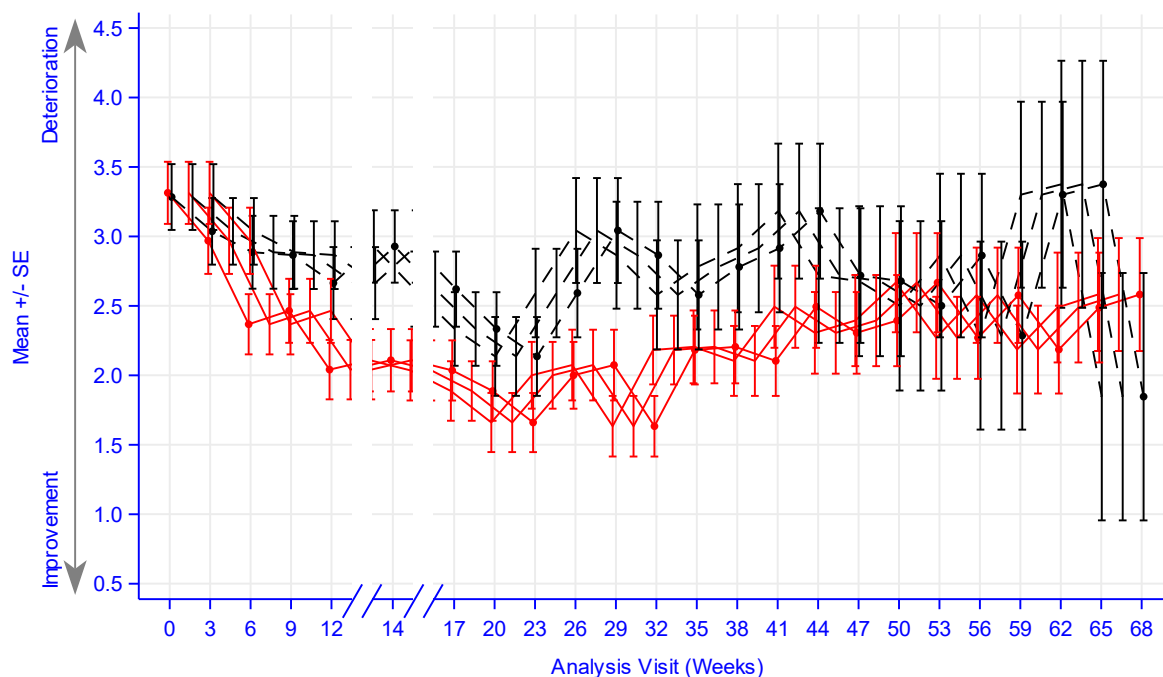
Tabelle 4G-31: Auswertung über den Studienverlauf der Symptomskala Stärkster Schmerz der vergangenen 24 Stunden des BPI-SF (Cisplatin ungeeignet)

BPI-SF Stärkster Schmerz in den vergangenen 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro	Plat+Gem
	N ^b = 166	N ^b = 166
Baseline		
N ^c	166	166
Mittelwert (SD)	3,3 (2,9)	3,3 (3,1)
Median (Q1; Q3)	3,0 (0,0; 6,0)	3,0 (0,0; 6,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 1		
N ^c	134	142
Mittelwert (SD)	3,4 (2,9)	3,7 (3,1)
Median (Q1; Q3)	3,0 (0,0; 6,0)	3,0 (0,0; 7,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 2		
N ^c	141	140
Mittelwert (SD)	3,5 (2,8)	3,3 (2,8)
Median (Q1; Q3)	3,0 (1,0; 6,0)	3,0 (1,0; 6,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	3,0 (2,7)	3,0 (2,8)
Median (Q1; Q3)	3,0 (0,0; 5,0)	2,5 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 9,0
Woche 4		
N ^c	134	137
Mittelwert (SD)	2,4 (2,5)	3,1 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,0)	3,0 (1,0; 5,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 5		
N ^c	126	141
Mittelwert (SD)	2,4 (2,4)	3,1 (2,9)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 6,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	2,4 (2,5)	2,9 (3,0)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,0 (0,0; 6,0)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 7		
N ^c	129	136
Mittelwert (SD)	2,2 (2,4)	2,8 (2,6)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,5 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 8		
N ^c	129	133
Mittelwert (SD)	2,2 (2,4)	3,1 (2,8)
Median (Q1; Q3)	2,0 (0,0; 3,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 10,0	0,0; 10,0

BPI-SF Stärkster Schmerz in den vergangenen 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	2,5 (2,6)	2,9 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,0)	3,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	2,2 (2,4)	3,0 (2,9)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 6,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	1,8 (2,2)	2,9 (2,9)
Median (Q1; Q3)	1,0 (0,0; 3,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 12		
N ^c	123	116
Mittelwert (SD)	2,0 (2,4)	2,7 (2,8)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	2,1 (2,5)	2,9 (2,7)
Median (Q1; Q3)	1,0 (0,0; 3,5)	2,5 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 10,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	2,0 (2,3)	2,6 (2,8)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 9,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	1,9 (2,2)	2,3 (2,6)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	1,7 (2,1)	2,1 (2,6)
Median (Q1; Q3)	1,0 (0,0; 3,0)	1,0 (0,0; 4,0)
Min, Max	0,0; 7,0	0,0; 8,0
Woche 26		
N ^c	97	76
Mittelwert (SD)	2,0 (2,4)	2,6 (2,8)
Median (Q1; Q3)	1,0 (0,0; 4,0)	1,5 (0,0; 4,5)
Min, Max	0,0; 8,0	0,0; 9,0

BPI-SF Stärkster Schmerz in den vergangenen 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 29		
N ^c	95	71
Mittelwert (SD)	2,1 (2,5)	3,0 (3,2)
Median (Q1; Q3)	1,0 (0,0; 4,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 32		
N ^c	90	59
Mittelwert (SD)	1,6 (2,1)	2,9 (3,0)
Median (Q1; Q3)	1,0 (0,0; 3,0)	2,0 (0,0; 5,0)
Min, Max	0,0; 7,0	0,0; 9,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	2,2 (2,3)	2,6 (3,0)
Median (Q1; Q3)	2,0 (0,0; 4,0)	1,0 (0,0; 5,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	2,2 (2,5)	2,8 (3,2)
Median (Q1; Q3)	1,0 (0,0; 5,0)	1,5 (0,0; 4,0)
Min, Max	0,0; 10,0	0,0; 9,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	2,1 (2,3)	2,9 (3,2)
Median (Q1; Q3)	1,0 (0,0; 4,0)	1,0 (0,0; 6,0)
Min, Max	0,0; 7,0	0,0; 9,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	2,5 (2,6)	3,2 (3,2)
Median (Q1; Q3)	2,0 (0,0; 5,0)	2,0 (0,0; 6,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	2,3 (2,5)	2,7 (3,0)
Median (Q1; Q3)	2,0 (0,0; 4,0)	1,0 (0,0; 6,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	2,4 (2,7)	2,7 (3,0)
Median (Q1; Q3)	2,0 (0,0; 5,0)	1,0 (0,0; 5,0)
Min, Max	0,0; 9,0	0,0; 9,0
Woche 53		
N ^c	66	28
Mittelwert (SD)	2,7 (2,9)	2,5 (3,2)
Median (Q1; Q3)	2,0 (0,0; 5,0)	1,0 (0,0; 4,5)
Min, Max	0,0; 9,0	0,0; 10,0

BPI-SF Stärkster Schmerz in den vergangenen 24 Stunden	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 56		
N ^c	63	29
Mittelwert (SD)	2,3 (2,3)	2,9 (3,2)
Median (Q1; Q3)	2,0 (0,0; 4,0)	1,0 (0,0; 6,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	2,6 (2,6)	2,3 (3,1)
Median (Q1; Q3)	2,0 (0,0; 5,0)	0,0 (0,0; 4,0)
Min, Max	0,0; 8,0	0,0; 9,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	2,2 (2,3)	3,3 (3,0)
Median (Q1; Q3)	2,0 (0,0; 4,0)	3,0 (0,0; 6,0)
Min, Max	0,0; 7,0	0,0; 8,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	2,5 (2,5)	3,4 (3,6)
Median (Q1; Q3)	2,0 (0,0; 4,0)	2,5 (0,0; 6,5)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	2,6 (2,7)	1,8 (3,2)
Median (Q1; Q3)	2,0 (0,0; 4,0)	0,0 (0,0; 2,0)
Min, Max	0,0; 8,0	0,0; 8,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
BPI-SF: Brief Pain Inventory - Short Form; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	166	126	128	125	123	120	114	106	100	97	95	90	88	88	87	77	72	66	66	63	59	54	41	43
- - - Plat+Gem	166	138	131	126	116	110	108	93	81	76	71	59	57	50	47	44	39	31	28	29	21	20	16	13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

BPI-SF Pain at its Worst in Last 24 Hours

Abbildung 4G-21: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden zu den verschiedenen Erhebungszeitpunkten des BPI-SF der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-32: Auswertung über den Studienverlauf der Symptomskala Schmerzbeeinträchtigung des BPI-SF (Cisplatin ungeeignet)

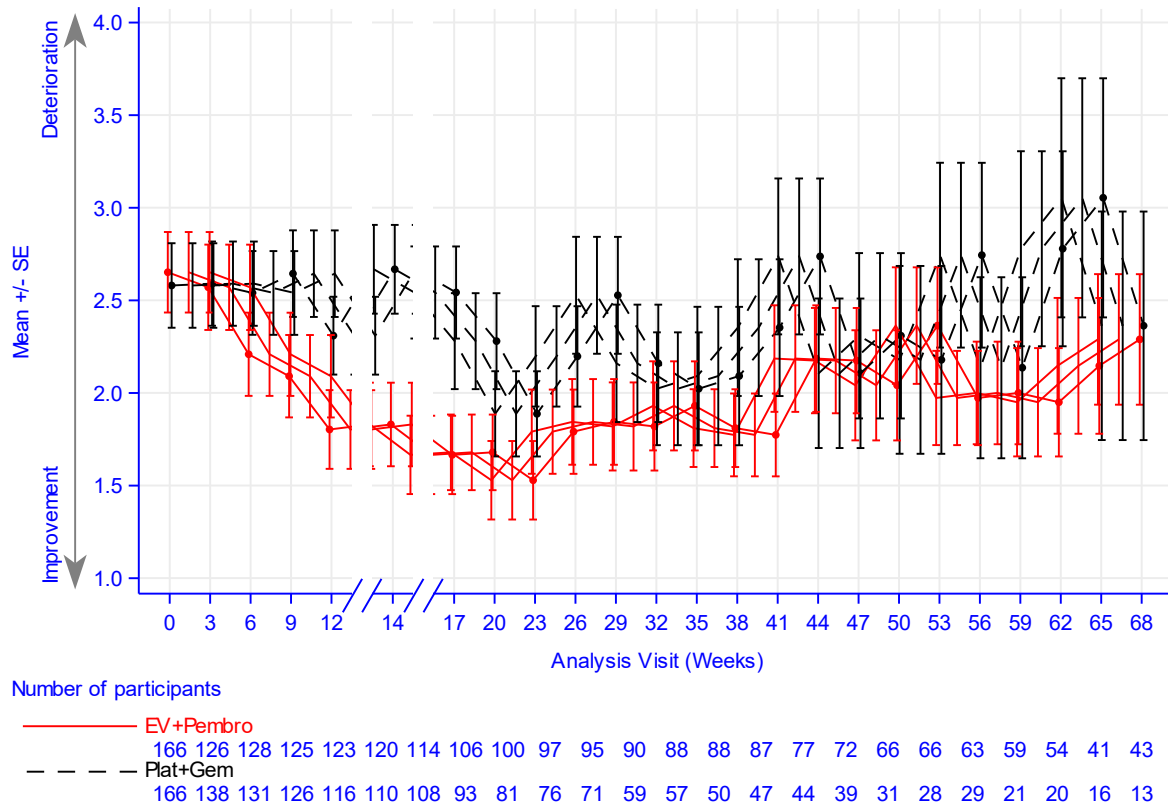
BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	166	166
Mittelwert (SD)	2,7 (2,8)	2,6 (2,9)
Median (Q1; Q3)	1,8 (0,0; 4,9)	1,1 (0,0; 5,0)
Min, Max	0,0; 9,7	0,0; 10,0
Woche 1		
N ^c	134	142
Mittelwert (SD)	2,8 (2,6)	3,1 (2,8)
Median (Q1; Q3)	2,7 (0,1; 5,0)	2,9 (0,1; 5,4)
Min, Max	0,0; 10,0	0,0; 10,0

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	141	140
Mittelwert (SD)	3,1 (2,7)	3,0 (2,7)
Median (Q1; Q3)	2,9 (0,3; 5,3)	2,5 (0,4; 5,4)
Min, Max	0,0; 9,7	0,0; 9,9
Woche 3		
N ^c	126	138
Mittelwert (SD)	2,6 (2,6)	2,6 (2,7)
Median (Q1; Q3)	2,0 (0,0; 4,4)	1,8 (0,0; 4,4)
Min, Max	0,0; 9,7	0,0; 10,0
Woche 4		
N ^c	134	137
Mittelwert (SD)	2,0 (2,3)	2,4 (2,4)
Median (Q1; Q3)	1,1 (0,0; 3,7)	1,7 (0,3; 4,6)
Min, Max	0,0; 8,0	0,0; 10,0
Woche 5		
N ^c	126	141
Mittelwert (SD)	2,0 (2,3)	2,5 (2,4)
Median (Q1; Q3)	1,0 (0,0; 3,6)	1,7 (0,3; 4,4)
Min, Max	0,0; 8,1	0,0; 8,6
Woche 6		
N ^c	128	131
Mittelwert (SD)	2,2 (2,5)	2,5 (2,6)
Median (Q1; Q3)	1,1 (0,0; 3,7)	2,0 (0,1; 4,3)
Min, Max	0,0; 9,4	0,0; 10,0
Woche 7		
N ^c	129	136
Mittelwert (SD)	1,9 (2,3)	2,5 (2,4)
Median (Q1; Q3)	1,1 (0,0; 3,1)	1,9 (0,0; 4,3)
Min, Max	0,0; 8,4	0,0; 9,0
Woche 8		
N ^c	129	133
Mittelwert (SD)	1,9 (2,3)	2,9 (2,7)
Median (Q1; Q3)	0,9 (0,0; 3,0)	2,3 (0,3; 5,1)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	2,1 (2,5)	2,6 (2,6)
Median (Q1; Q3)	1,3 (0,0; 3,3)	1,9 (0,1; 4,3)
Min, Max	0,0; 10,0	0,0; 10,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	1,9 (2,3)	2,5 (2,5)
Median (Q1; Q3)	1,1 (0,0; 3,3)	1,9 (0,0; 4,3)
Min, Max	0,0; 9,1	0,0; 10,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	1,5 (2,0)	2,7 (2,6)
Median (Q1; Q3)	0,4 (0,0; 2,4)	2,0 (0,0; 4,3)
Min, Max	0,0; 8,7	0,0; 10,0

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	1,8 (2,4)	2,3 (2,3)
Median (Q1; Q3)	0,7 (0,0; 2,7)	1,9 (0,0; 4,1)
Min, Max	0,0; 9,3	0,0; 10,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	1,8 (2,5)	2,7 (2,5)
Median (Q1; Q3)	0,8 (0,0; 3,4)	2,0 (0,1; 4,9)
Min, Max	0,0; 9,9	0,0; 10,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	1,7 (2,3)	2,5 (2,6)
Median (Q1; Q3)	0,6 (0,0; 2,6)	1,8 (0,0; 4,1)
Min, Max	0,0; 10,0	0,0; 8,6
Woche 20		
N ^c	106	93
Mittelwert (SD)	1,7 (2,1)	2,3 (2,5)
Median (Q1; Q3)	0,8 (0,0; 2,9)	1,3 (0,0; 4,3)
Min, Max	0,0; 9,0	0,0; 8,6
Woche 23		
N ^c	100	81
Mittelwert (SD)	1,5 (2,1)	1,9 (2,1)
Median (Q1; Q3)	0,3 (0,0; 2,3)	1,0 (0,0; 3,7)
Min, Max	0,0; 8,0	0,0; 6,9
Woche 26		
N ^c	97	76
Mittelwert (SD)	1,8 (2,2)	2,2 (2,4)
Median (Q1; Q3)	0,9 (0,0; 3,0)	1,0 (0,0; 4,1)
Min, Max	0,0; 8,3	0,0; 8,1
Woche 29		
N ^c	95	71
Mittelwert (SD)	1,8 (2,3)	2,5 (2,7)
Median (Q1; Q3)	0,7 (0,0; 3,3)	2,1 (0,0; 4,1)
Min, Max	0,0; 8,9	0,0; 10,0
Woche 32		
N ^c	90	59
Mittelwert (SD)	1,8 (2,3)	2,2 (2,4)
Median (Q1; Q3)	0,8 (0,0; 3,1)	0,9 (0,0; 4,4)
Min, Max	0,0; 9,4	0,0; 8,6
Woche 35		
N ^c	88	57
Mittelwert (SD)	1,9 (2,3)	2,0 (2,3)
Median (Q1; Q3)	1,0 (0,0; 3,2)	1,0 (0,0; 3,9)
Min, Max	0,0; 10,0	0,0; 8,1
Woche 38		
N ^c	88	50
Mittelwert (SD)	1,8 (2,0)	2,1 (2,6)
Median (Q1; Q3)	1,0 (0,0; 3,3)	0,9 (0,0; 3,4)
Min, Max	0,0; 8,1	0,0; 9,0

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	1,8 (2,1)	2,4 (2,5)
Median (Q1; Q3)	1,0 (0,0; 3,3)	1,4 (0,0; 4,0)
Min, Max	0,0; 7,7	0,0; 7,9
Woche 44		
N ^c	77	44
Mittelwert (SD)	2,2 (2,5)	2,7 (2,8)
Median (Q1; Q3)	1,0 (0,0; 3,7)	2,0 (0,0; 5,1)
Min, Max	0,0; 9,4	0,0; 8,4
Woche 47		
N ^c	72	39
Mittelwert (SD)	2,2 (2,4)	2,1 (2,5)
Median (Q1; Q3)	1,3 (0,0; 3,9)	1,1 (0,0; 3,7)
Min, Max	0,0; 10,0	0,0; 8,6
Woche 50		
N ^c	66	31
Mittelwert (SD)	2,0 (2,4)	2,3 (2,5)
Median (Q1; Q3)	1,2 (0,0; 3,6)	1,7 (0,0; 4,4)
Min, Max	0,0; 9,9	0,0; 7,1
Woche 53		
N ^c	66	28
Mittelwert (SD)	2,4 (2,6)	2,2 (2,7)
Median (Q1; Q3)	1,6 (0,0; 4,3)	1,0 (0,0; 3,6)
Min, Max	0,0; 8,3	0,0; 8,7
Woche 56		
N ^c	63	29
Mittelwert (SD)	2,0 (2,0)	2,7 (2,7)
Median (Q1; Q3)	1,4 (0,0; 3,9)	2,3 (0,0; 5,0)
Min, Max	0,0; 7,1	0,0; 7,7
Woche 59		
N ^c	59	21
Mittelwert (SD)	2,0 (2,1)	2,1 (2,2)
Median (Q1; Q3)	1,3 (0,0; 3,3)	1,7 (0,0; 3,4)
Min, Max	0,0; 7,1	0,0; 6,4
Woche 62		
N ^c	54	20
Mittelwert (SD)	1,9 (2,1)	2,8 (2,4)
Median (Q1; Q3)	1,3 (0,0; 3,3)	2,6 (1,0; 4,0)
Min, Max	0,0; 7,4	0,0; 7,9
Woche 65		
N ^c	41	16
Mittelwert (SD)	2,1 (2,3)	3,1 (2,6)
Median (Q1; Q3)	1,1 (0,0; 4,0)	3,0 (0,6; 4,8)
Min, Max	0,0; 7,7	0,0; 8,4
Woche 68		
N ^c	43	13
Mittelwert (SD)	2,3 (2,3)	2,4 (2,2)
Median (Q1; Q3)	1,7 (0,0; 3,7)	2,4 (0,1; 3,1)
Min, Max	0,0; 8,1	0,0; 6,7

BPI-SF Schmerzbeeinträchtigung	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
BPI-SF: Brief Pain Inventory - Short Form; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



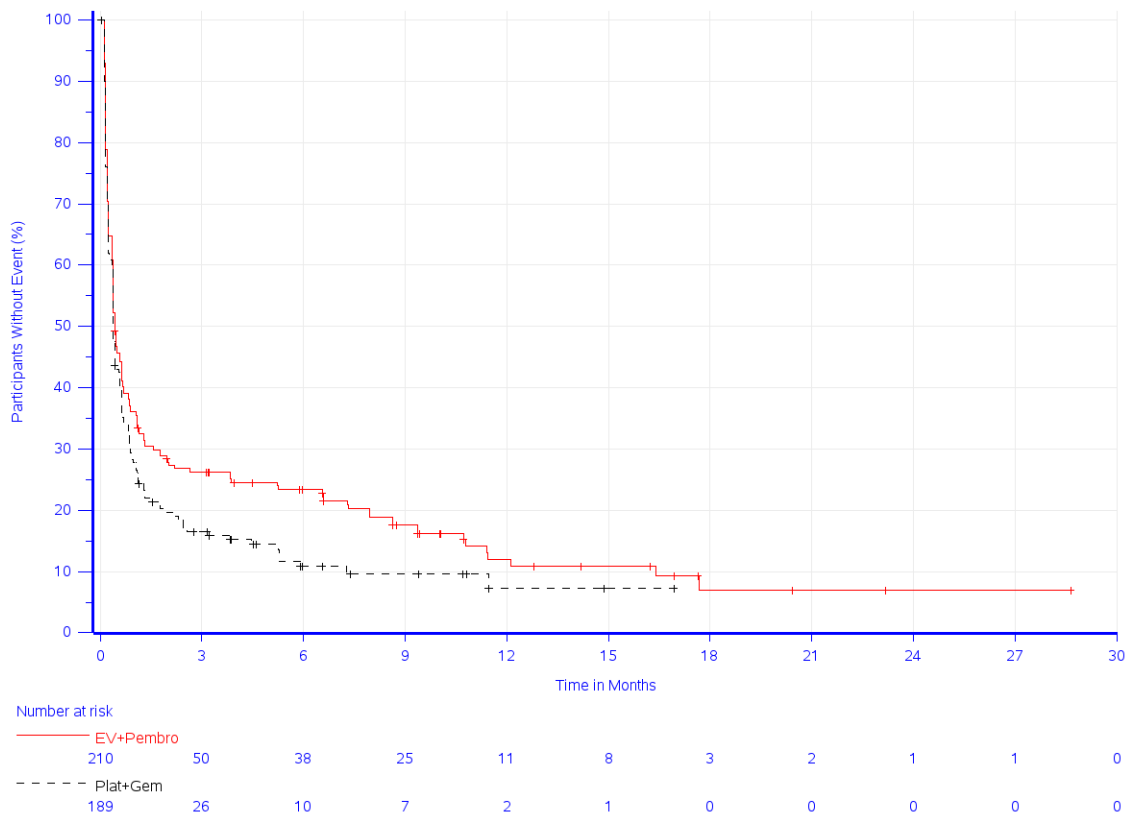
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 BPI-SF Pain Interference

Abbildung 4G-22: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerzbeeinträchtigung zu den verschiedenen Erhebungszeitpunkten des BPI-SF der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Anhang 4-G4: Analyse der Endpunkte Krankheitssymptomatik und Gesundheitszustand anhand von EORTC QLQ-C30 und EQ-5D VAS – Kaplan-Meier-Kurven der statistisch nicht signifikanten ($p \geq 0,05$) Symptomskalen bzw. der EQ-5D VAS

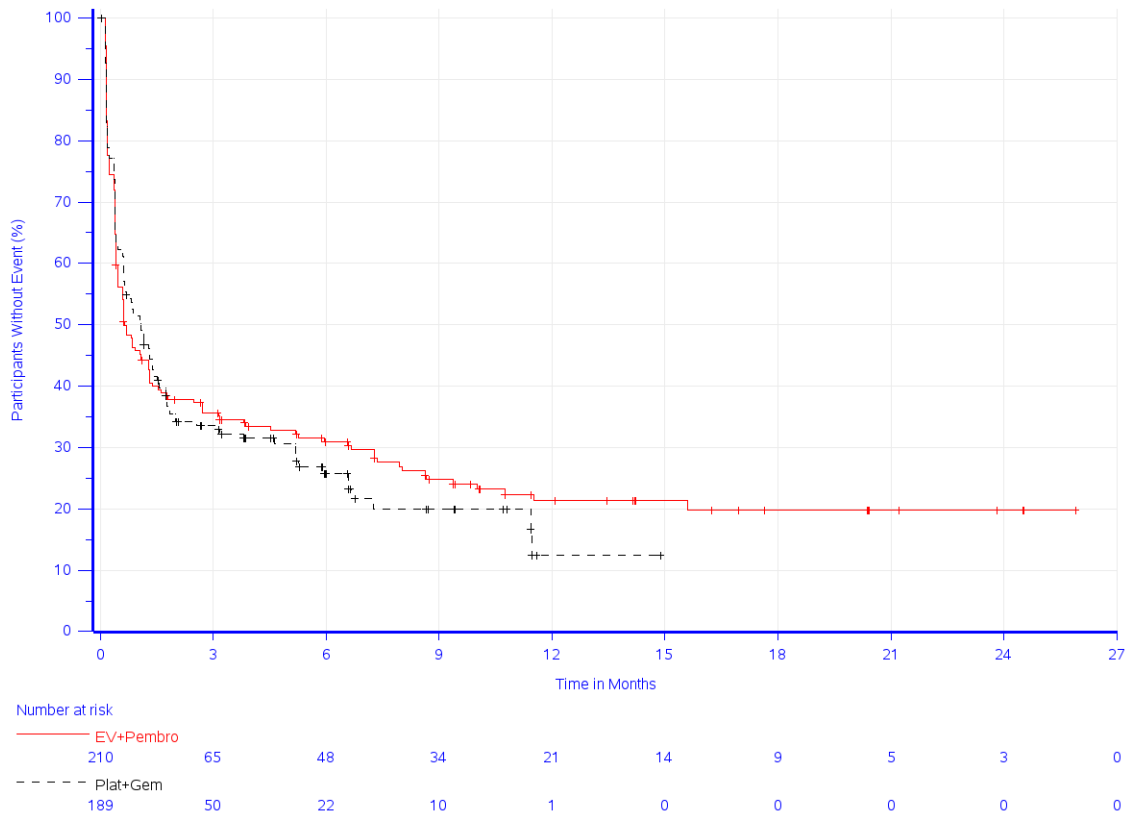
Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Kaplan-Meier-Kurven der nicht signifikanten ($p \geq 0,05$) Symptomskalen des EORTC QLQ-C30, der EQ-5D VAS und des BPI-SF dargestellt.

Cisplatin geeignet



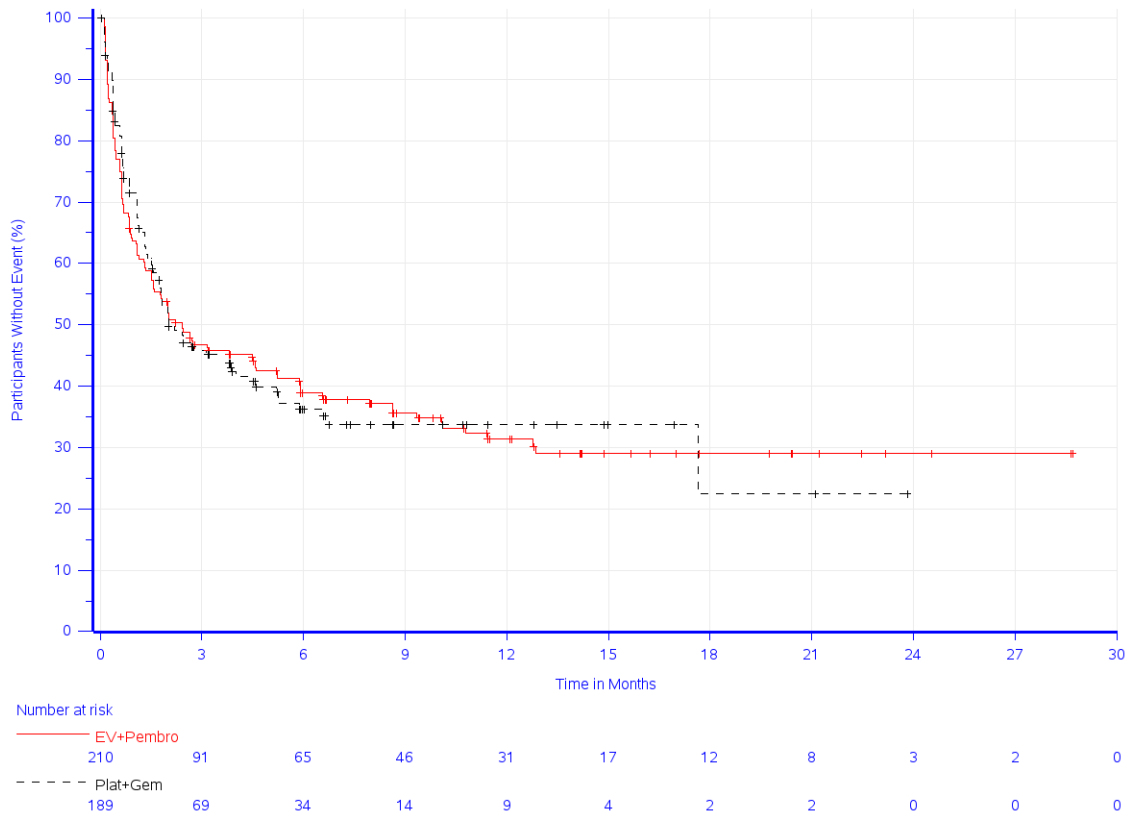
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Time to Deterioration for EORTC QLQ-C30 Fatigue (10 points)

Abbildung 4G-23: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



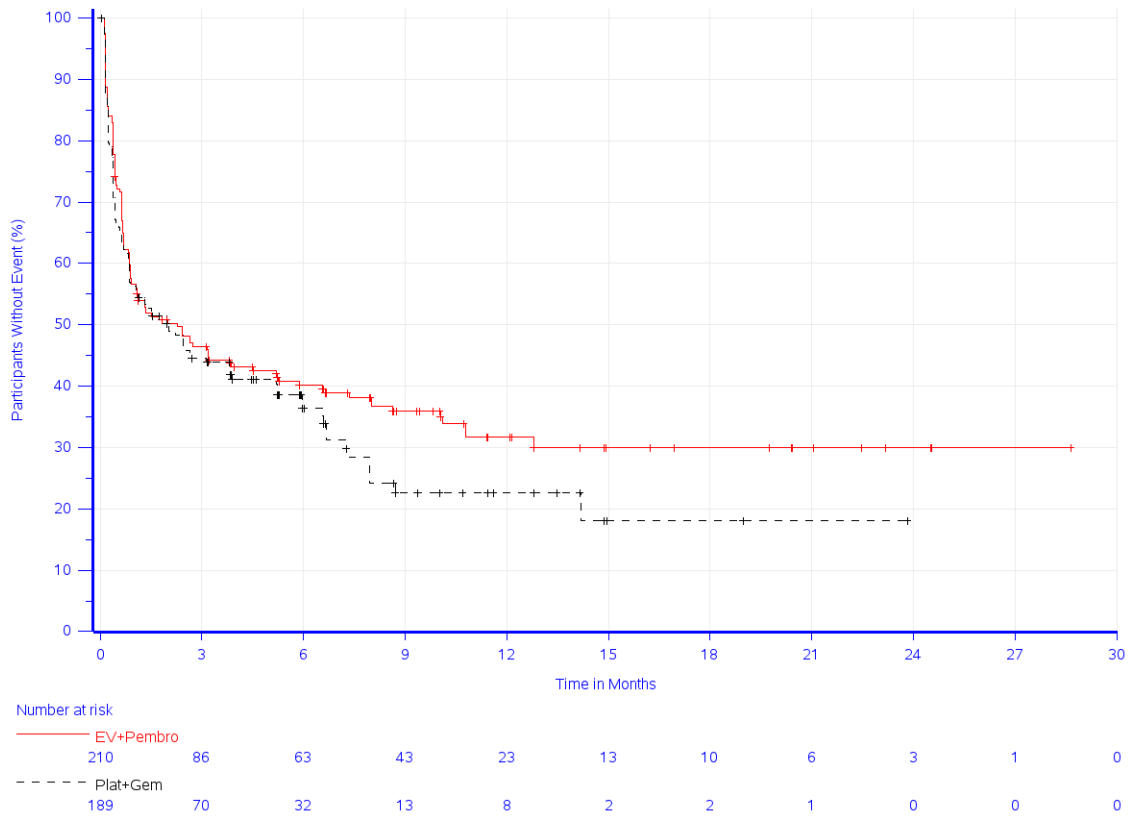
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Pain (10 points)

Abbildung 4G-24: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Schmerzen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



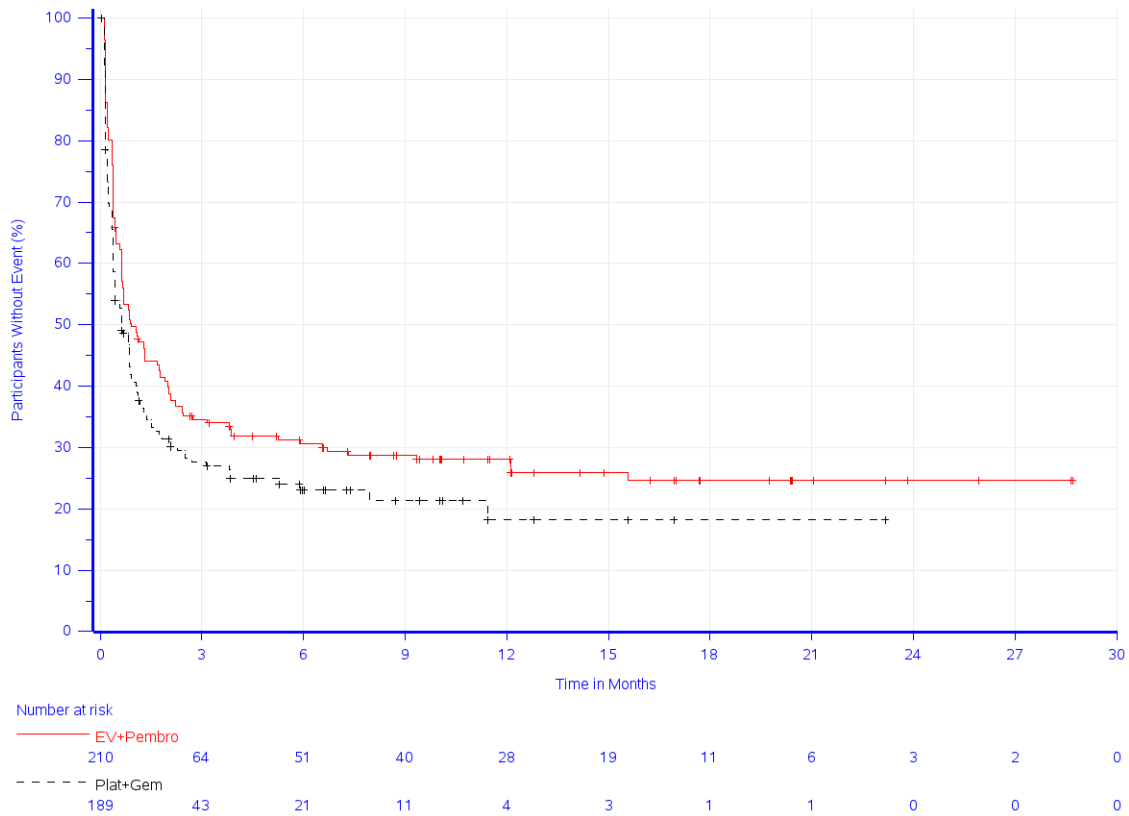
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Dyspnoea (10 points)

Abbildung 4G-25: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



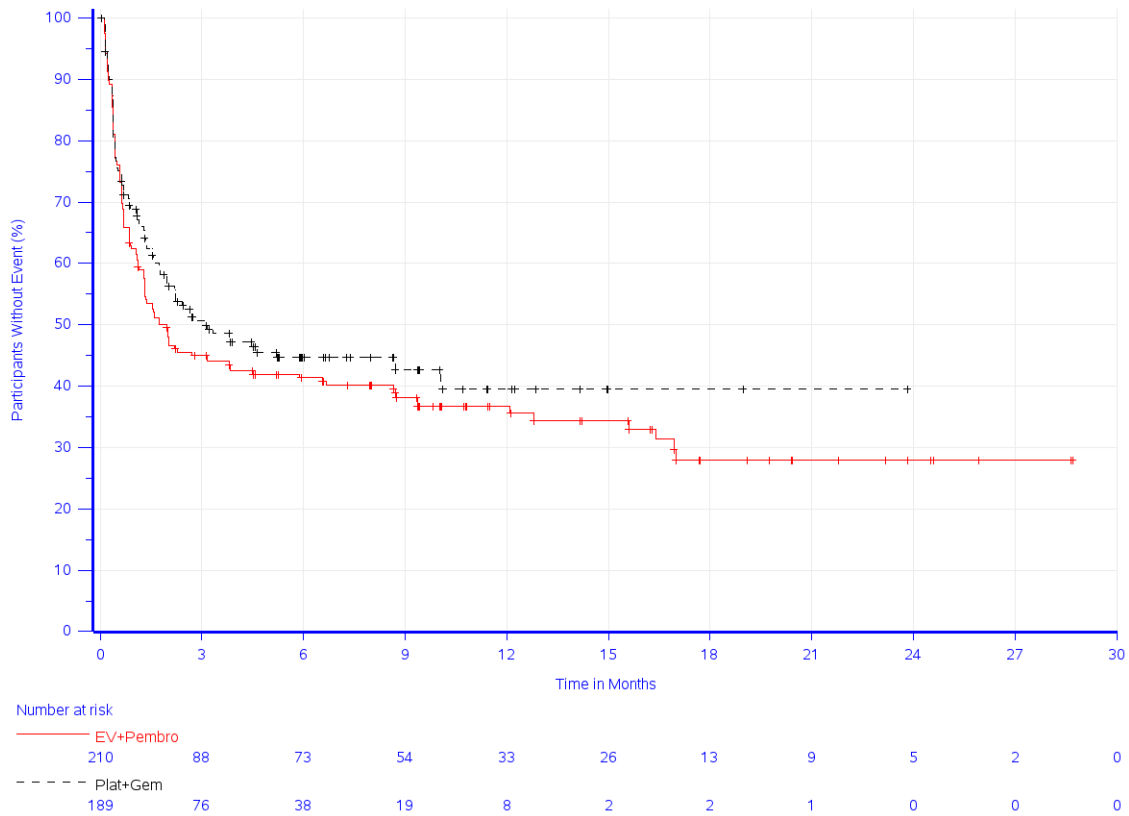
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Insomnia (10 points)

Abbildung 4G-26: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Schlaflosigkeit des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



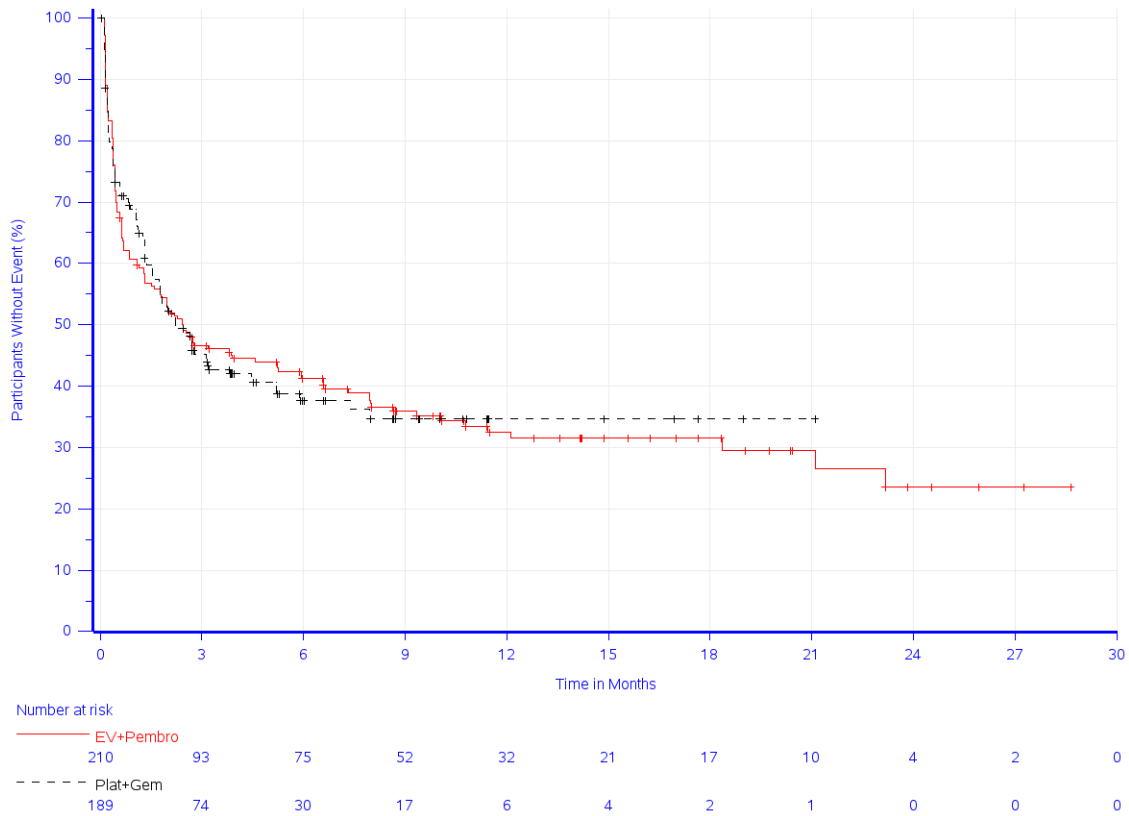
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Appetite Loss (10 points)

Abbildung 4G-27: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



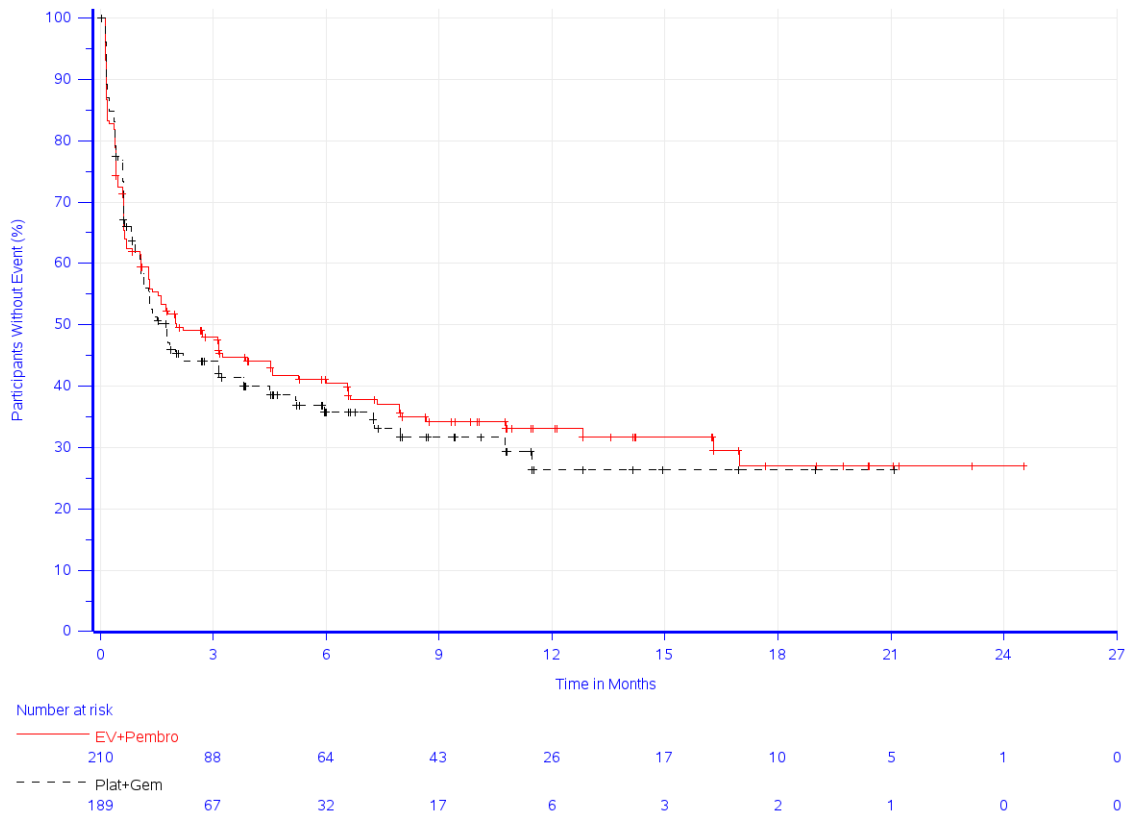
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Diarrhoea (10 points)

Abbildung 4G-28: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Diarrhoe des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



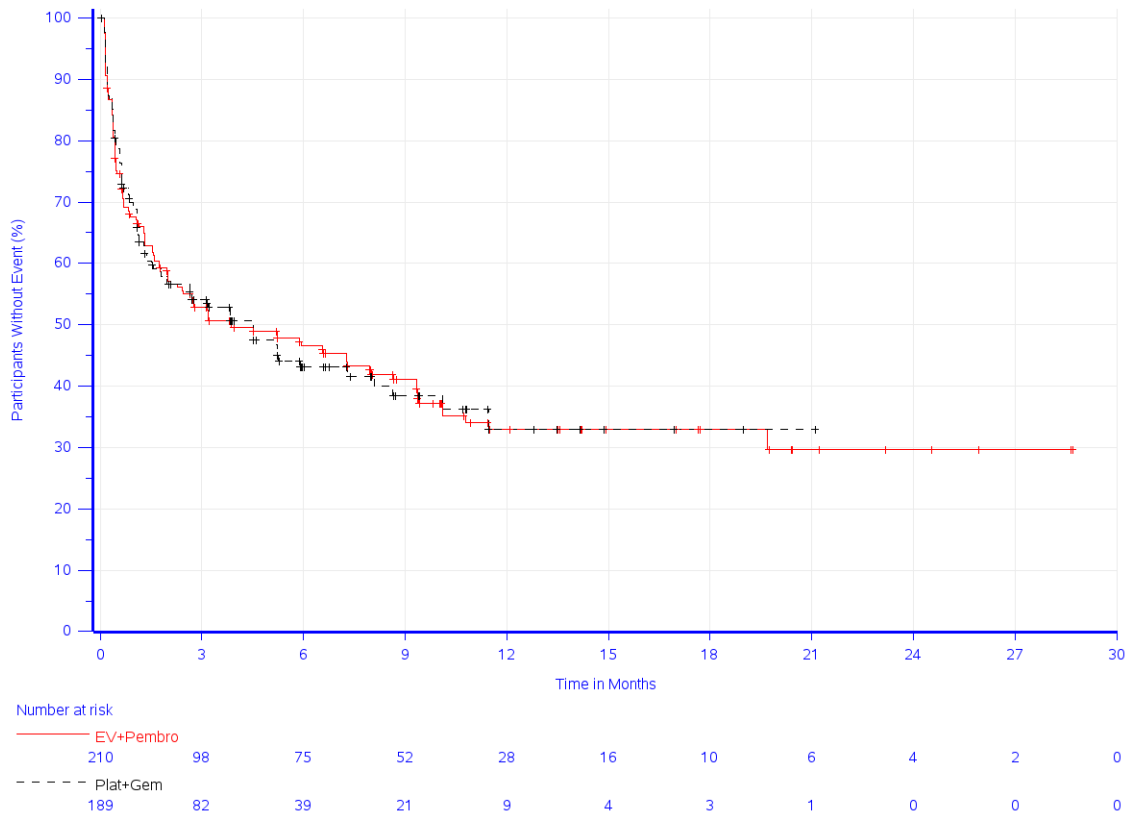
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EQ-5D VAS Score (15 points)

Abbildung 4G-29: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zur ersten Verschlechterung für den Gesundheitszustand anhand der VAS des EQ-5D (15 Punkte) der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for BPI-SF Pain at its Worst in Last 24 Hours (2 points)

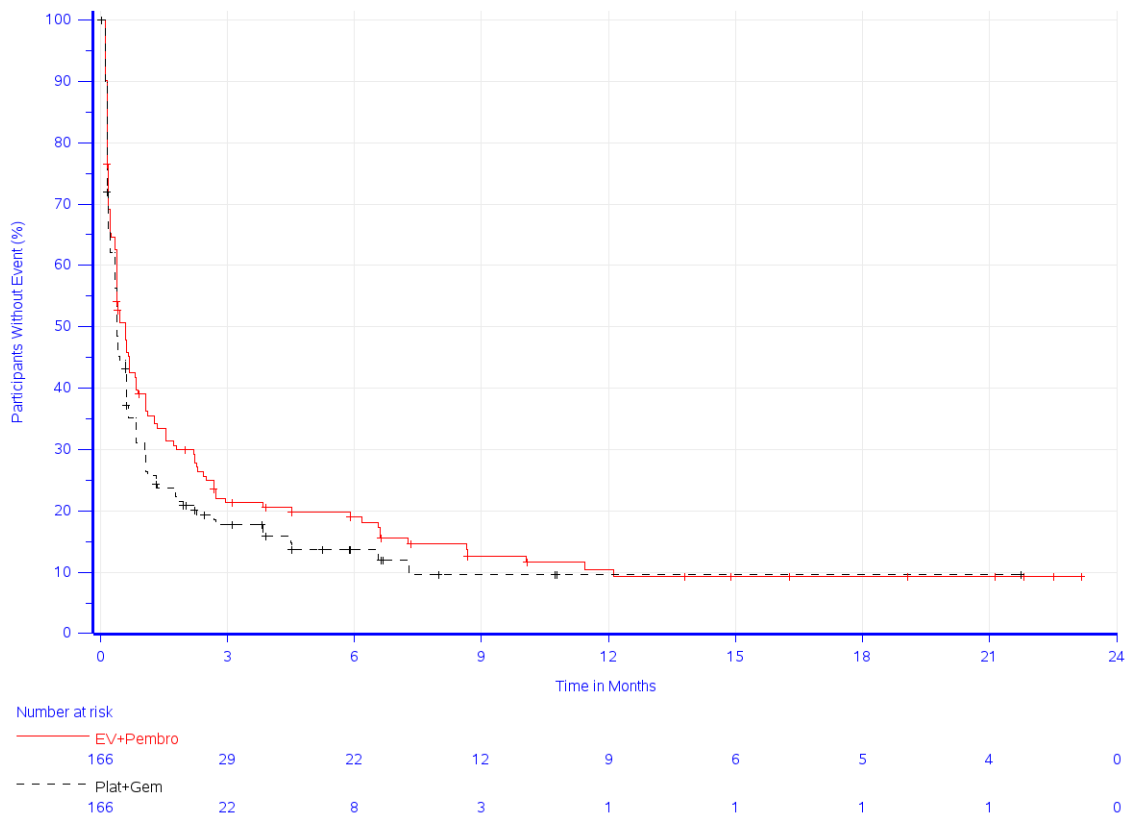
Abbildung 4G-30: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden des BPI-SF (2 Punkte) der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for BPI-SF Pain Interference (2 points)

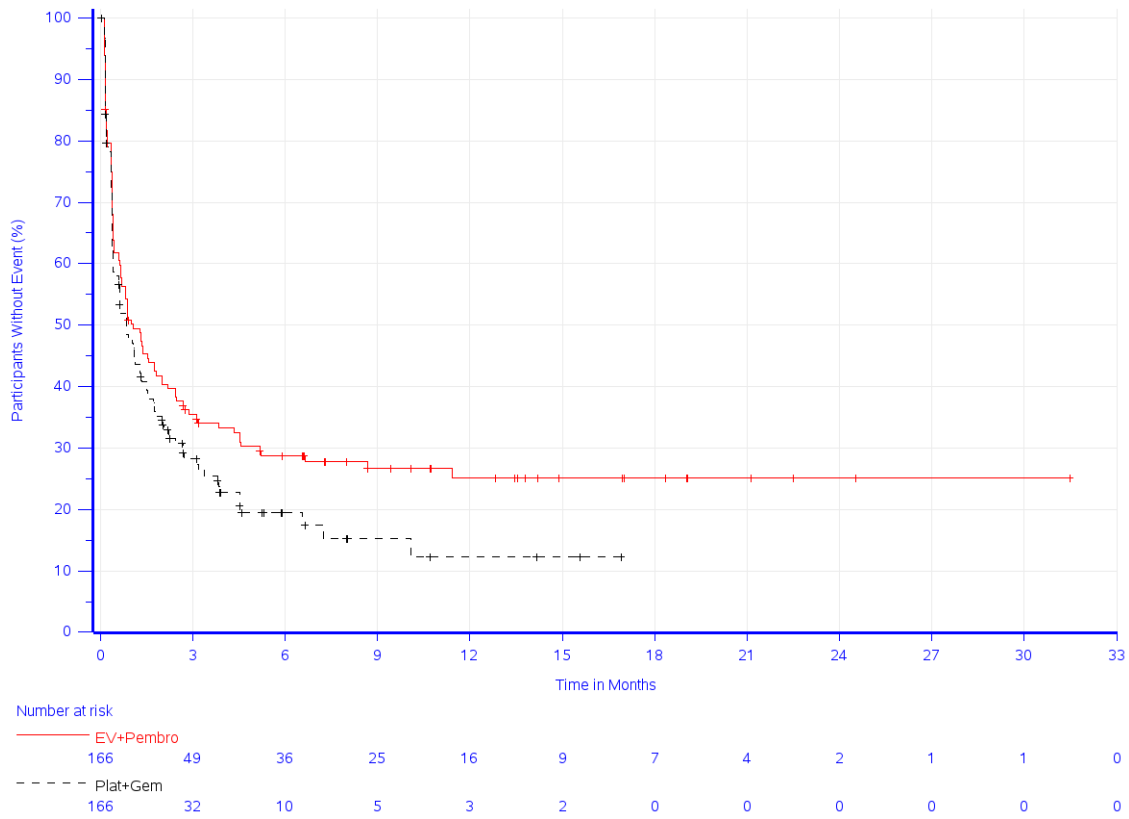
Abbildung 4G-31: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Stärkster Schmerzbeeinträchtigung des BPI-SF (2 Punkte) der Studie KEYNOTE A39 (Cisplatin geeignet)

Cisplatin ungeeignet



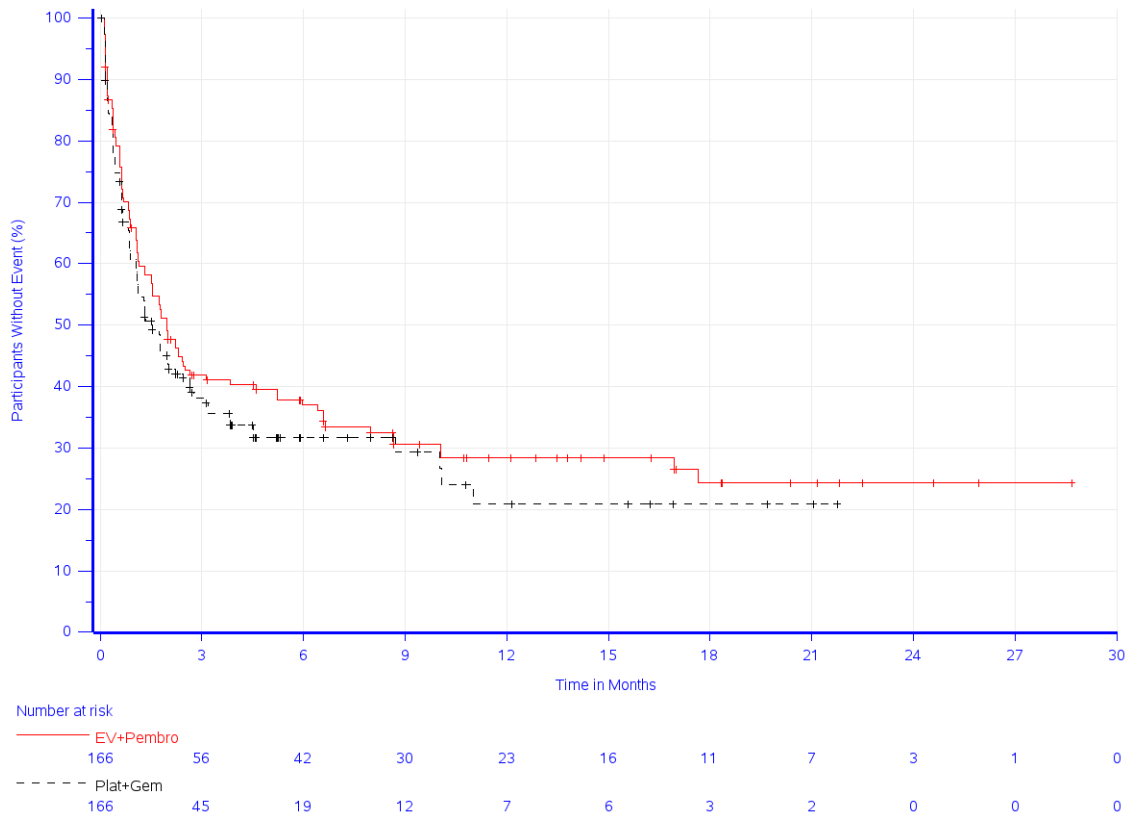
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Fatigue (10 points)

Abbildung 4G-32: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)



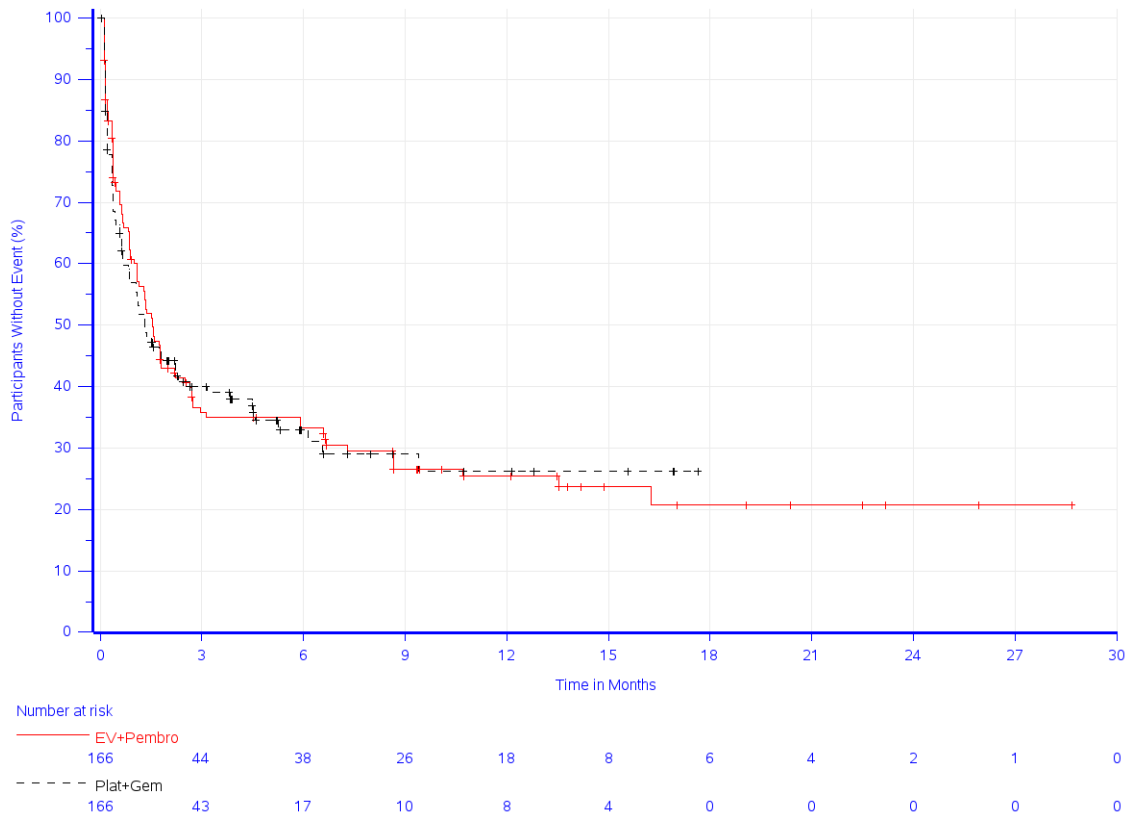
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Pain (10 points)

Abbildung 4G-33: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Schmerzen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)



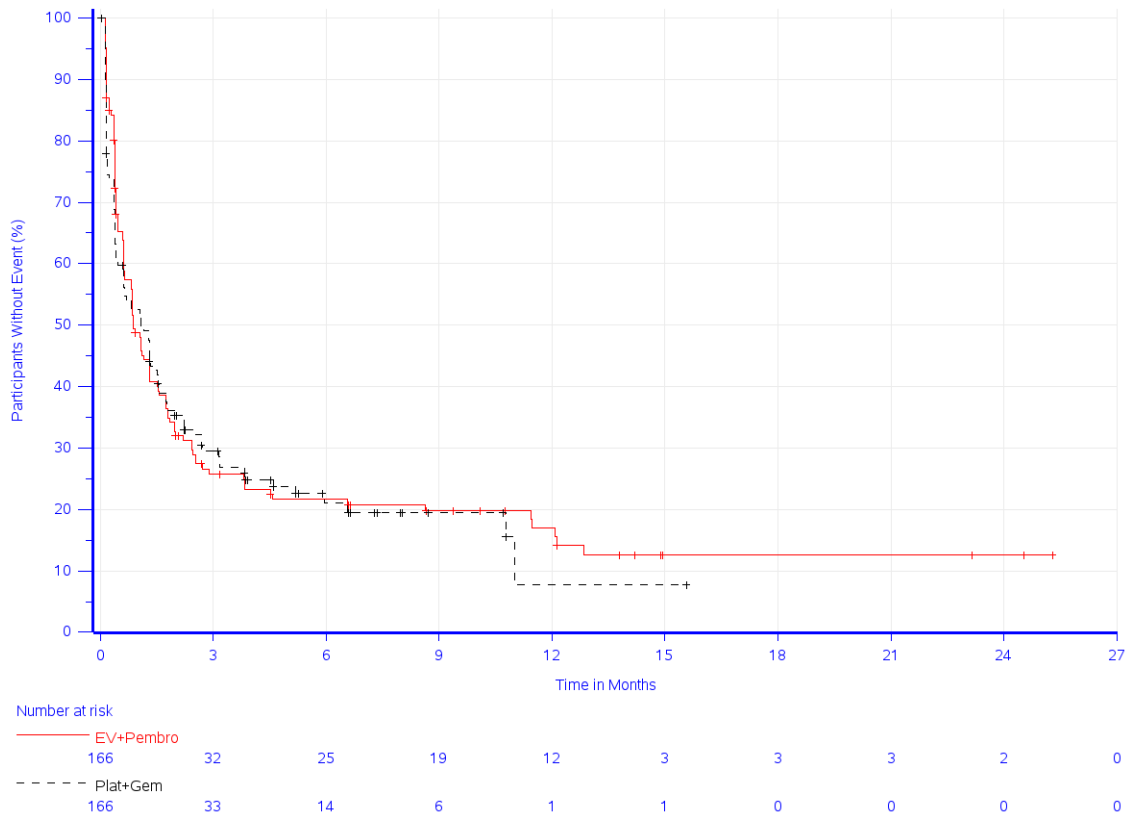
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Dyspnoea (10 points)

Abbildung 4G-34: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)



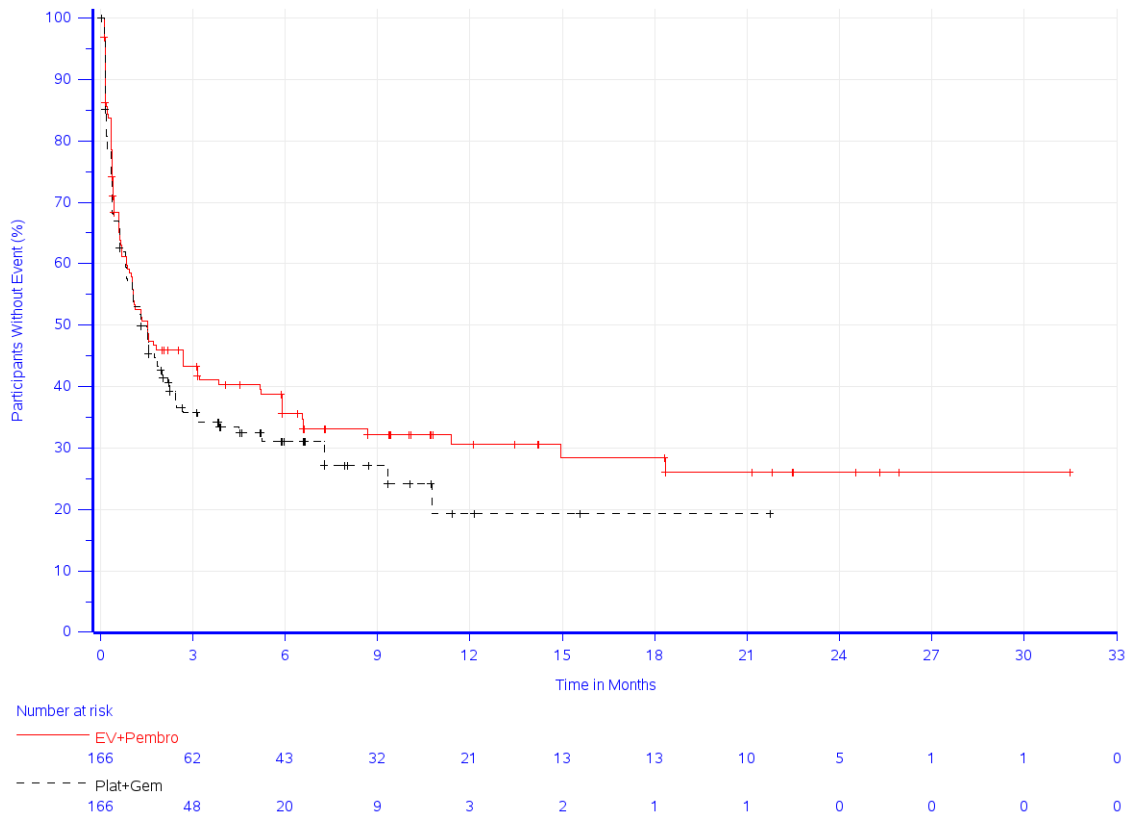
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Insomnia (10 points)

Abbildung 4G-35: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Schlaflosigkeit des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EORTC QLQ-C30 Appetite Loss (10 points)

Abbildung 4G-36: Zeit bis zur ersten klinisch relevanten Verschlechterung: Kaplan-Meier-Kurve für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Time to Deterioration for EQ-5D VAS Score (15 points)

Abbildung 4G-37: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zur ersten Verschlechterung für den Gesundheitszustand anhand der VAS des EQ-5D (15 Punkte) der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Anhang 4-G5: Auswertungen über den Studienverlauf für den Endpunkt Gesundheitsbezogene Lebensqualität anhand von EORTC QLQ-C30

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.3.1 die Auswertungen über den Studienverlauf des EORTC QLQ-C30 dargestellt.

Cisplatin geeignet

EORTC QLQ-C30 Globaler Gesundheitsstatus

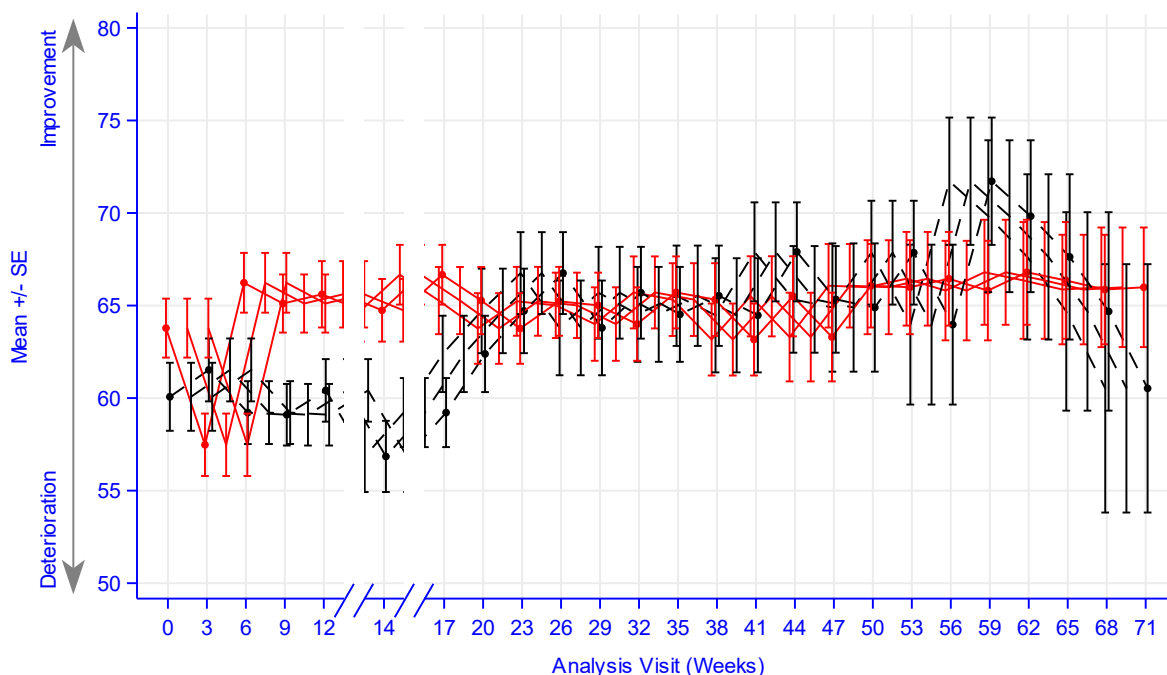
Tabelle 4G-33: Auswertung über den Studienverlauf des Globalen Gesundheitsstatus des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	63,8 (22,8)	60,1 (25,1)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (41,7; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	61,3 (23,2)	57,3 (22,7)
Median (Q1; Q3)	66,7 (50,0; 83,3)	58,3 (41,7; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	60,0 (22,1)	55,6 (22,6)
Median (Q1; Q3)	66,7 (50,0; 75,0)	50,0 (33,3; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	57,5 (22,9)	61,5 (21,6)
Median (Q1; Q3)	58,3 (41,7; 75,0)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	64,0 (22,1)	59,7 (21,4)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	65,8 (21,5)	57,1 (21,0)
Median (Q1; Q3)	66,7 (50,0; 83,3)	58,3 (41,7; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	66,2 (21,2)	59,2 (20,9)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 7			
N ^c		178	159
Mittelwert (SD)		65,6 (22,4)	58,4 (21,4)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (41,7; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 8			
N ^c		173	146
Mittelwert (SD)		65,9 (22,0)	57,2 (22,3)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 9			
N ^c		182	152
Mittelwert (SD)		65,1 (21,2)	59,1 (20,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (45,8; 75,0)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 10			
N ^c		177	141
Mittelwert (SD)		66,5 (21,1)	57,3 (20,7)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (50,0; 66,7)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 11			
N ^c		177	145
Mittelwert (SD)		67,1 (21,2)	59,4 (19,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 12			
N ^c		173	140
Mittelwert (SD)		65,6 (23,6)	60,4 (20,0)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 14			
N ^c		169	129
Mittelwert (SD)		64,7 (22,0)	56,8 (21,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	50,0 (41,7; 66,7)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 17			
N ^c		164	132
Mittelwert (SD)		66,7 (20,7)	59,2 (21,4)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 20			
N ^c		155	111
Mittelwert (SD)		65,3 (22,6)	62,4 (21,7)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 23			
N ^c		152	98
Mittelwert (SD)		63,8 (23,5)	64,7 (22,6)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Min, Max		8,3; 100,0	0,0; 100,0
Woche 26			
N ^c		145	96
Mittelwert (SD)		65,2 (22,4)	66,8 (21,7)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 29			
N ^c		146	87
Mittelwert (SD)		65,0 (21,3)	63,8 (23,9)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 32			
N ^c		125	77
Mittelwert (SD)		64,0 (22,2)	65,7 (21,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	8,3; 100,0
Woche 35			
N ^c		122	70
Mittelwert (SD)		65,7 (21,5)	64,5 (21,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 38			
N ^c		124	66
Mittelwert (SD)		65,3 (21,9)	65,5 (22,0)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	16,7; 100,0
Woche 41			
N ^c		119	57
Mittelwert (SD)		63,2 (21,2)	64,5 (23,3)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 44			
N ^c		100	54
Mittelwert (SD)		65,5 (21,6)	67,9 (19,7)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	33,3; 100,0
Woche 47			
N ^c		94	50
Mittelwert (SD)		63,3 (23,2)	65,3 (20,4)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 50			
N ^c		84	47
Mittelwert (SD)		66,1 (20,7)	64,9 (23,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 53			
N ^c		74	42
Mittelwert (SD)		66,0 (21,8)	67,9 (18,2)

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	33,3; 100,0
Woche 56			
N ^c		76	34
Mittelwert (SD)		66,4 (22,1)	64,0 (25,2)
Median (Q1; Q3)		66,7 (50,0; 83,3)	70,8 (41,7; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 59			
N ^c		68	33
Mittelwert (SD)		65,8 (22,2)	71,7 (19,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	75,0 (66,7; 83,3)
Min, Max		0,0; 100,0	16,7; 100,0
Woche 62			
N ^c		63	29
Mittelwert (SD)		66,8 (22,5)	69,8 (22,1)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	16,7; 100,0
Woche 65			
N ^c		54	26
Mittelwert (SD)		66,4 (23,2)	67,6 (22,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 68			
N ^c		52	21
Mittelwert (SD)		65,9 (21,3)	64,7 (24,6)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 71			
N ^c		49	19
Mittelwert (SD)		66,0 (22,6)	60,5 (29,2)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (33,3; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
a: Datenschnitt: 08. August 2023			
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet			
c: Anzahl der Beobachtungen zu jedem Zeitpunkt			
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; QoL: Quality of Life; SD: Standardabweichung			



Number of participants

— EV+Pembro

205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49

- - - Plat+Gem

187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Global Health Status/QoL

Abbildung 4G-38: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler des Globalen Gesundheitsstatus zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

EORTC QLQ-C30 Funktionsskalen

Tabelle 4G-34: Auswertung über den Studienverlauf der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	79,3 (21,9)	73,9 (23,5)
Median (Q1; Q3)	86,7 (66,7; 100,0)	80,0 (60,0; 93,3)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	76,2 (23,7)	71,2 (23,4)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

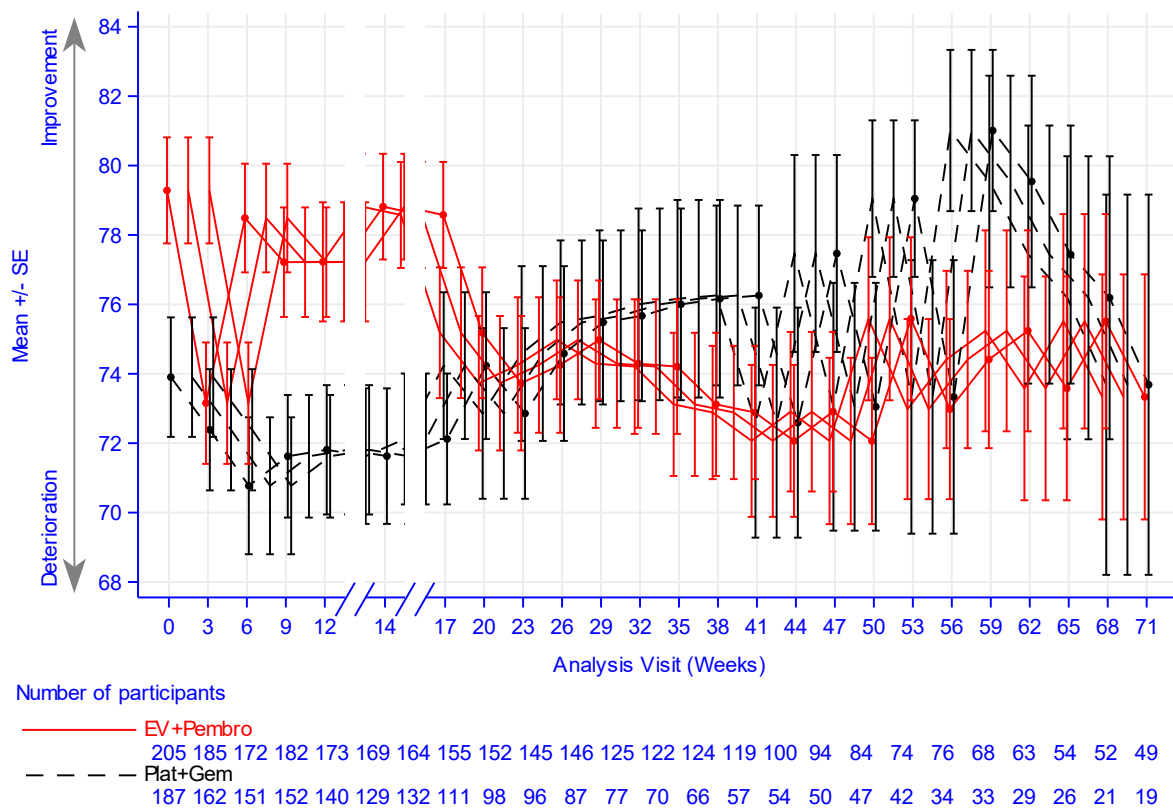
EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	74,2 (23,8)	70,1 (22,6)
Median (Q1; Q3)	80,0 (60,0; 93,3)	73,3 (53,3; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	73,2 (23,8)	72,4 (22,2)
Median (Q1; Q3)	80,0 (60,0; 93,3)	76,7 (60,0; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	77,5 (22,1)	72,3 (21,7)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (60,0; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	77,7 (21,4)	71,5 (23,1)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (60,0; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	78,5 (20,5)	70,8 (24,2)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (60,0; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	78,2 (20,1)	72,2 (22,2)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (60,0; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	78,3 (21,0)	69,8 (24,7)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	182	152
Mittelwert (SD)	77,2 (21,3)	71,6 (21,8)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (60,0; 86,7)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	78,1 (19,6)	71,2 (22,7)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (60,0; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	78,3 (20,5)	72,7 (21,7)
Median (Q1; Q3)	80,0 (73,3; 93,3)	80,0 (60,0; 86,7)

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Min, Max	0,0; 100,0	13,3; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	77,2 (22,6)	71,8 (22,1)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (60,0; 86,7)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	78,8 (19,8)	71,6 (22,2)
Median (Q1; Q3)	86,7 (66,7; 93,3)	73,3 (53,3; 93,3)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	78,6 (19,6)	72,1 (21,7)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (53,3; 86,7)
Min, Max	26,7; 100,0	13,3; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	75,2 (23,4)	74,2 (22,3)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (60,0; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	73,7 (23,9)	72,9 (24,3)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (53,3; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	74,3 (23,5)	74,6 (24,7)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (60,0; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	75,0 (20,7)	75,5 (22,1)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	74,3 (20,7)	75,7 (21,6)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (66,7; 93,3)
Min, Max	13,3; 100,0	6,7; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	74,2 (21,4)	76,0 (23,1)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	73,1 (23,0)	76,2 (23,1)

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Median (Q1; Q3)	76,7 (60,0; 93,3)	86,7 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	72,9 (21,0)	76,3 (19,6)
Median (Q1; Q3)	73,3 (60,0; 86,7)	80,0 (60,0; 93,3)
Min, Max	6,7; 100,0	13,3; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	72,1 (21,9)	72,6 (24,4)
Median (Q1; Q3)	73,3 (60,0; 86,7)	76,7 (60,0; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	72,9 (22,3)	77,5 (20,1)
Median (Q1; Q3)	73,3 (60,0; 86,7)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	72,1 (22,0)	73,1 (24,5)
Median (Q1; Q3)	73,3 (60,0; 86,7)	73,3 (66,7; 86,7)
Min, Max	20,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	75,6 (20,2)	79,0 (14,6)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (66,7; 86,7)
Min, Max	6,7; 100,0	53,3; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	73,0 (22,6)	73,3 (23,0)
Median (Q1; Q3)	80,0 (60,0; 86,7)	76,7 (66,7; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	74,4 (21,1)	81,0 (13,3)
Median (Q1; Q3)	80,0 (66,7; 86,7)	80,0 (73,3; 93,3)
Min, Max	0,0; 100,0	53,3; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	75,2 (23,0)	79,5 (16,4)
Median (Q1; Q3)	80,0 (66,7; 93,3)	86,7 (73,3; 86,7)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	73,6 (23,7)	77,4 (19,0)
Median (Q1; Q3)	73,3 (60,0; 93,3)	80,0 (66,7; 93,3)
Min, Max	6,7; 100,0	13,3; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 68		
N ^c	52	21
Mittelwert (SD)	75,5 (22,3)	76,2 (18,7)
Median (Q1; Q3)	80,0 (60,0; 93,3)	80,0 (66,7; 86,7)
Min, Max	20,0; 100,0	33,3; 100,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	73,3 (24,7)	73,7 (23,9)
Median (Q1; Q3)	80,0 (66,7; 100,0)	80,0 (60,0; 86,7)
Min, Max	13,3; 100,0	13,3; 100,0

a: Datenschnitt: 08. August 2023
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet
c: Anzahl der Beobachtungen zu jedem Zeitpunkt
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Physical Functioning

Abbildung 4G-39: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Körperliche Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

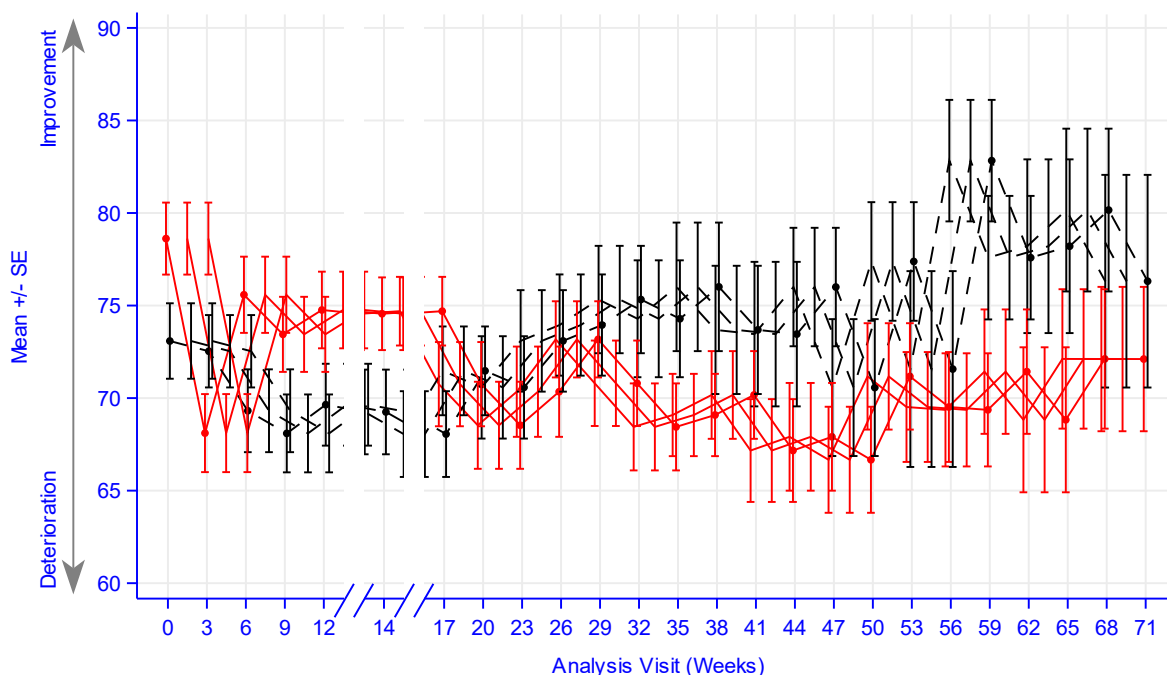
Tabelle 4G-35: Auswertung über den Studienverlauf der Funktionsskala Rollenfunktion des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	78,6 (27,8)	73,1 (27,9)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	74,0 (29,0)	67,9 (26,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	70,5 (28,9)	63,7 (29,4)
Median (Q1; Q3)	66,7 (58,3; 100,0)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	68,1 (28,7)	72,5 (24,9)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	74,2 (26,7)	68,0 (27,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	73,8 (28,3)	65,3 (27,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	75,6 (27,0)	69,3 (27,5)
Median (Q1; Q3)	75,0 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	74,2 (26,1)	69,2 (28,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	75,8 (26,2)	68,3 (28,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	182	152
Mittelwert (SD)	73,4 (27,4)	68,1 (25,9)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	76,9 (25,7)	67,1 (27,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	74,2 (27,3)	69,4 (26,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	74,8 (27,2)	69,6 (26,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	74,6 (25,5)	69,3 (26,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	74,7 (23,7)	68,1 (26,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 91,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	70,8 (28,3)	71,5 (25,3)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	68,5 (29,0)	70,6 (27,4)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	70,3 (29,4)	73,1 (26,9)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	73,2 (24,9)	73,9 (25,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 32		
N ^c	125	77
Mittelwert (SD)	70,8 (25,8)	75,3 (25,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	68,4 (26,0)	74,3 (26,4)
Median (Q1; Q3)	66,7 (50,0; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	69,1 (24,8)	76,0 (28,2)
Median (Q1; Q3)	66,7 (50,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	70,2 (25,8)	73,7 (26,2)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	67,2 (27,8)	73,5 (28,7)
Median (Q1; Q3)	66,7 (50,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	67,9 (28,2)	76,0 (22,6)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	66,7 (26,3)	70,6 (25,4)
Median (Q1; Q3)	66,7 (50,0; 91,7)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	71,2 (24,7)	77,4 (20,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	69,5 (25,9)	71,6 (30,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	69,4 (25,2)	82,8 (18,9)
Median (Q1; Q3)	66,7 (58,3; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62		
N ^c	63	29
Mittelwert (SD)	71,4 (26,7)	77,6 (18,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	68,8 (28,8)	78,2 (23,9)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	72,1 (27,2)	80,2 (20,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	72,1 (27,3)	76,3 (25,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	205	185	172	182	173	169	164	155	152	145	146	125	122	124	119	100	94	84	74	76	68	63	54	52	49
- - - Plat+Gem	187	162	151	152	140	129	132	111	98	96	87	77	70	66	57	54	50	47	42	34	33	29	26	21	19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Role Functioning

Abbildung 4G-40: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Rollenfunktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Tabelle 4G-36: Auswertung über den Studienverlauf der Funktionsskala Soziale Funktion des EORTC QLQ-C30 (Cisplatin geeignet)

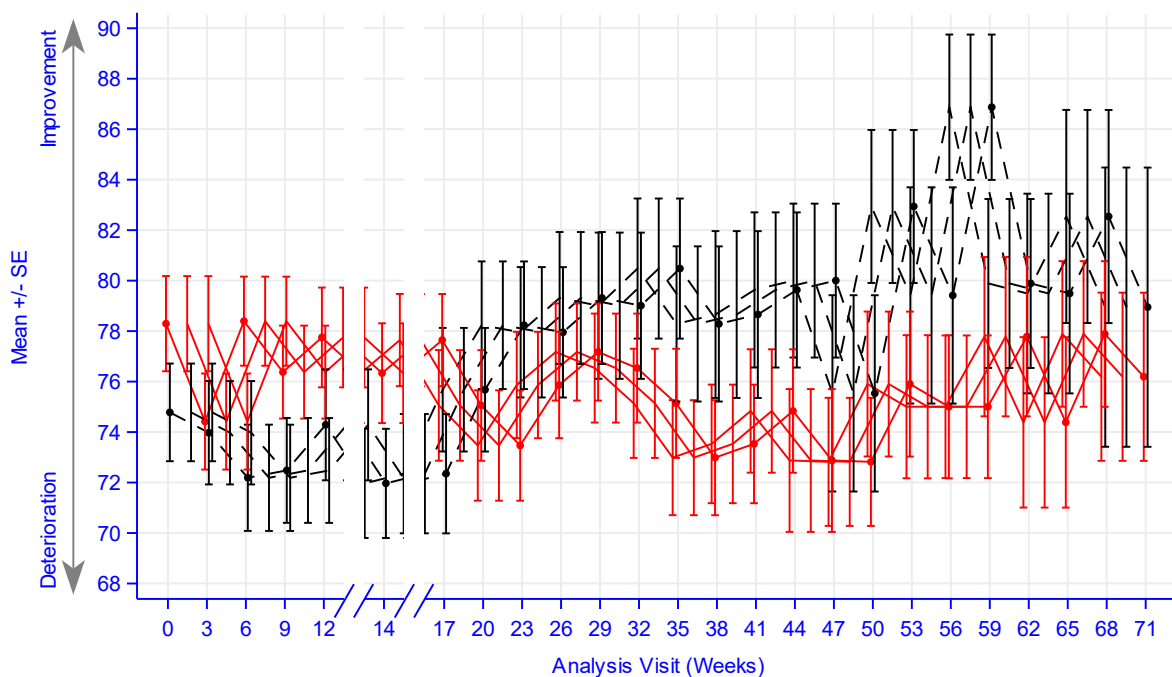
EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	78,3 (27,0)	74,8 (26,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	76,8 (25,6)	73,0 (24,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2		
N ^c	192	151
Mittelwert (SD)	76,0 (24,5)	69,9 (28,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	74,4 (25,9)	74,0 (26,1)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	77,6 (24,4)	71,1 (27,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	76,4 (25,2)	70,9 (26,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	78,4 (23,1)	72,2 (25,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	77,3 (23,4)	73,8 (25,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	77,1 (24,7)	71,9 (25,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	182	152
Mittelwert (SD)	76,4 (24,8)	72,5 (25,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (58,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	77,1 (23,6)	72,8 (25,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	77,4 (25,0)	73,0 (25,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 12		
N ^c	173	140
Mittelwert (SD)	77,7 (26,0)	74,3 (26,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	76,3 (25,7)	72,0 (24,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	77,6 (23,4)	72,3 (27,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	75,1 (27,3)	75,7 (25,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	73,5 (26,9)	78,2 (25,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	75,9 (25,4)	78,0 (25,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	146	87
Mittelwert (SD)	77,2 (23,2)	79,3 (24,4)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	76,5 (24,1)	79,0 (25,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	75,1 (23,9)	80,5 (23,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	73,0 (25,4)	78,3 (25,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 41		
N ^c	119	57
Mittelwert (SD)	73,5 (25,6)	78,7 (25,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	74,8 (24,4)	79,6 (22,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	72,9 (27,4)	80,0 (21,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	72,8 (23,3)	75,5 (26,7)
Median (Q1; Q3)	66,7 (50,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	75,9 (24,7)	82,9 (19,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 56		
N ^c	76	34
Mittelwert (SD)	75,0 (24,7)	79,4 (25,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	75,0 (23,3)	86,9 (16,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	77,8 (25,0)	79,9 (18,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	74,4 (24,8)	79,5 (20,2)
Median (Q1; Q3)	75,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	77,9 (20,8)	82,5 (19,3)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	50,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 71		
N ^c	49	19
Mittelwert (SD)	76,2 (23,3)	78,9 (24,1)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
a: Datenschnitt: 08. August 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49
- - - Plat+Gem	187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Social Functioning

Abbildung 4G-41: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Soziale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Tabelle 4G-37: Auswertung über den Studienverlauf der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 (Cisplatin geeignet)

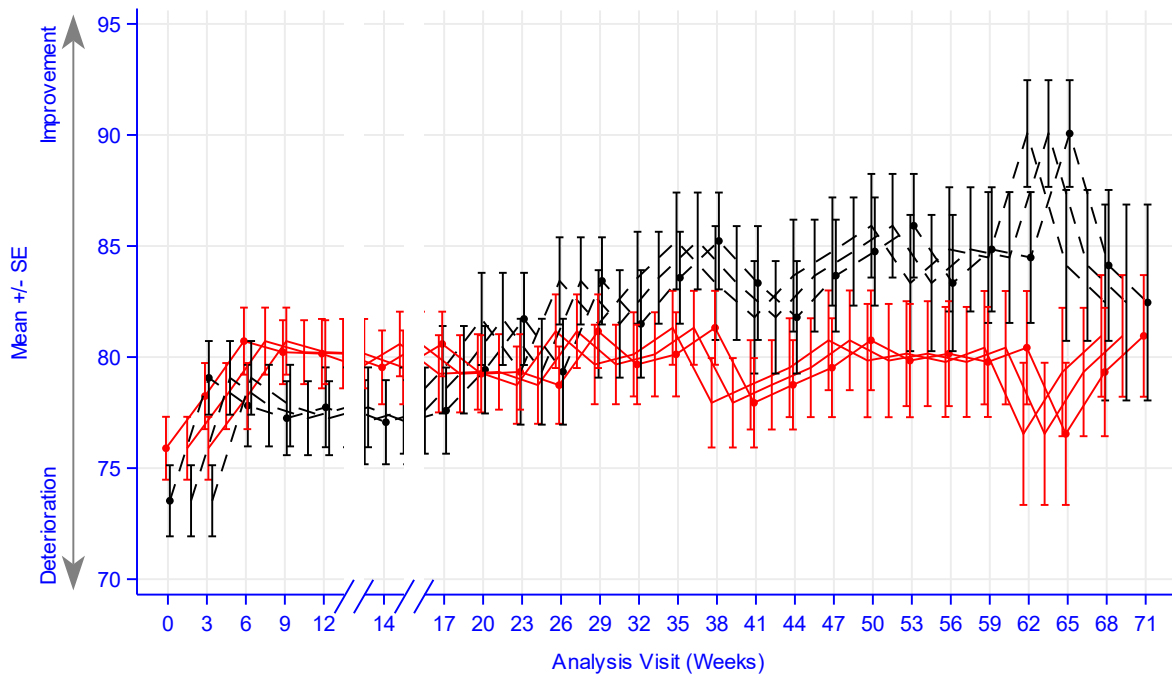
EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline		
N ^c	205	187
Mittelwert (SD)	75,9 (20,3)	73,5 (21,9)
Median (Q1; Q3)	75,0 (66,7; 91,7)	75,0 (66,7; 91,7)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 1		
N ^c	188	159
Mittelwert (SD)	78,9 (19,4)	76,5 (21,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 91,7)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 2		
N ^c	192	151
Mittelwert (SD)	78,8 (19,6)	75,3 (21,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 91,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	185	162
Mittelwert (SD)	78,2 (20,2)	79,1 (21,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	8,3; 100,0
Woche 4		
N ^c	181	157
Mittelwert (SD)	80,1 (19,9)	78,8 (20,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	175	157
Mittelwert (SD)	81,8 (17,5)	76,9 (21,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 6		
N ^c	172	151
Mittelwert (SD)	80,7 (19,8)	77,8 (22,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 7		
N ^c	178	159
Mittelwert (SD)	80,3 (21,0)	78,1 (20,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	8,3; 100,0
Woche 8		
N ^c	173	146
Mittelwert (SD)	79,3 (21,6)	76,0 (23,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	79,2 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 9		
N ^c	182	152
Mittelwert (SD)	80,2 (19,4)	77,2 (20,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	16,7; 100,0	16,7; 100,0
Woche 10		
N ^c	177	141
Mittelwert (SD)	80,8 (19,9)	76,8 (22,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	177	145
Mittelwert (SD)	80,8 (20,8)	77,3 (22,6)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 12		
N ^c	173	140
Mittelwert (SD)	80,2 (20,5)	77,7 (21,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 14		
N ^c	169	129
Mittelwert (SD)	79,5 (21,6)	77,1 (21,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 17		
N ^c	164	132
Mittelwert (SD)	80,6 (18,6)	77,6 (22,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 20		
N ^c	155	111
Mittelwert (SD)	79,2 (21,6)	79,4 (20,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 23		
N ^c	152	98
Mittelwert (SD)	79,3 (20,9)	81,7 (20,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	0,0; 100,0	8,3; 100,0
Woche 26		
N ^c	145	96
Mittelwert (SD)	78,7 (20,9)	79,3 (23,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 29		
N ^c	146	87
Mittelwert (SD)	81,2 (20,0)	83,4 (18,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 32		
N ^c	125	77
Mittelwert (SD)	79,7 (20,0)	81,5 (21,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 35		
N ^c	122	70
Mittelwert (SD)	80,1 (20,9)	83,6 (17,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 38		
N ^c	124	66
Mittelwert (SD)	81,3 (18,5)	85,2 (17,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	25,0; 100,0	25,0; 100,0
Woche 41		
N ^c	119	57
Mittelwert (SD)	77,9 (22,0)	83,3 (19,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 44		
N ^c	100	54
Mittelwert (SD)	78,8 (20,1)	81,8 (18,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	33,3; 100,0
Woche 47		
N ^c	94	50
Mittelwert (SD)	79,5 (21,6)	83,7 (17,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 50		
N ^c	84	47
Mittelwert (SD)	80,8 (20,6)	84,8 (16,7)
Median (Q1; Q3)	87,5 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	16,7; 100,0	50,0; 100,0
Woche 53		
N ^c	74	42
Mittelwert (SD)	79,8 (21,9)	85,9 (15,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	50,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 56		
N ^c	76	34
Mittelwert (SD)	80,2 (20,6)	83,3 (17,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	16,7; 100,0	50,0; 100,0
Woche 59		
N ^c	68	33
Mittelwert (SD)	79,8 (20,4)	84,8 (16,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	25,0; 100,0	41,7; 100,0
Woche 62		
N ^c	63	29
Mittelwert (SD)	80,4 (20,3)	84,5 (15,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	50,0; 100,0
Woche 65		
N ^c	54	26
Mittelwert (SD)	76,5 (23,5)	90,1 (12,3)
Median (Q1; Q3)	75,0 (66,7; 100,0)	91,7 (83,3; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 68		
N ^c	52	21
Mittelwert (SD)	79,3 (20,8)	84,1 (15,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (75,0; 100,0)
Min, Max	33,3; 100,0	50,0; 100,0
Woche 71		
N ^c	49	19
Mittelwert (SD)	81,0 (19,2)	82,5 (19,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	33,3; 100,0	25,0; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

—	EV+Pembro
205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49	
- - -	Plat+Gem
187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19	

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Emotional Functioning

Abbildung 4G-42: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Emotionale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Tabelle 4G-38: Auswertung über den Studienverlauf der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 (Cisplatin geeignet)

EORTC Funktion	QLQ-C30 Kognitive	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Baseline			
N ^c		205	187
Mittelwert (SD)		86,3 (19,5)	83,0 (20,1)
Median (Q1; Q3)		100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max		0,0; 100,0	16,7; 100,0
Woche 1			
N ^c		188	159
Mittelwert (SD)		86,2 (18,3)	81,1 (20,8)
Median (Q1; Q3)		100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max		0,0; 100,0	0,0; 100,0

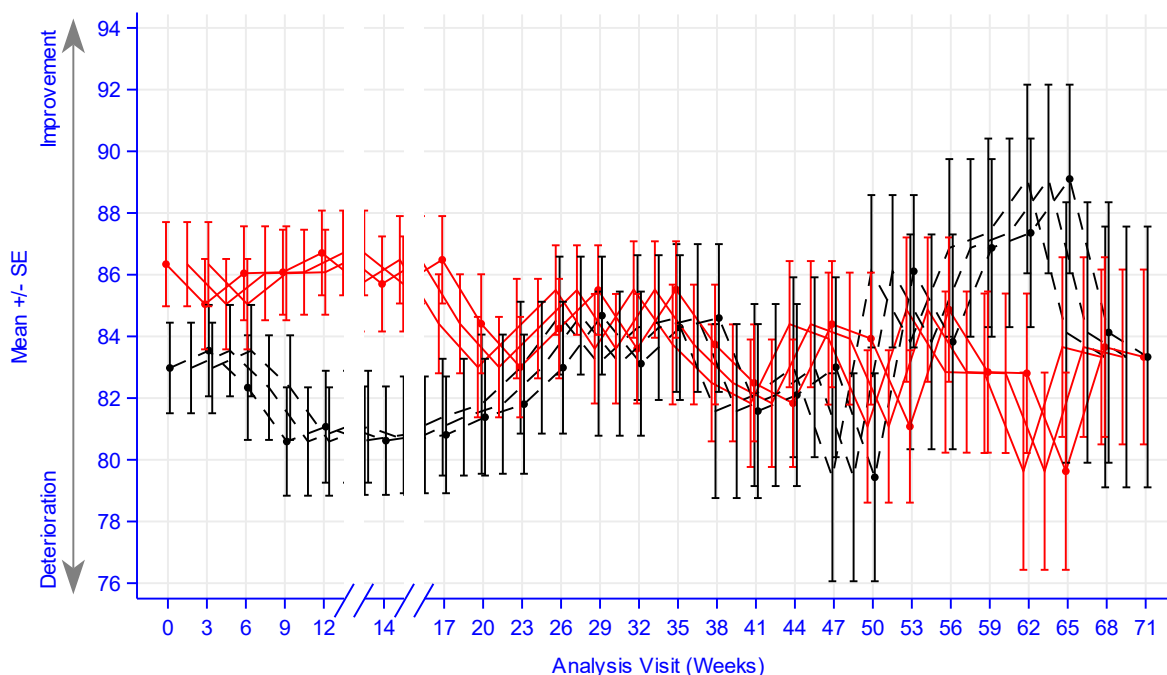
EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 2				
N ^c			192	151
Mittelwert (SD)			84,5 (19,5)	80,1 (21,1)
Median (Q1; Q3)			91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 3				
N ^c			185	162
Mittelwert (SD)			85,0 (19,9)	83,5 (18,9)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	16,7; 100,0
Woche 4				
N ^c			181	157
Mittelwert (SD)			85,5 (19,2)	82,8 (20,4)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 5				
N ^c			175	157
Mittelwert (SD)			86,2 (19,5)	81,3 (20,7)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	16,7; 100,0
Woche 6				
N ^c			172	151
Mittelwert (SD)			86,0 (20,0)	82,3 (20,8)
Median (Q1; Q3)			100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 7				
N ^c			178	159
Mittelwert (SD)			86,7 (19,7)	82,4 (19,9)
Median (Q1; Q3)			100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	33,3; 100,0
Woche 8				
N ^c			173	146
Mittelwert (SD)			85,7 (20,5)	80,0 (21,1)
Median (Q1; Q3)			100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	16,7; 100,0
Woche 9				
N ^c			182	152
Mittelwert (SD)			86,1 (18,6)	80,6 (21,7)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 10				
N ^c			177	141
Mittelwert (SD)			86,6 (19,0)	78,5 (22,0)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	16,7; 100,0

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 11				
N ^c			177	145
Mittelwert (SD)			87,5 (18,9)	81,3 (21,9)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 12				
N ^c			173	140
Mittelwert (SD)			86,7 (18,1)	81,1 (21,5)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 14				
N ^c			169	129
Mittelwert (SD)			85,7 (20,0)	80,6 (20,0)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 17				
N ^c			164	132
Mittelwert (SD)			86,5 (18,1)	80,8 (21,7)
Median (Q1; Q3)			100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 20				
N ^c			155	111
Mittelwert (SD)			84,4 (20,0)	81,4 (19,9)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 23				
N ^c			152	98
Mittelwert (SD)			83,0 (20,1)	81,8 (22,3)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 26				
N ^c			145	96
Mittelwert (SD)			84,3 (19,4)	83,0 (20,9)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	0,0; 100,0
Woche 29				
N ^c			146	87
Mittelwert (SD)			85,5 (17,5)	84,7 (17,8)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	33,3; 100,0
Woche 32				
N ^c			125	77
Mittelwert (SD)			83,6 (19,9)	83,1 (20,5)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 35				
N ^c			122	70
Mittelwert (SD)			85,5 (17,3)	84,3 (19,6)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	16,7; 100,0
Woche 38				
N ^c			124	66
Mittelwert (SD)			83,7 (21,6)	84,6 (19,5)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 41				
N ^c			119	57
Mittelwert (SD)			82,5 (20,7)	81,6 (21,3)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	0,0; 100,0
Woche 44				
N ^c			100	54
Mittelwert (SD)			81,8 (20,7)	82,1 (21,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 47				
N ^c			94	50
Mittelwert (SD)			84,4 (19,8)	83,0 (20,6)
Median (Q1; Q3)			100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	0,0; 100,0
Woche 50				
N ^c			84	47
Mittelwert (SD)			83,9 (19,6)	79,4 (23,1)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	0,0; 100,0
Woche 53				
N ^c			74	42
Mittelwert (SD)			81,1 (21,2)	86,1 (16,0)
Median (Q1; Q3)			83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max			16,7; 100,0	50,0; 100,0
Woche 56				
N ^c			76	34
Mittelwert (SD)			84,9 (20,4)	83,8 (20,3)
Median (Q1; Q3)			100,0 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max			16,7; 100,0	16,7; 100,0
Woche 59				
N ^c			68	33
Mittelwert (SD)			82,8 (21,5)	86,9 (16,5)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			16,7; 100,0	50,0; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 210	Plat+Gem N ^b = 189
Woche 62				
N ^c			63	29
Mittelwert (SD)			82,8 (20,5)	87,4 (16,5)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			16,7; 100,0	50,0; 100,0
Woche 65				
N ^c			54	26
Mittelwert (SD)			79,6 (23,5)	89,1 (15,6)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max			16,7; 100,0	50,0; 100,0
Woche 68				
N ^c			52	21
Mittelwert (SD)			83,7 (21,0)	84,1 (19,3)
Median (Q1; Q3)			91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	33,3; 100,0
Woche 71				
N ^c			49	19
Mittelwert (SD)			83,3 (19,8)	83,3 (18,4)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	50,0; 100,0
a: Datenschnitt: 08. August 2023				
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-geeignet				
c: Anzahl der Beobachtungen zu jedem Zeitpunkt				
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung				



Number of participants

— EV+Pembro

205 185 172 182 173 169 164 155 152 145 146 125 122 124 119 100 94 84 74 76 68 63 54 52 49

- - - Plat+Gem

187 162 151 152 140 129 132 111 98 96 87 77 70 66 57 54 50 47 42 34 33 29 26 21 19

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)

EORTC QLQ-C30 Cognitive Functioning

Abbildung 4G-43: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Kognitive Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Cisplatin ungeeignet

EORTC QLQ-C30 Globaler Gesundheitsstatus

Tabelle 4G-39: Auswertung über den Studienverlauf des Globalen Gesundheitsstatus des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline			
N ^c		160	163
Mittelwert (SD)		60,7 (22,0)	60,6 (25,8)
Median (Q1; Q3)		66,7 (50,0; 75,0)	66,7 (41,7; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 1			
N ^c		133	141
Mittelwert (SD)		60,0 (21,3)	61,4 (23,0)
Median (Q1; Q3)		58,3 (50,0; 75,0)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2			
N ^c		138	137
Mittelwert (SD)		56,4 (22,2)	58,0 (23,0)
Median (Q1; Q3)		50,0 (41,7; 75,0)	66,7 (41,7; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 3			
N ^c		126	138
Mittelwert (SD)		57,4 (22,3)	60,0 (24,0)
Median (Q1; Q3)		54,2 (41,7; 75,0)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 4			
N ^c		133	137
Mittelwert (SD)		61,9 (21,5)	60,5 (23,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 5			
N ^c		125	139
Mittelwert (SD)		63,3 (19,7)	59,4 (21,7)
Median (Q1; Q3)		66,7 (50,0; 75,0)	66,7 (50,0; 75,0)
Min, Max		0,0; 100,0	8,3; 100,0
Woche 6			
N ^c		128	131
Mittelwert (SD)		60,1 (23,3)	60,4 (24,5)
Median (Q1; Q3)		58,3 (50,0; 83,3)	66,7 (41,7; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 7			
N ^c		128	135
Mittelwert (SD)		62,3 (22,8)	60,7 (20,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 8			
N ^c		128	133
Mittelwert (SD)		60,1 (22,7)	58,2 (22,5)
Median (Q1; Q3)		66,7 (45,8; 83,3)	58,3 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 9			
N ^c		125	126
Mittelwert (SD)		60,9 (23,2)	59,5 (22,6)
Median (Q1; Q3)		66,7 (41,7; 83,3)	62,5 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 10			
N ^c		122	130
Mittelwert (SD)		60,0 (23,9)	60,5 (22,4)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 11			
N ^c		119	115
Mittelwert (SD)		64,4 (20,9)	59,6 (21,9)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 12			
N ^c		123	116
Mittelwert (SD)		62,9 (23,2)	59,4 (22,9)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (41,7; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 14			
N ^c		120	110
Mittelwert (SD)		63,5 (21,5)	56,4 (23,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	58,3 (41,7; 75,0)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 17			
N ^c		114	108
Mittelwert (SD)		65,9 (18,3)	60,0 (21,8)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (41,7; 75,0)
Min, Max		16,7; 100,0	16,7; 100,0
Woche 20			
N ^c		106	93
Mittelwert (SD)		64,9 (19,5)	65,2 (20,9)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	16,7; 100,0
Woche 23			
N ^c		100	81
Mittelwert (SD)		64,7 (21,9)	67,9 (22,0)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	25,0; 100,0
Woche 26			
N ^c		96	76
Mittelwert (SD)		65,0 (19,9)	66,6 (22,1)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	8,3; 100,0
Woche 29			
N ^c		95	71
Mittelwert (SD)		62,7 (19,8)	64,9 (25,2)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 32			
N ^c		90	58
Mittelwert (SD)		64,0 (20,3)	65,2 (22,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	0,0; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 35			
N ^c		88	57
Mittelwert (SD)		61,2 (22,0)	66,1 (21,4)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	16,7; 100,0
Woche 38			
N ^c		88	50
Mittelwert (SD)		62,7 (18,0)	61,2 (25,2)
Median (Q1; Q3)		66,7 (50,0; 75,0)	66,7 (50,0; 83,3)
Min, Max		25,0; 100,0	0,0; 100,0
Woche 41			
N ^c		87	47
Mittelwert (SD)		65,0 (19,1)	62,9 (24,3)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	0,0; 100,0
Woche 44			
N ^c		77	44
Mittelwert (SD)		60,7 (19,7)	56,4 (25,4)
Median (Q1; Q3)		66,7 (50,0; 75,0)	62,5 (37,5; 70,8)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 47			
N ^c		72	39
Mittelwert (SD)		65,5 (18,8)	62,2 (25,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (41,7; 83,3)
Min, Max		16,7; 100,0	16,7; 100,0
Woche 50			
N ^c		66	31
Mittelwert (SD)		61,0 (20,6)	65,6 (24,6)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		0,0; 100,0	8,3; 100,0
Woche 53			
N ^c		64	28
Mittelwert (SD)		59,1 (23,1)	62,5 (24,1)
Median (Q1; Q3)		66,7 (41,7; 83,3)	58,3 (50,0; 83,3)
Min, Max		0,0; 100,0	8,3; 100,0
Woche 56			
N ^c		63	29
Mittelwert (SD)		63,2 (19,9)	59,2 (20,2)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (41,7; 75,0)
Min, Max		0,0; 100,0	16,7; 91,7
Woche 59			
N ^c		59	21
Mittelwert (SD)		62,4 (19,6)	62,3 (23,5)
Median (Q1; Q3)		66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max		16,7; 100,0	16,7; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC QLQ-C30 Gesundheitsstatus	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62			
N ^c		54	20
Mittelwert (SD)		61,3 (17,5)	58,3 (19,1)
Median (Q1; Q3)		66,7 (50,0; 75,0)	58,3 (50,0; 70,8)
Min, Max		33,3; 100,0	16,7; 83,3
Woche 65			
N ^c		41	16
Mittelwert (SD)		61,0 (18,6)	60,9 (19,4)
Median (Q1; Q3)		58,3 (50,0; 75,0)	66,7 (45,8; 75,0)
Min, Max		33,3; 100,0	33,3; 91,7
Woche 68			
N ^c		43	13
Mittelwert (SD)		61,4 (19,8)	61,5 (20,8)
Median (Q1; Q3)		66,7 (50,0; 75,0)	66,7 (50,0; 75,0)
Min, Max		25,0; 100,0	16,7; 91,7
Woche 71			
N ^c		39	13
Mittelwert (SD)		61,3 (17,2)	62,2 (19,1)
Median (Q1; Q3)		58,3 (50,0; 75,0)	66,7 (50,0; 75,0)
Min, Max		33,3; 91,7	33,3; 83,3
a: Datenschnitt: 08. August 2023			
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin ungeeignet			
c: Anzahl der Beobachtungen zu jedem Zeitpunkt			
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; QoL: Quality of Life; SD: Standardabweichung			

EORTC QLQ-C30 Funktionsskalen

Tabelle 4G-40: Auswertung über den Studienverlauf der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 (Cisplatin ungeeignet)

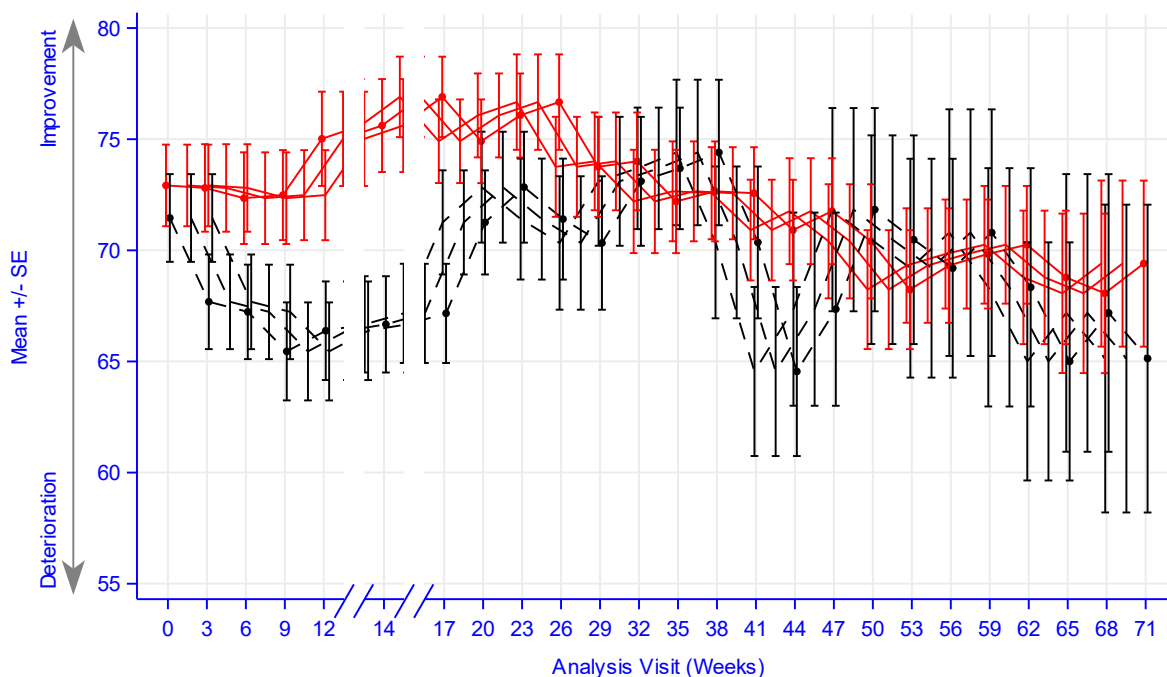
EORTC QLQ-C30 Körperliche Funktion	Globaler	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline			
N ^c		160	163
Mittelwert (SD)		72,9 (23,2)	71,5 (25,2)
Median (Q1; Q3)		80,0 (60,0; 93,3)	80,0 (53,3; 93,3)
Min, Max		20,0; 100,0	0,0; 100,0
Woche 1			
N ^c		133	141
Mittelwert (SD)		72,2 (22,4)	67,5 (25,2)
Median (Q1; Q3)		73,3 (53,3; 93,3)	73,3 (46,7; 86,7)
Min, Max		0,0; 100,0	0,0; 100,0
Woche 2			
N ^c		138	137
Mittelwert (SD)		71,1 (22,5)	66,6 (23,9)
Median (Q1; Q3)		73,3 (60,0; 86,7)	73,3 (53,3; 86,7)
Min, Max		6,7; 100,0	0,0; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 3		
N ^c	126	138
Mittelwert (SD)	72,8 (22,1)	67,7 (25,0)
Median (Q1; Q3)	76,7 (60,0; 93,3)	73,3 (53,3; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	74,5 (21,1)	68,9 (22,2)
Median (Q1; Q3)	80,0 (60,0; 86,7)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	74,2 (21,2)	69,4 (22,0)
Median (Q1; Q3)	80,0 (66,7; 86,7)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	72,3 (23,3)	67,2 (24,3)
Median (Q1; Q3)	80,0 (60,0; 86,7)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	75,2 (21,2)	67,4 (22,6)
Median (Q1; Q3)	80,0 (66,7; 90,0)	73,3 (60,0; 86,7)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	72,9 (22,2)	66,6 (24,5)
Median (Q1; Q3)	80,0 (60,0; 86,7)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	72,5 (22,6)	65,4 (24,7)
Median (Q1; Q3)	80,0 (66,7; 86,7)	70,0 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	74,0 (23,4)	67,9 (23,5)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	76,0 (21,1)	66,3 (24,1)
Median (Q1; Q3)	80,0 (66,7; 93,3)	73,3 (53,3; 80,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	75,0 (23,5)	66,4 (23,9)
Median (Q1; Q3)	80,0 (66,7; 93,3)	70,0 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	75,6 (22,9)	66,7 (22,7)
Median (Q1; Q3)	80,0 (66,7; 93,3)	70,0 (53,3; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	76,9 (19,3)	67,2 (23,2)
Median (Q1; Q3)	80,0 (66,7; 93,3)	66,7 (53,3; 86,7)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	74,9 (19,4)	71,3 (22,6)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (60,0; 86,7)
Min, Max	20,0; 100,0	6,7; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	76,1 (18,9)	72,8 (22,5)
Median (Q1; Q3)	80,0 (66,7; 86,7)	73,3 (60,0; 93,3)
Min, Max	20,0; 100,0	13,3; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	76,7 (21,0)	71,4 (23,7)
Median (Q1; Q3)	80,0 (63,3; 93,3)	80,0 (60,0; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	73,8 (21,9)	70,3 (25,3)
Median (Q1; Q3)	80,0 (60,0; 86,7)	80,0 (60,0; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	74,0 (20,9)	73,1 (22,1)
Median (Q1; Q3)	80,0 (66,7; 86,7)	80,0 (60,0; 86,7)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	72,2 (21,8)	73,7 (20,6)
Median (Q1; Q3)	76,7 (60,0; 86,7)	80,0 (66,7; 86,7)
Min, Max	0,0; 100,0	20,0; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 38		
N ^c	88	50
Mittelwert (SD)	72,7 (21,1)	74,4 (23,1)
Median (Q1; Q3)	73,3 (60,0; 86,7)	80,0 (60,0; 93,3)
Min, Max	13,3; 100,0	6,7; 100,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	72,6 (19,3)	70,4 (23,4)
Median (Q1; Q3)	73,3 (60,0; 86,7)	73,3 (60,0; 86,7)
Min, Max	26,7; 100,0	6,7; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	70,9 (19,9)	64,5 (25,2)
Median (Q1; Q3)	73,3 (60,0; 86,7)	66,7 (46,7; 86,7)
Min, Max	6,7; 100,0	6,7; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	71,8 (20,2)	67,4 (27,1)
Median (Q1; Q3)	73,3 (60,0; 86,7)	73,3 (46,7; 93,3)
Min, Max	13,3; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	70,4 (20,9)	71,8 (25,5)
Median (Q1; Q3)	73,3 (60,0; 80,0)	80,0 (60,0; 93,3)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	68,2 (21,4)	70,5 (24,8)
Median (Q1; Q3)	66,7 (56,7; 83,3)	80,0 (56,7; 90,0)
Min, Max	6,7; 100,0	20,0; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	69,3 (20,4)	69,2 (26,5)
Median (Q1; Q3)	66,7 (53,3; 86,7)	80,0 (53,3; 86,7)
Min, Max	26,7; 100,0	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	69,8 (18,8)	70,8 (25,4)
Median (Q1; Q3)	73,3 (53,3; 86,7)	80,0 (46,7; 93,3)
Min, Max	20,0; 100,0	20,0; 100,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	70,2 (19,5)	68,3 (24,0)
Median (Q1; Q3)	73,3 (60,0; 80,0)	80,0 (46,7; 86,7)
Min, Max	13,3; 100,0	26,7; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 65		
N ^c	41	16
Mittelwert (SD)	68,8 (19,2)	65,0 (21,4)
Median (Q1; Q3)	73,3 (60,0; 80,0)	70,0 (46,7; 83,3)
Min, Max	20,0; 100,0	26,7; 93,3
Woche 68		
N ^c	43	13
Mittelwert (SD)	68,1 (23,5)	67,2 (22,5)
Median (Q1; Q3)	66,7 (60,0; 80,0)	66,7 (53,3; 86,7)
Min, Max	6,7; 100,0	26,7; 93,3
Woche 71		
N ^c	39	13
Mittelwert (SD)	69,4 (23,3)	65,1 (25,0)
Median (Q1; Q3)	73,3 (60,0; 86,7)	73,3 (53,3; 86,7)
Min, Max	13,3; 100,0	13,3; 93,3
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— — — — —	EV+Pembro
160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39	
- - - - -	Plat+Gem
163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13	

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Physical Functioning

Abbildung 4G-44: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Körperliche Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-41: Auswertung über den Studienverlauf der Funktionsskala Rollenfunktion des EORTC QLQ-C30 (Cisplatin ungeeignet)

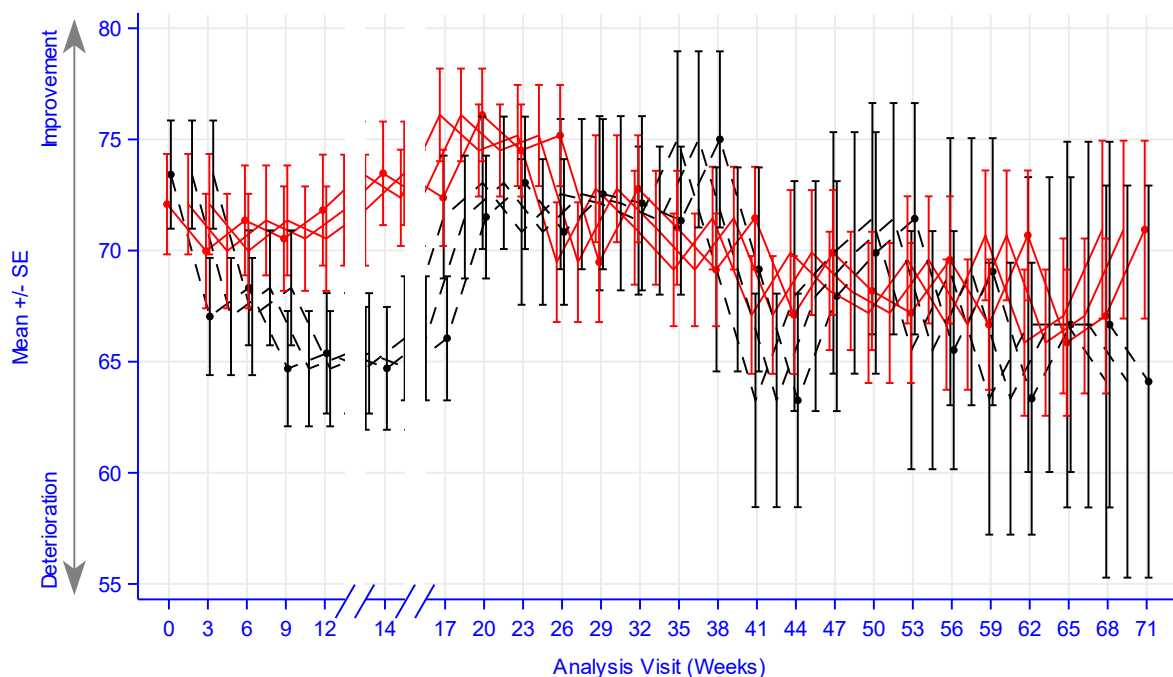
EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	72,1 (28,6)	73,4 (31,1)
Median (Q1; Q3)	66,7 (50,0; 100,0)	83,3 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	71,4 (26,8)	69,9 (29,9)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	67,6 (28,5)	67,0 (29,4)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	70,0 (28,9)	67,0 (31,0)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	71,1 (25,9)	70,1 (28,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	72,4 (26,4)	66,9 (28,9)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	71,4 (28,0)	68,3 (29,6)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	73,3 (25,9)	67,7 (29,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	71,0 (27,7)	65,5 (28,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	70,5 (26,3)	64,7 (29,1)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	73,0 (27,0)	66,8 (28,3)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	73,5 (25,0)	66,7 (28,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 12		
N ^c	123	116
Mittelwert (SD)	71,8 (27,7)	65,4 (29,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	73,5 (25,5)	64,7 (29,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	72,4 (23,1)	66,0 (29,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	76,1 (21,5)	71,5 (26,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	74,5 (20,7)	73,0 (26,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	75,2 (22,3)	70,8 (28,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	69,5 (26,3)	72,5 (28,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	72,8 (22,8)	72,1 (29,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	71,0 (24,0)	71,3 (25,1)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	69,1 (23,8)	75,0 (28,0)
Median (Q1; Q3)	66,7 (66,7; 83,3)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 41		
N ^c	87	47
Mittelwert (SD)	71,5 (21,6)	69,1 (31,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	67,1 (23,3)	63,3 (31,9)
Median (Q1; Q3)	66,7 (66,7; 83,3)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	69,9 (23,8)	67,9 (32,3)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	68,2 (21,6)	69,9 (30,3)
Median (Q1; Q3)	66,7 (66,7; 83,3)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	67,2 (25,2)	71,4 (27,5)
Median (Q1; Q3)	66,7 (50,0; 91,7)	66,7 (58,3; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	69,6 (22,7)	65,5 (28,8)
Median (Q1; Q3)	66,7 (66,7; 83,3)	66,7 (33,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	66,7 (22,5)	69,0 (27,5)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 62		
N ^c	54	20
Mittelwert (SD)	70,7 (21,5)	63,3 (27,4)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 83,3)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	65,9 (21,1)	66,7 (26,5)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 91,7)
Min, Max	33,3; 100,0	16,7; 100,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	67,1 (22,9)	66,7 (29,7)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (66,7; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 71		
N ^c	39	13
Mittelwert (SD)	70,9 (25,0)	64,1 (31,8)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
a: Datenschnitt: 08. August 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

— EV+Pembro	160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39
- - - Plat+Gem	163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Role Functioning

Abbildung 4G-45: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Rollenfunktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

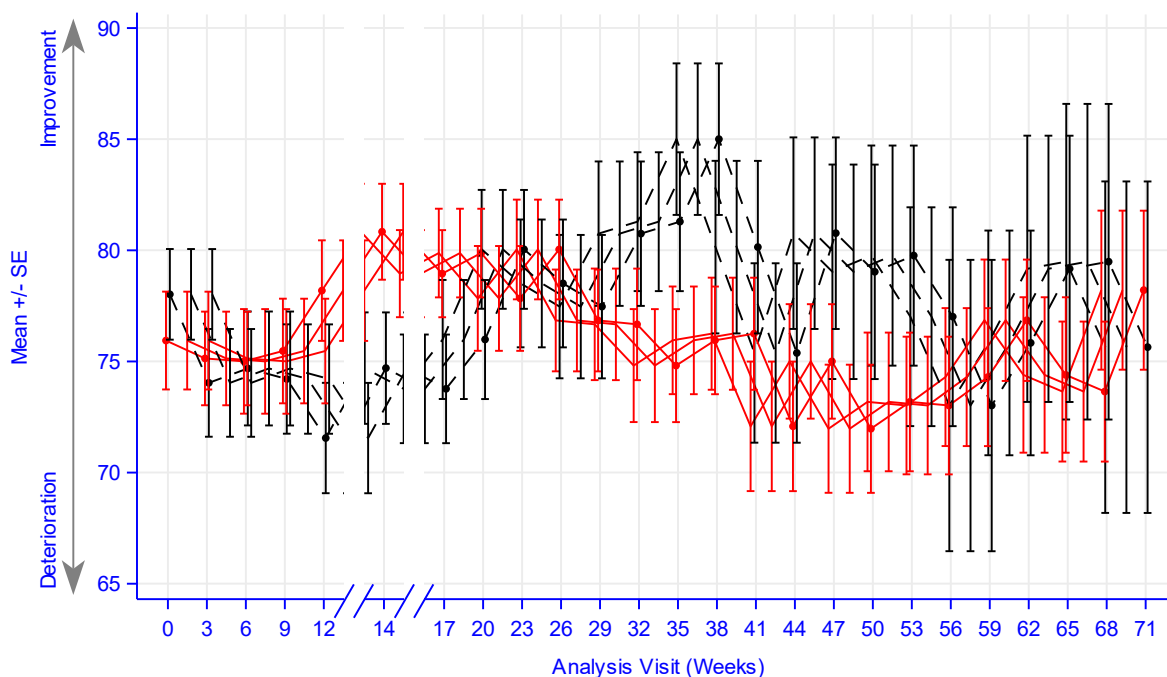
Tabelle 4G-42: Auswertung über den Studienverlauf der Funktionsskala Soziale Funktion des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline		
N ^c	160	163
Mittelwert (SD)	75,9 (27,8)	78,0 (26,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 1		
N ^c	133	141
Mittelwert (SD)	78,7 (23,2)	77,2 (27,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 2		
N ^c	138	137
Mittelwert (SD)	72,2 (27,1)	75,4 (27,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	75,1 (23,6)	74,0 (28,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	76,2 (23,2)	76,9 (26,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	77,2 (22,8)	74,7 (26,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	75,0 (26,6)	74,7 (29,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	77,3 (24,5)	76,2 (26,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	75,3 (25,4)	74,4 (27,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 9		
N ^c	125	126
Mittelwert (SD)	75,5 (26,3)	74,2 (27,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	75,8 (25,8)	76,0 (26,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 11		
N ^c	119	115
Mittelwert (SD)	78,0 (23,9)	73,9 (27,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N ^c	123	116
Mittelwert (SD)	78,2 (25,1)	71,6 (26,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	80,8 (23,6)	74,7 (26,3)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	78,9 (20,9)	73,8 (25,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	79,9 (20,5)	76,0 (25,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	77,8 (23,6)	80,0 (24,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	80,0 (22,0)	78,5 (25,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	76,8 (22,3)	77,5 (27,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 32		
N ^c	90	58
Mittelwert (SD)	76,7 (23,8)	80,7 (24,7)
Median (Q1; Q3)	75,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 35		
N ^c	88	57
Mittelwert (SD)	74,8 (23,8)	81,3 (23,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	75,9 (22,7)	85,0 (24,1)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	76,2 (23,5)	80,1 (26,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	72,1 (25,6)	75,4 (26,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	75,0 (21,8)	80,8 (26,9)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	72,0 (23,4)	79,0 (26,9)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	73,2 (25,0)	79,8 (26,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	73,0 (24,6)	77,0 (26,5)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	74,3 (23,8)	73,0 (30,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	16,7; 100,0	16,7; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62		
N ^c	54	20
Mittelwert (SD)	76,9 (20,1)	75,8 (22,6)
Median (Q1; Q3)	75,0 (66,7; 100,0)	83,3 (58,3; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	74,4 (22,4)	79,2 (24,0)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	73,6 (20,6)	79,5 (25,6)
Median (Q1; Q3)	66,7 (66,7; 83,3)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 71		
N ^c	39	13
Mittelwert (SD)	78,2 (22,3)	75,6 (26,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

—	EV+Pembro																							
160	126	128	125	123	120	114	106	100	96	95	90	88	88	87	77	72	66	64	63	59	54	41	43	39
---	Plat+Gem																							
163	138	131	126	116	110	108	93	81	76	71	58	57	50	47	44	39	31	28	29	21	20	16	13	13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Social Functioning

Abbildung 4G-46: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Soziale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-43: Auswertung über den Studienverlauf der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC QLQ-C30 Funktion	Emotionale Funktion	Studie: KEYNOTE A39 ^a	
		EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline			
N ^c		160	163
Mittelwert (SD)		75,0 (21,3)	75,8 (22,1)
Median (Q1; Q3)		75,0 (66,7; 91,7)	83,3 (66,7; 91,7)
Min, Max		0,0; 100,0	8,3; 100,0
Woche 1			
N ^c		133	141
Mittelwert (SD)		78,1 (21,8)	77,7 (21,4)
Median (Q1; Q3)		83,3 (66,7; 100,0)	83,3 (66,7; 91,7)
Min, Max		0,0; 100,0	8,3; 100,0

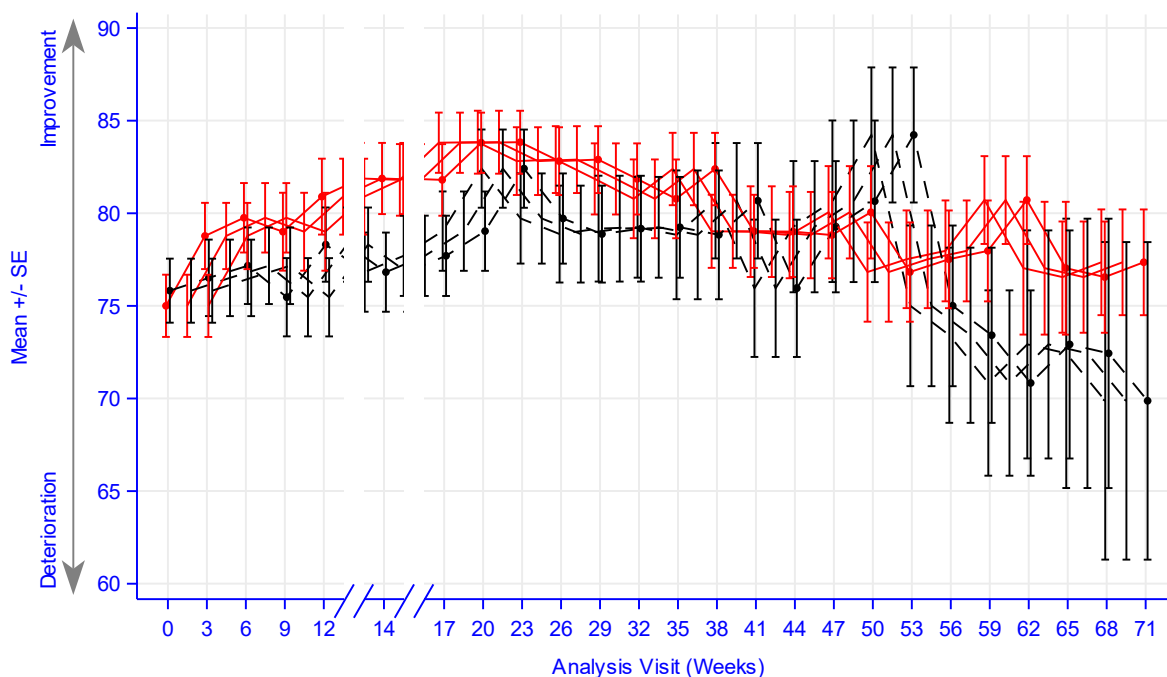
Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2		
N ^c	138	137
Mittelwert (SD)	75,8 (22,6)	77,0 (22,5)
Median (Q1; Q3)	75,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	126	138
Mittelwert (SD)	78,8 (20,1)	76,5 (24,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 4		
N ^c	133	137
Mittelwert (SD)	80,4 (21,7)	78,3 (21,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 5		
N ^c	125	139
Mittelwert (SD)	81,7 (18,8)	76,2 (21,3)
Median (Q1; Q3)	91,7 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	33,3; 100,0	8,3; 100,0
Woche 6		
N ^c	128	131
Mittelwert (SD)	79,8 (21,2)	77,2 (23,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 7		
N ^c	128	135
Mittelwert (SD)	80,3 (21,4)	77,2 (21,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	8,3; 100,0	8,3; 100,0
Woche 8		
N ^c	128	133
Mittelwert (SD)	80,4 (21,7)	76,1 (22,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	125	126
Mittelwert (SD)	79,0 (23,5)	75,5 (23,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 10		
N ^c	122	130
Mittelwert (SD)	81,4 (21,5)	77,4 (22,7)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	8,3; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 11		
N ^c	119	115
Mittelwert (SD)	82,6 (20,8)	77,2 (23,4)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 12		
N ^c	123	116
Mittelwert (SD)	80,9 (22,7)	78,3 (21,6)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 14		
N ^c	120	110
Mittelwert (SD)	81,9 (21,1)	76,8 (22,4)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 17		
N ^c	114	108
Mittelwert (SD)	81,8 (20,6)	77,7 (22,5)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	8,3; 100,0
Woche 20		
N ^c	106	93
Mittelwert (SD)	83,8 (16,7)	79,0 (20,7)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	16,7; 100,0
Woche 23		
N ^c	100	81
Mittelwert (SD)	83,8 (17,0)	82,4 (19,0)
Median (Q1; Q3)	87,5 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	25,0; 100,0
Woche 26		
N ^c	96	76
Mittelwert (SD)	82,8 (17,9)	79,7 (21,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 29		
N ^c	95	71
Mittelwert (SD)	82,9 (17,6)	78,9 (22,0)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 32		
N ^c	90	58
Mittelwert (SD)	81,9 (18,2)	79,2 (21,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	16,7; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 35		
N ^c	88	57
Mittelwert (SD)	80,8 (20,0)	79,2 (20,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 38		
N ^c	88	50
Mittelwert (SD)	82,4 (18,3)	78,8 (24,6)
Median (Q1; Q3)	83,3 (70,8; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 41		
N ^c	87	47
Mittelwert (SD)	79,0 (18,4)	80,7 (21,4)
Median (Q1; Q3)	83,3 (66,7; 91,7)	91,7 (66,7; 100,0)
Min, Max	0,0; 100,0	25,0; 100,0
Woche 44		
N ^c	77	44
Mittelwert (SD)	79,0 (21,5)	75,9 (24,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (62,5; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 47		
N ^c	72	39
Mittelwert (SD)	78,8 (19,8)	79,3 (22,1)
Median (Q1; Q3)	79,2 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	25,0; 100,0
Woche 50		
N ^c	66	31
Mittelwert (SD)	80,1 (20,2)	80,6 (24,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	25,0; 100,0	16,7; 100,0
Woche 53		
N ^c	64	28
Mittelwert (SD)	76,8 (21,4)	84,2 (19,3)
Median (Q1; Q3)	75,0 (66,7; 100,0)	91,7 (70,8; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 56		
N ^c	63	29
Mittelwert (SD)	77,5 (20,9)	75,0 (23,4)
Median (Q1; Q3)	83,3 (66,7; 91,7)	83,3 (66,7; 91,7)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 59		
N ^c	59	21
Mittelwert (SD)	78,0 (20,9)	73,4 (21,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (58,3; 91,7)
Min, Max	25,0; 100,0	25,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE A39 ^a	
	EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62		
N ^c	54	20
Mittelwert (SD)	80,7 (17,4)	70,8 (22,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (54,2; 91,7)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 65		
N ^c	41	16
Mittelwert (SD)	77,0 (23,0)	72,9 (24,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	79,2 (50,0; 91,7)
Min, Max	25,0; 100,0	33,3; 100,0
Woche 68		
N ^c	43	13
Mittelwert (SD)	76,6 (19,7)	72,4 (26,2)
Median (Q1; Q3)	83,3 (66,7; 91,7)	75,0 (50,0; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 71		
N ^c	39	13
Mittelwert (SD)	77,4 (17,8)	69,9 (30,9)
Median (Q1; Q3)	75,0 (66,7; 100,0)	75,0 (50,0; 100,0)
Min, Max	33,3; 100,0	8,3; 100,0
a: Datenschnitt: 08. August 2023		
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet		
c: Anzahl der Beobachtungen zu jedem Zeitpunkt		
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		



Number of participants

—	EV+Pembro
160 126 128 125 123 120 114 106 100 96 95 90 88 88 87 77 72 66 64 63 59 54 41 43 39	
---	Plat+Gem
163 138 131 126 116 110 108 93 81 76 71 58 57 50 47 44 39 31 28 29 21 20 16 13 13	

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
EORTC QLQ-C30 Emotional Functioning

Abbildung 4G-47: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Emotionale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Tabelle 4G-44: Auswertung über den Studienverlauf der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 (Cisplatin ungeeignet)

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Baseline				
N ^c			160	163
Mittelwert (SD)			81,8 (19,5)	85,0 (19,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (83,3; 100,0)
Min, Max			16,7; 100,0	16,7; 100,0
Woche 1				
N ^c			133	141
Mittelwert (SD)			83,3 (20,3)	84,5 (19,9)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0

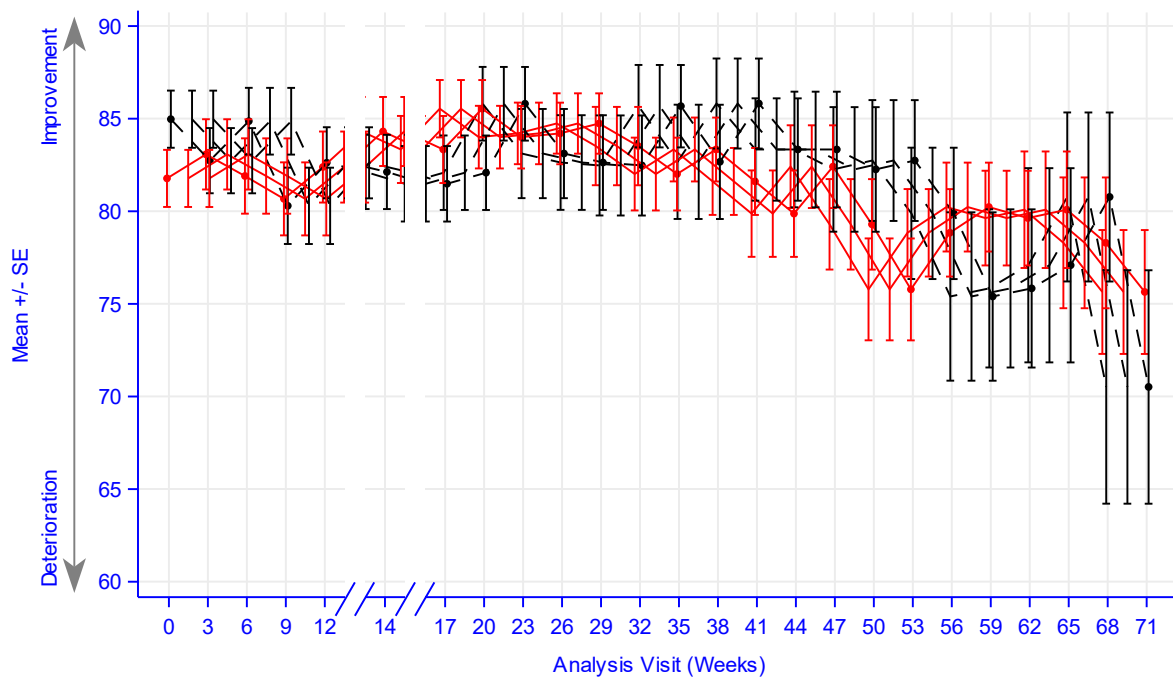
EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 2				
N ^c			138	137
Mittelwert (SD)			80,8 (22,0)	83,5 (21,2)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 3				
N ^c			126	138
Mittelwert (SD)			83,1 (21,3)	82,7 (20,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 4				
N ^c			133	137
Mittelwert (SD)			83,3 (20,4)	85,2 (18,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 5				
N ^c			125	139
Mittelwert (SD)			84,4 (21,6)	83,8 (20,9)
Median (Q1; Q3)			100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 6				
N ^c			128	131
Mittelwert (SD)			81,9 (23,0)	84,9 (20,6)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 7				
N ^c			128	135
Mittelwert (SD)			81,6 (20,7)	82,6 (21,2)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 8				
N ^c			128	133
Mittelwert (SD)			80,7 (22,8)	80,7 (23,5)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 9				
N ^c			125	126
Mittelwert (SD)			80,7 (22,0)	80,3 (23,1)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 10				
N ^c			122	130
Mittelwert (SD)			81,7 (22,9)	82,2 (22,8)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 11				
N ^c			119	115
Mittelwert (SD)			81,4 (23,6)	81,0 (22,4)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 12				
N ^c			123	116
Mittelwert (SD)			82,4 (21,3)	82,6 (20,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 14				
N ^c			120	110
Mittelwert (SD)			84,3 (20,4)	82,1 (21,0)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	0,0; 100,0
Woche 17				
N ^c			114	108
Mittelwert (SD)			83,3 (19,3)	81,5 (21,2)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	0,0; 100,0
Woche 20				
N ^c			106	93
Mittelwert (SD)			85,5 (15,9)	82,1 (19,4)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	33,3; 100,0
Woche 23				
N ^c			100	81
Mittelwert (SD)			84,0 (16,9)	85,8 (17,9)
Median (Q1; Q3)			83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max			16,7; 100,0	33,3; 100,0
Woche 26				
N ^c			96	76
Mittelwert (SD)			84,2 (16,3)	83,1 (21,0)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	16,7; 100,0
Woche 29				
N ^c			95	71
Mittelwert (SD)			84,7 (15,9)	82,6 (21,5)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	0,0; 100,0
Woche 32				
N ^c			90	58
Mittelwert (SD)			83,5 (20,1)	82,5 (20,6)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	16,7; 100,0

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 35				
N ^c			88	57
Mittelwert (SD)			82,0 (18,4)	85,7 (16,8)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	50,0; 100,0
Woche 38				
N ^c			88	50
Mittelwert (SD)			83,3 (16,2)	82,7 (21,8)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			50,0; 100,0	0,0; 100,0
Woche 41				
N ^c			87	47
Mittelwert (SD)			81,6 (16,9)	85,8 (16,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	50,0; 100,0
Woche 44				
N ^c			77	44
Mittelwert (SD)			79,9 (20,5)	83,3 (18,3)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	50,0; 100,0
Woche 47				
N ^c			72	39
Mittelwert (SD)			82,4 (18,9)	83,3 (19,5)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	33,3; 100,0
Woche 50				
N ^c			66	31
Mittelwert (SD)			79,3 (19,8)	82,3 (18,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	50,0; 100,0
Woche 53				
N ^c			64	28
Mittelwert (SD)			75,8 (22,0)	82,7 (17,3)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			0,0; 100,0	50,0; 100,0
Woche 56				
N ^c			63	29
Mittelwert (SD)			78,8 (18,7)	79,9 (19,1)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	33,3; 100,0
Woche 59				
N ^c			59	21
Mittelwert (SD)			80,2 (18,4)	75,4 (20,8)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			33,3; 100,0	33,3; 100,0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

EORTC Funktion	QLQ-C30	Kognitive	Studie: KEYNOTE A39 ^a	
			EV+Pembro N ^b = 166	Plat+Gem N ^b = 166
Woche 62				
N ^c			54	20
Mittelwert (SD)			79,6 (18,8)	75,8 (19,1)
Median (Q1; Q3)			83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max			33,3; 100,0	50,0; 100,0
Woche 65				
N ^c			41	16
Mittelwert (SD)			80,1 (20,1)	77,1 (21,0)
Median (Q1; Q3)			83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max			16,7; 100,0	33,3; 100,0
Woche 68				
N ^c			43	13
Mittelwert (SD)			78,3 (23,2)	80,8 (16,4)
Median (Q1; Q3)			83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max			0,0; 100,0	66,7; 100,0
Woche 71				
N ^c			39	13
Mittelwert (SD)			75,6 (20,9)	70,5 (22,7)
Median (Q1; Q3)			83,3 (66,7; 100,0)	66,7 (66,7; 83,3)
Min, Max			33,3; 100,0	16,7; 100,0
a: Datenschnitt: 08. August 2023				
b: Anzahl der Patient:innen: Full-Analysis-Set Population, Cisplatin-ungeeignet				
c: Anzahl der Beobachtungen zu jedem Zeitpunkt				
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; Max: Maximum; Min: Minimum; PRO: Patient Reported Outcome; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung				



Number of participants

—	EV+Pembro																							
160	126	128	125	123	120	114	106	100	96	95	90	88	88	87	77	72	66	64	63	59	54	41	43	39
- - -	Plat+Gem																							
163	138	131	126	116	110	108	93	81	76	71	58	57	50	47	44	39	31	28	29	21	20	16	13	13

Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 EORTC QLQ-C30 Cognitive Functioning

Abbildung 4G-48: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Kognitive Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin ungeeignet)

Anhang 4-G6: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest (p < 0,05)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Kaplan-Meier-Kurven der Subgruppenanalysen, für die ein signifikanter Interaktionstest (p < 0,05) vorliegt, dargestellt.

Cisplatin geeignet

Morbidität

Zeit bis zur ersten Folgetherapie oder Tod

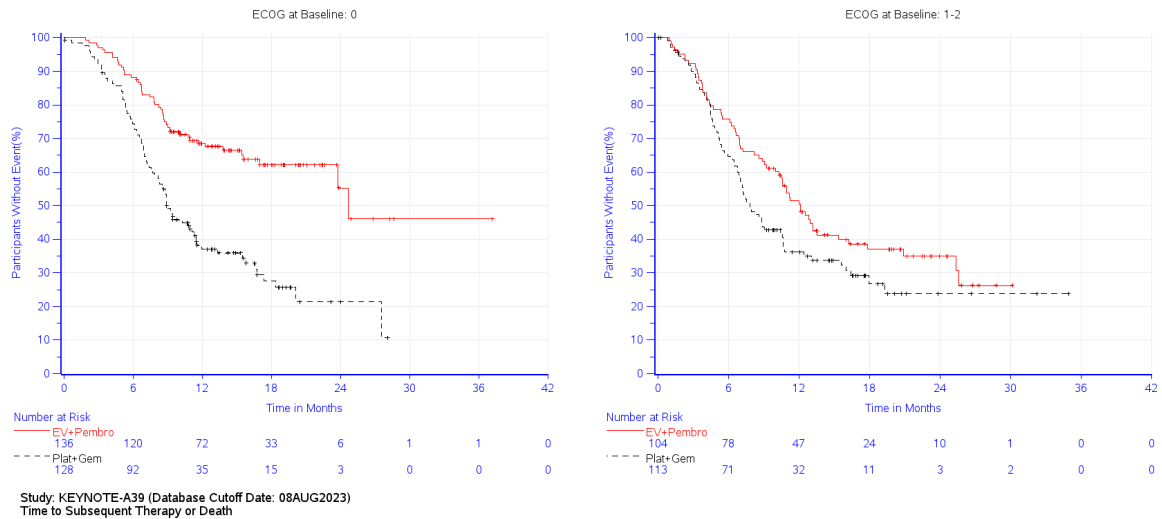
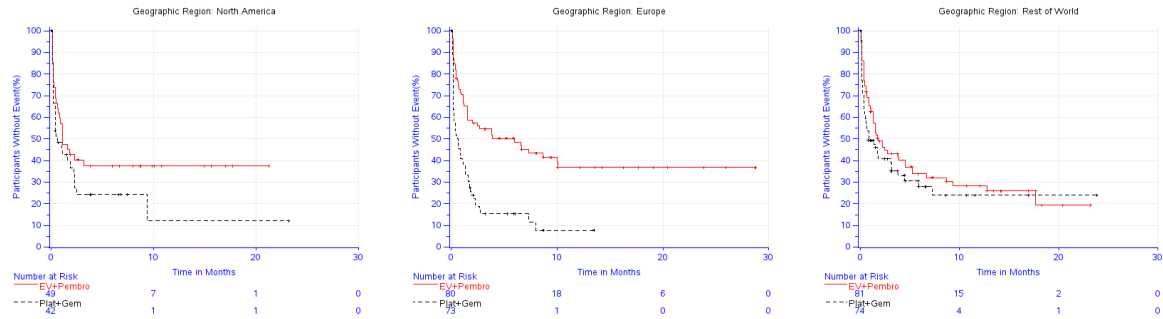


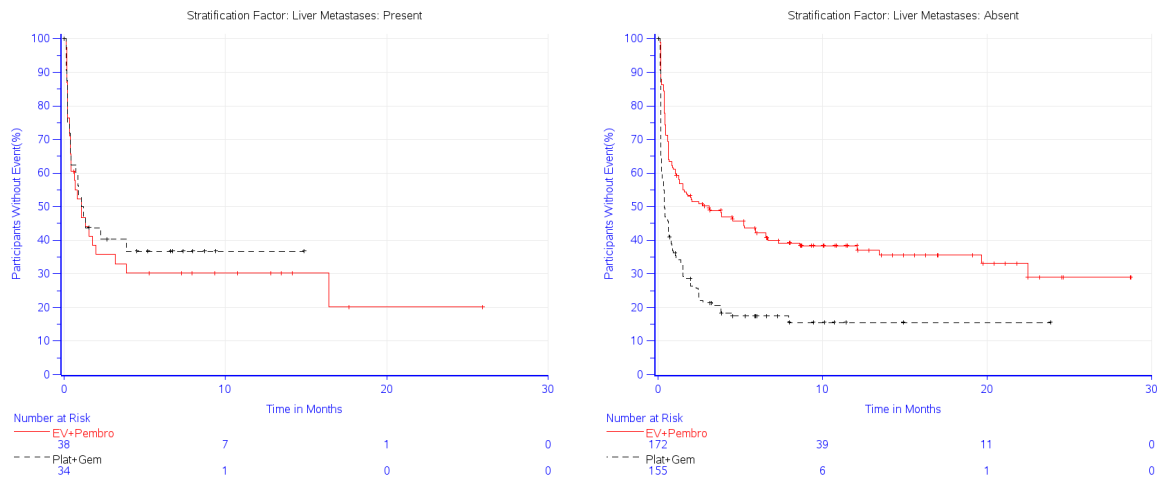
Abbildung 4G-49: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus für den Endpunkt Zeit bis zur ersten Folgetherapie oder Tod der Studie KEYNOTE A39 (Cisplatin geeignet)

Krankheitssymptomatik und Gesundheitszustand



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Time to Deterioration for EORTC QLQ-C30 Constipation (10 points)

Abbildung 4G-50: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Time to Deterioration for EORTC QLQ-C30 Nausea and Vomiting (10 points)

Abbildung 4G-51: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

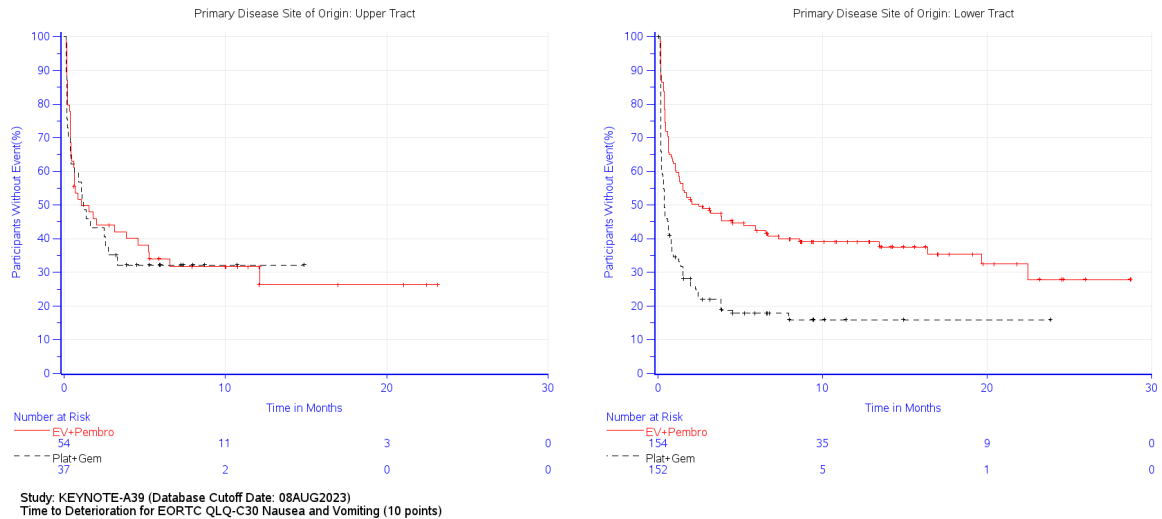


Abbildung 4G-52: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für die Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

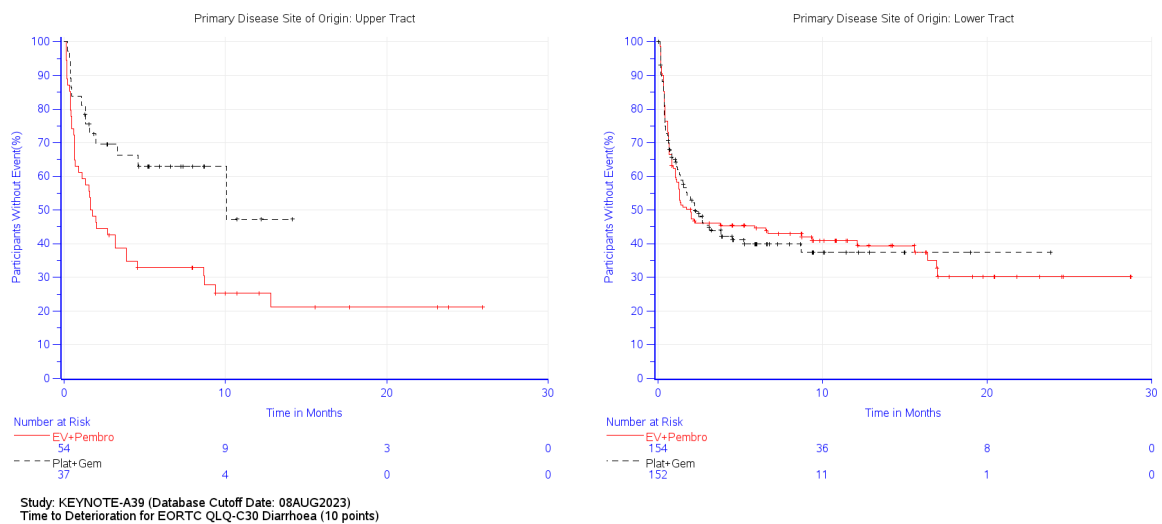


Abbildung 4G-53: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für die Symptomskala Diarrhö des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

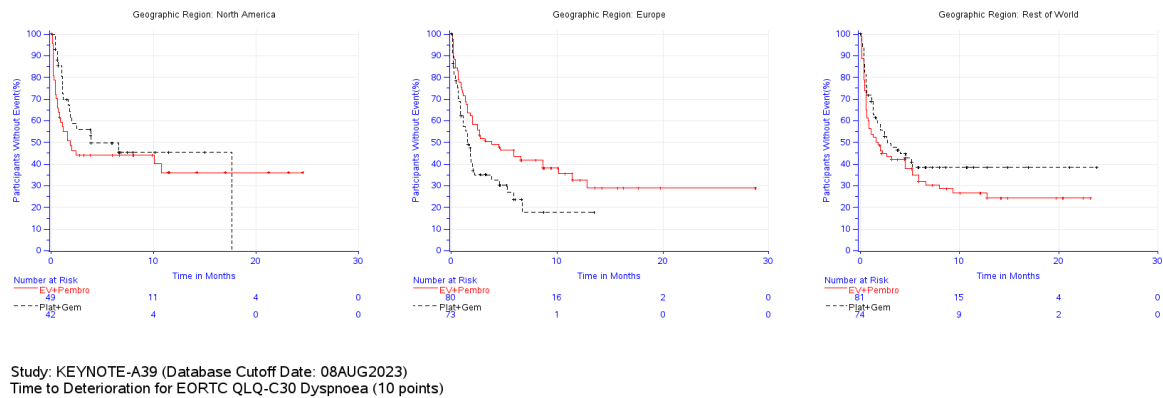


Abbildung 4G-54: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

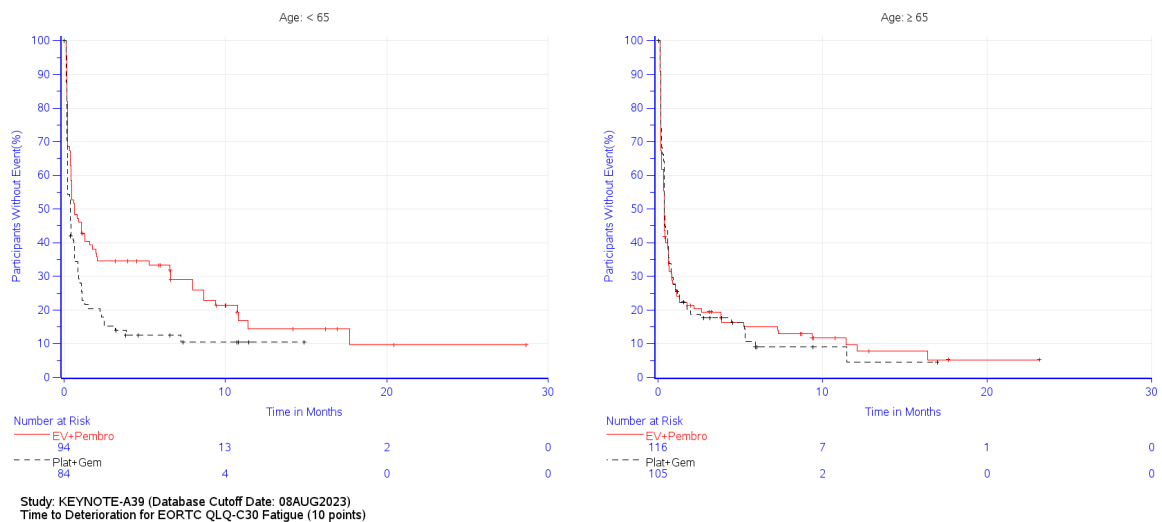


Abbildung 4G-55: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

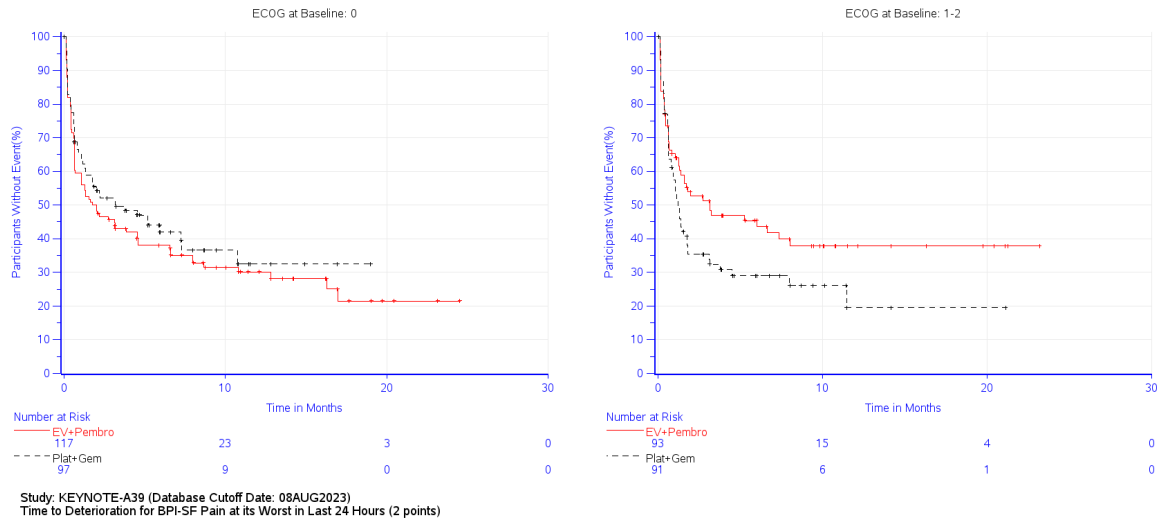


Abbildung 4G-56: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus für die Symptomskala Stärkster Schmerz der vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39 (Cisplatin geeignet)

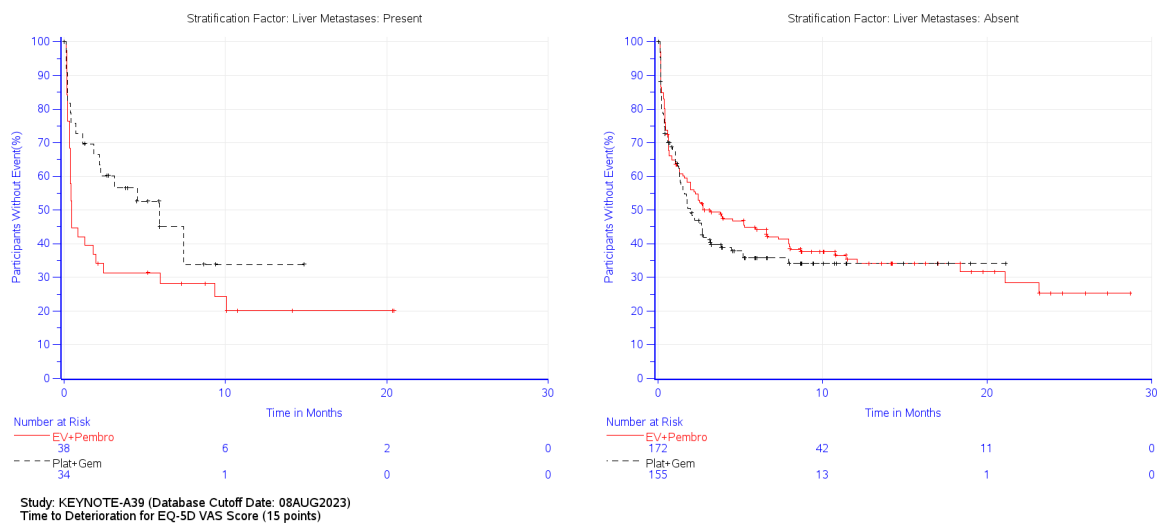


Abbildung 4G-57: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen der EQ-5D VAS der Studie KEYNOTE A39 (Cisplatin geeignet)

Gesundheitsbezogene Lebensqualität

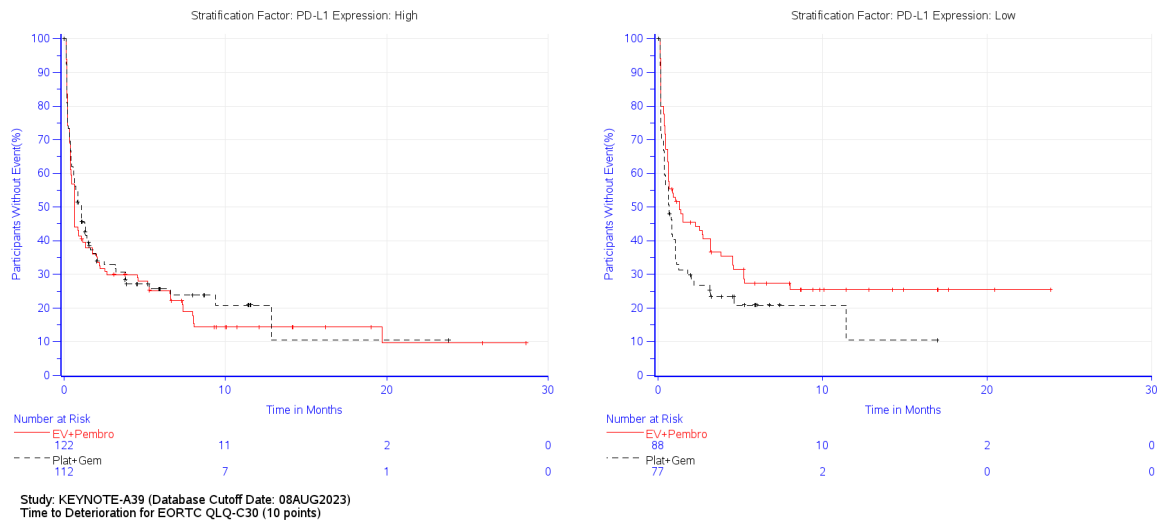


Abbildung 4G-58: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den Globalen Gesundheitsstatus des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

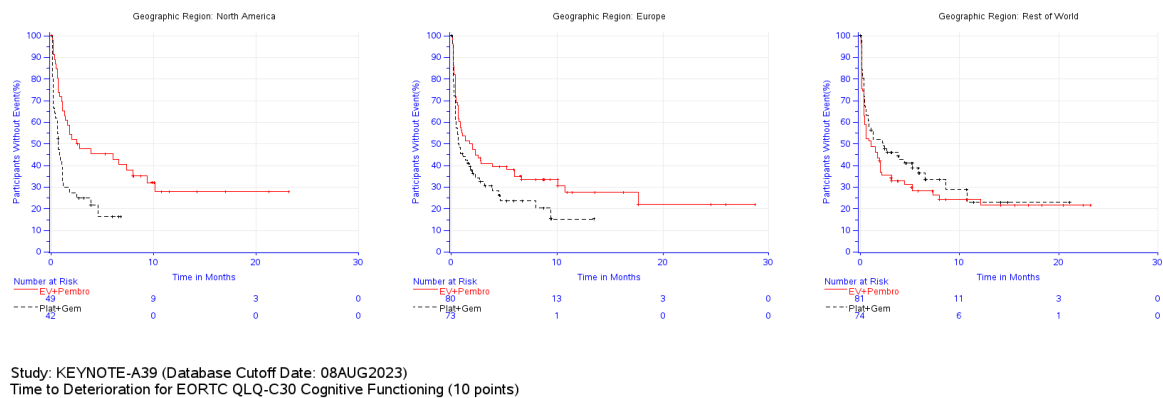


Abbildung 4G-59: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für die Funktionsskala Kognitive Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

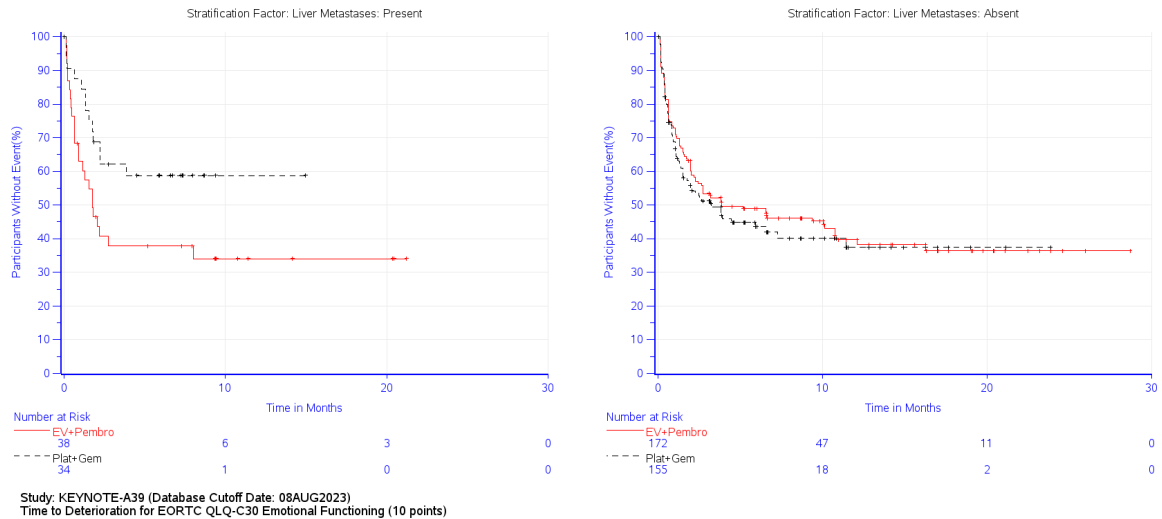


Abbildung 4G-60: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die Funktionsskala Emotionale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

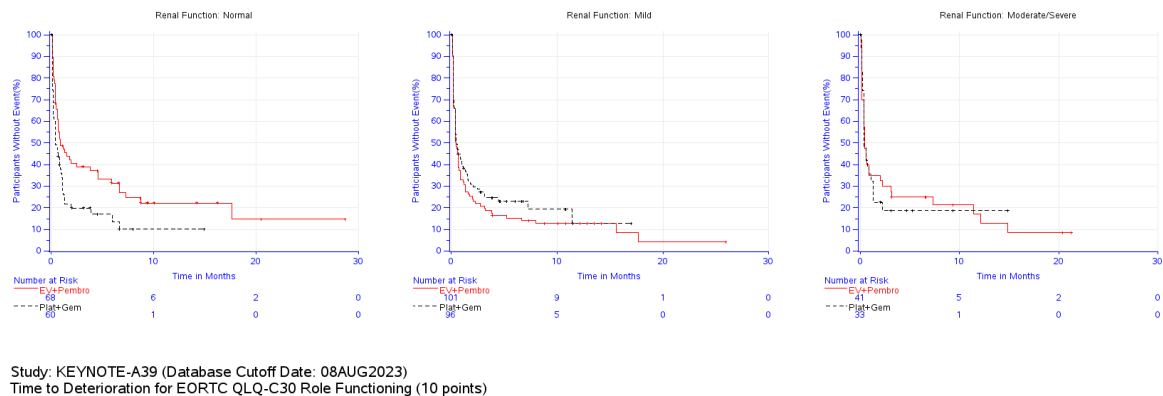


Abbildung 4G-61: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die Funktionsskala Rollenfunktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

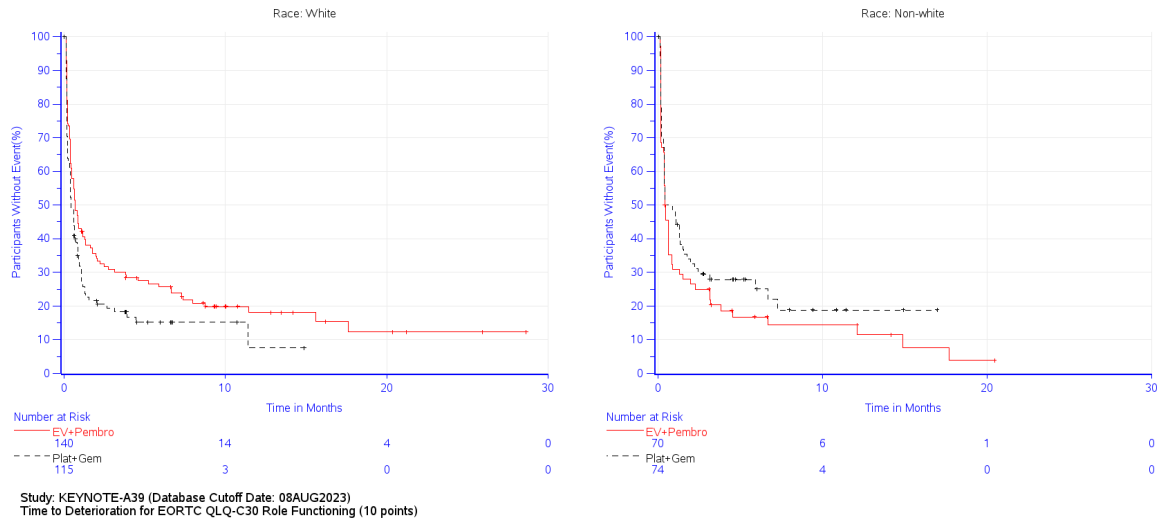


Abbildung 4G-62: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die Funktionsskala Rollenfunktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

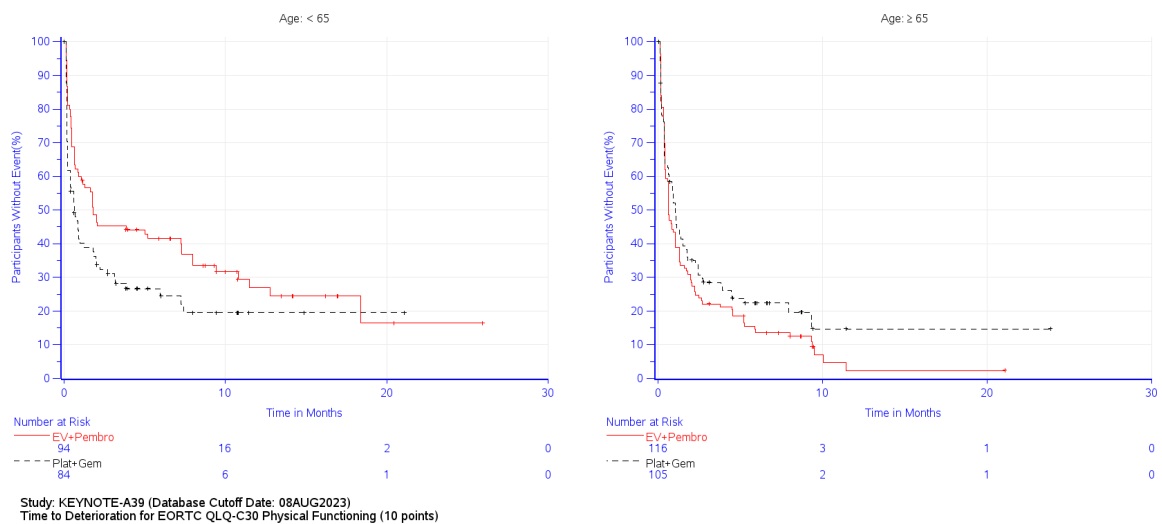


Abbildung 4G-63: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die Funktionsskala Körperliche Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

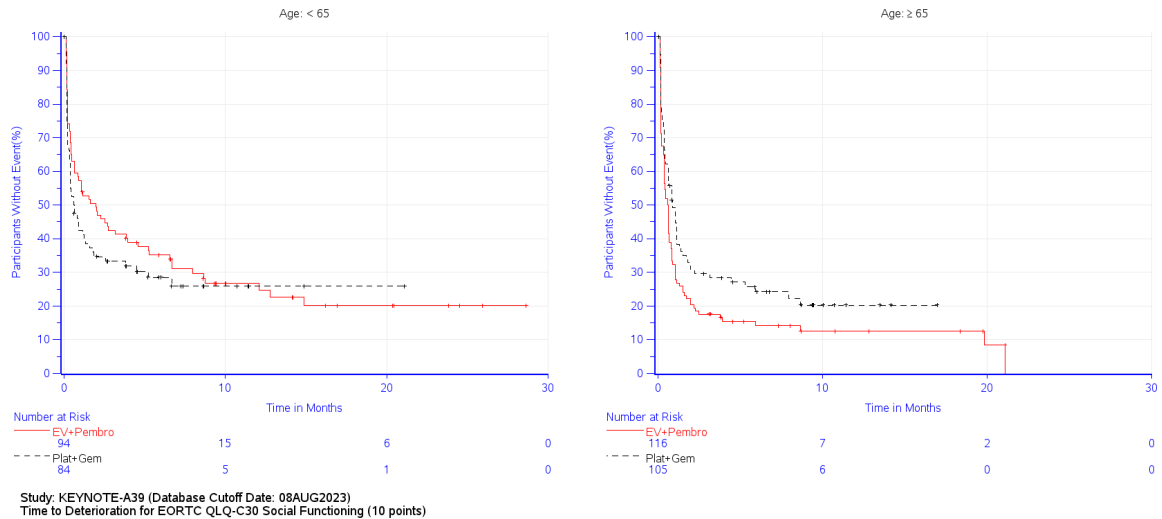


Abbildung 4G-64: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Nebenwirkungen

Unerwünschte Ereignisse gesamt

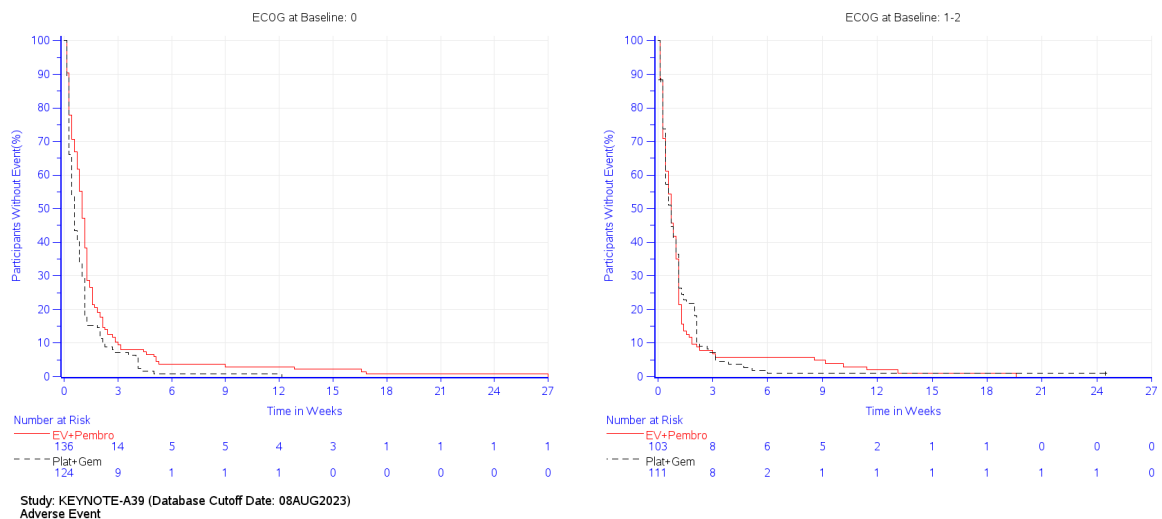


Abbildung 4G-65: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für Unerwünschte Ereignisse gesamt der Studie KEYNOTE A39 (Cisplatin geeignet)

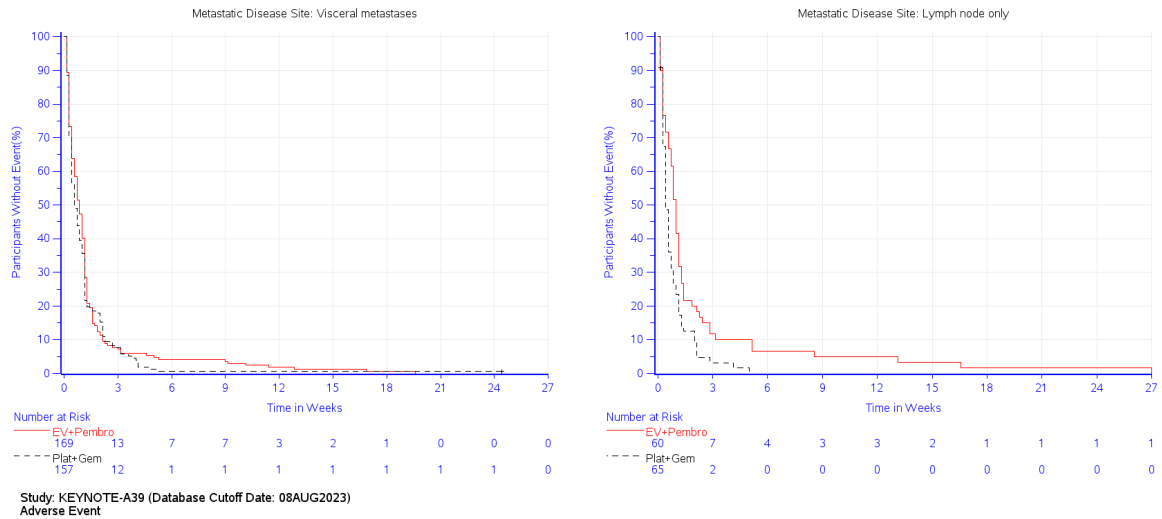


Abbildung 4G-66: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für Unerwünschte Ereignisse gesamt der Studie KEYNOTE A39 (Cisplatin geeignet)

Schwerwiegende unerwünschte Ereignisse

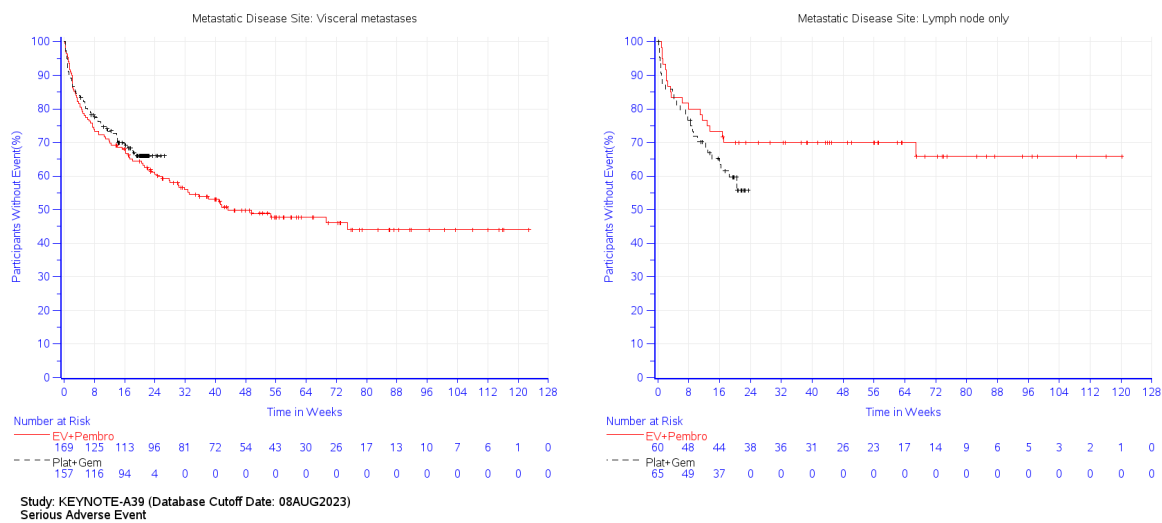


Abbildung 4G-67: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für Schwerwiegende unerwünschte Ereignisse der Studie KEYNOTE A39 (Cisplatin geeignet)

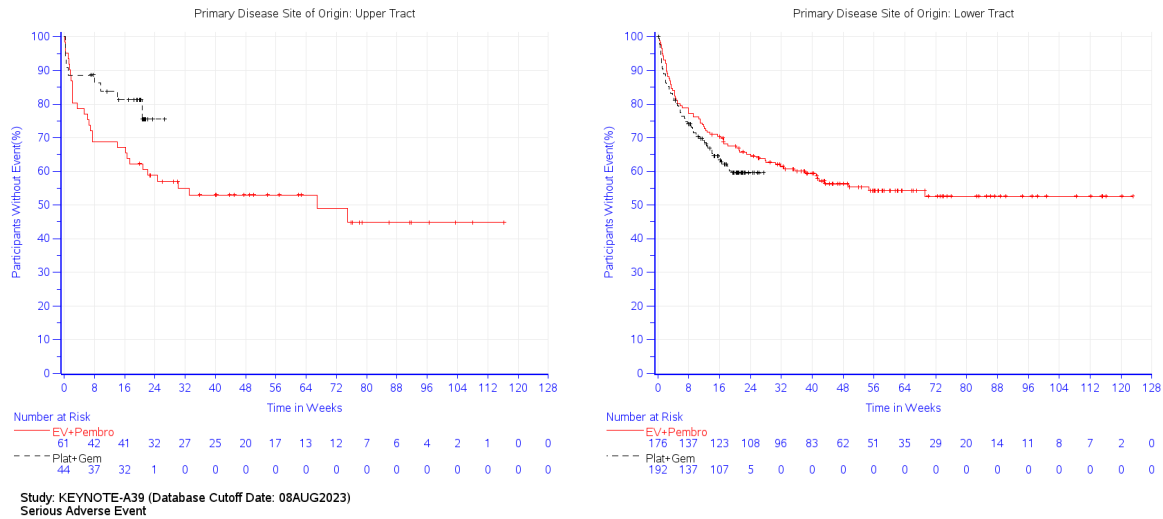


Abbildung 4G-68: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für Schwerwiegende unerwünschte Ereignisse der Studie KEYNOTE A39 (Cisplatin geeignet)

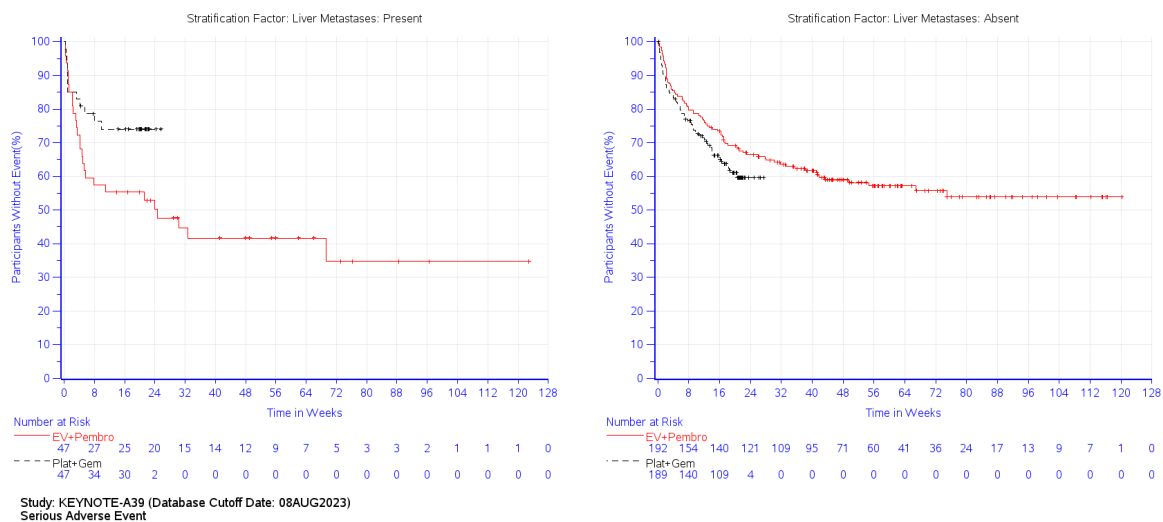
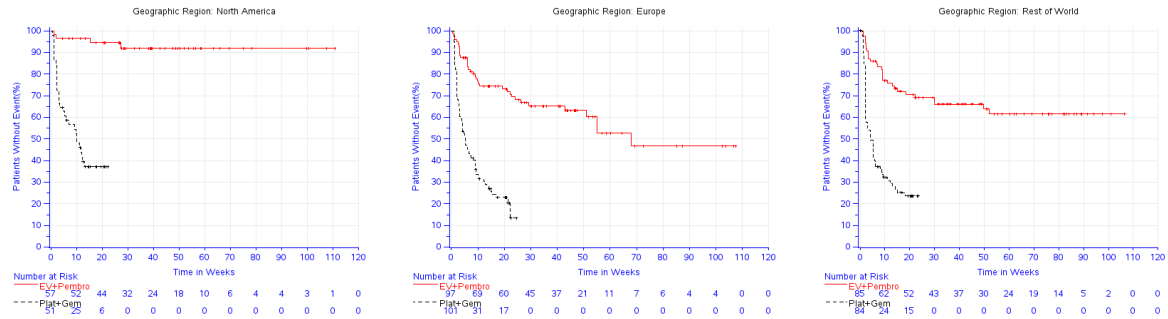


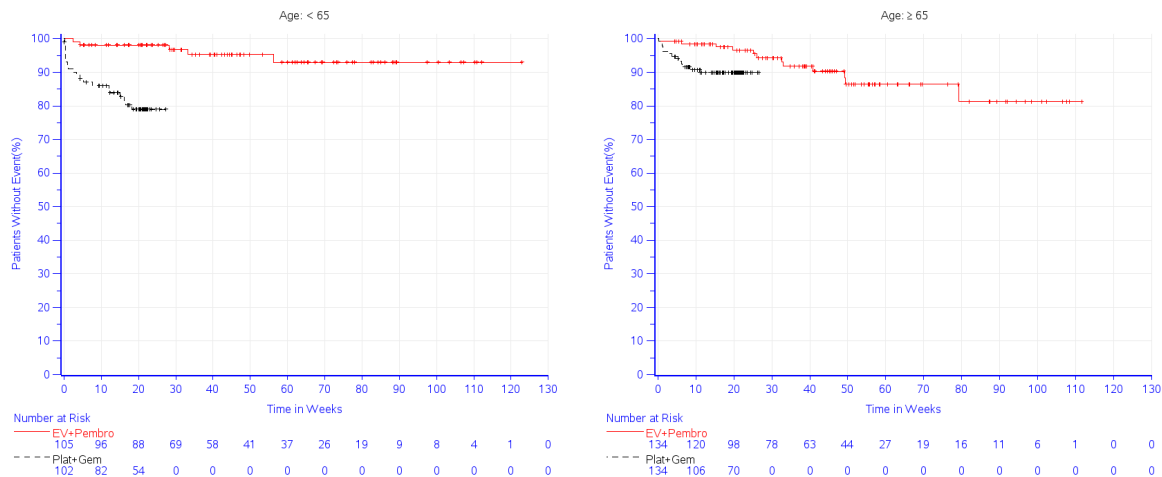
Abbildung 4G-69: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für Schwerwiegende unerwünschte Ereignisse der Studie KEYNOTE A39 (Cisplatin geeignet)

Unerwünschte Ereignisse gesamt (SOC und PT)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Adverse Event - System Organ Class: Blood and lymphatic system disorders

Abbildung 4G-70: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für die SOC Erkrankungen des Blutes und des Lymphsystems für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
 Adverse Event - System Organ Class: Ear and labyrinth disorders

Abbildung 4G-71: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die SOC Erkrankungen des Ohrs und des Labyrinths für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

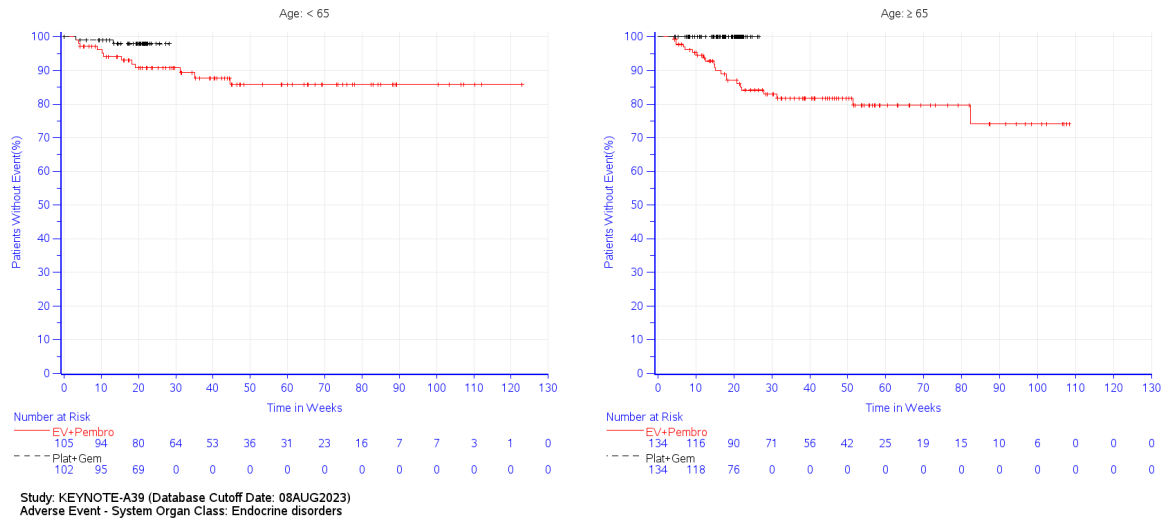


Abbildung 4G-72: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die SOC Endokrine Erkrankungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

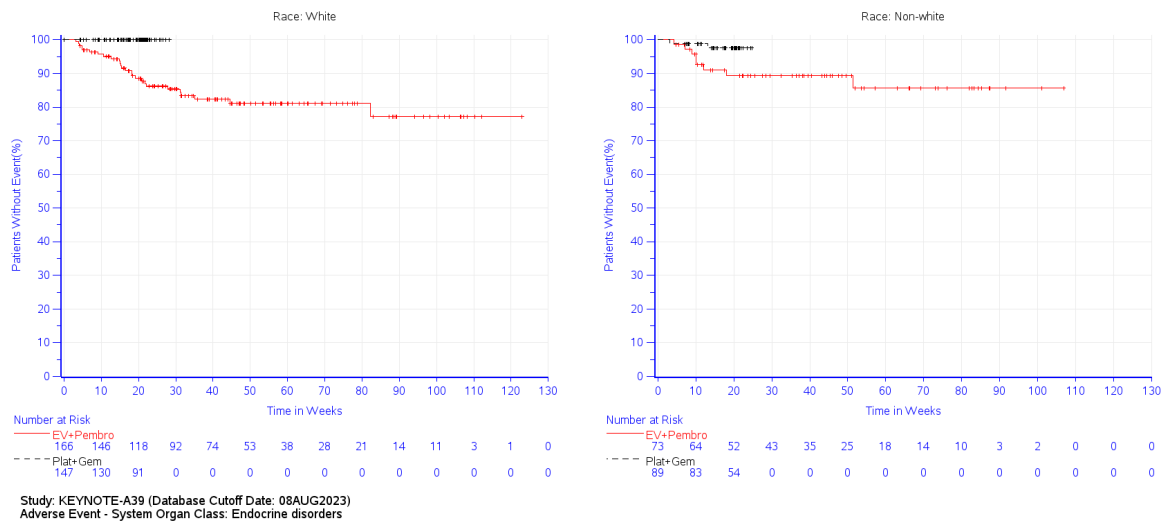


Abbildung 4G-73: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Endokrine Erkrankungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

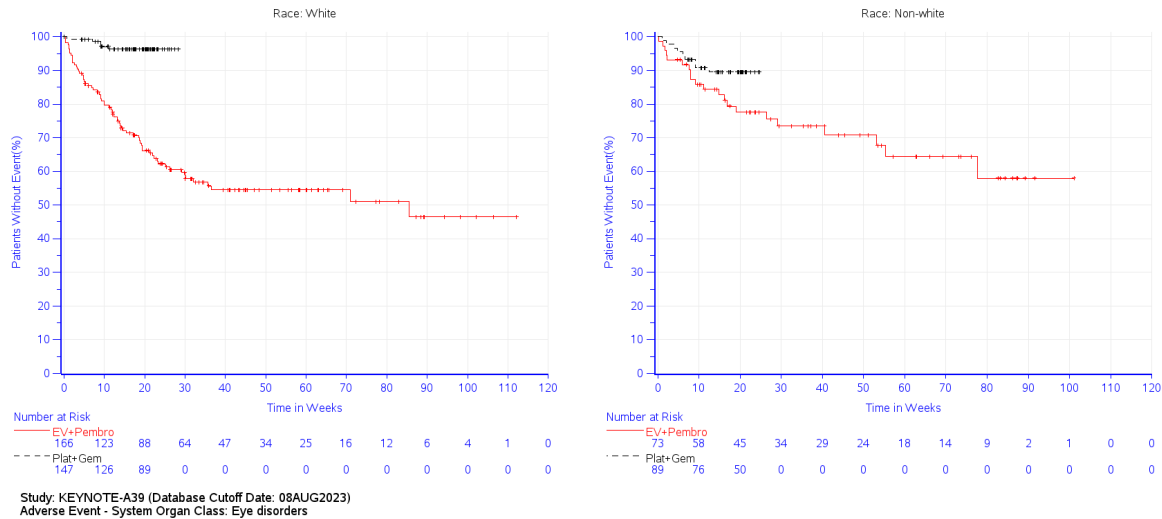


Abbildung 4G-74: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Augenerkrankungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

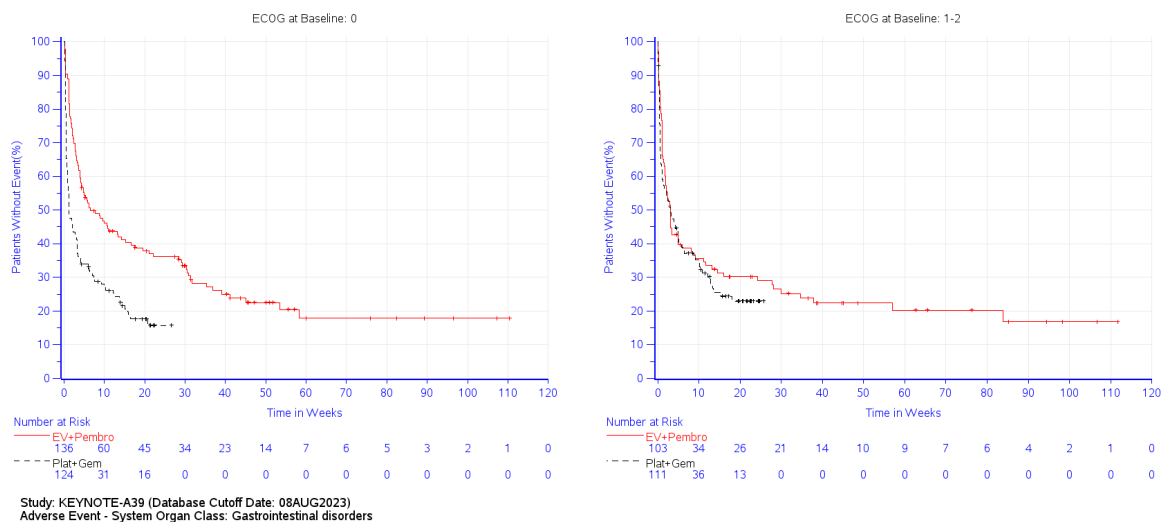


Abbildung 4G-75: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für die SOC Erkrankungen des Gastrointestinaltrakts für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

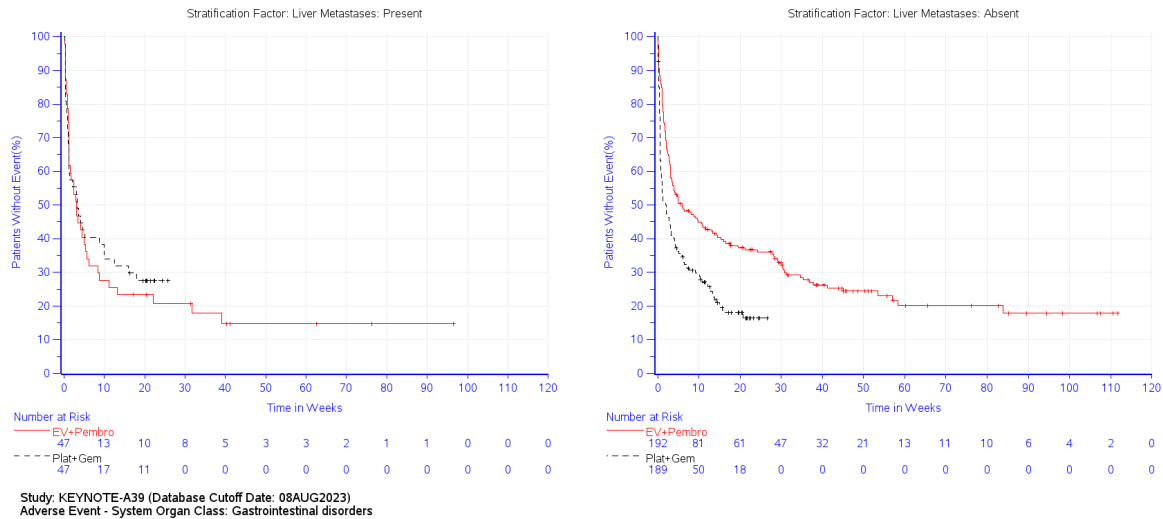


Abbildung 4G-76: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die SOC Erkrankungen des Gastrointestinaltrakts für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

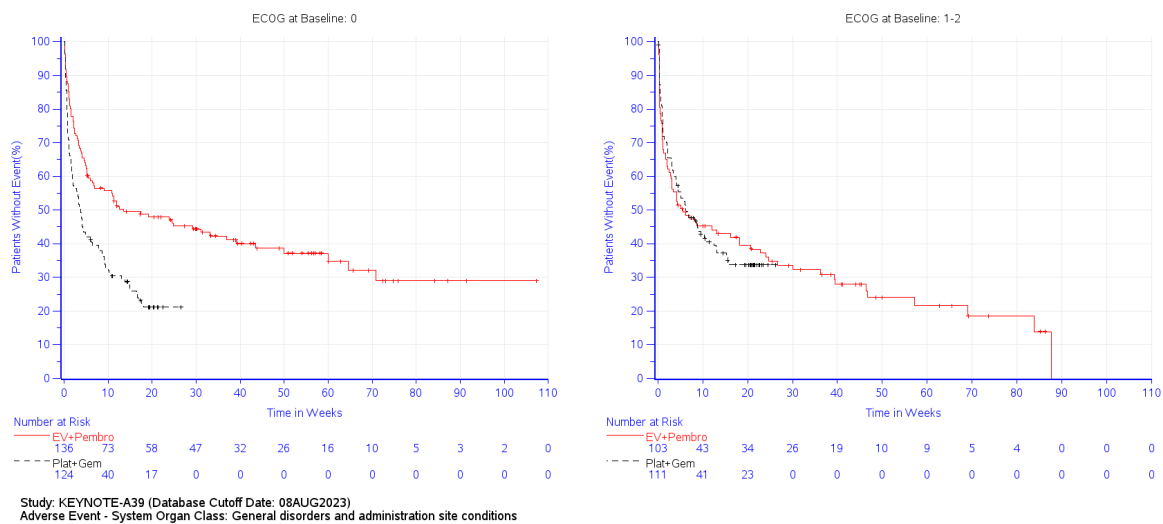


Abbildung 4G-77: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für die SOC Allgemeine Erkrankungen und Beschwerden am Verabreichungsort für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

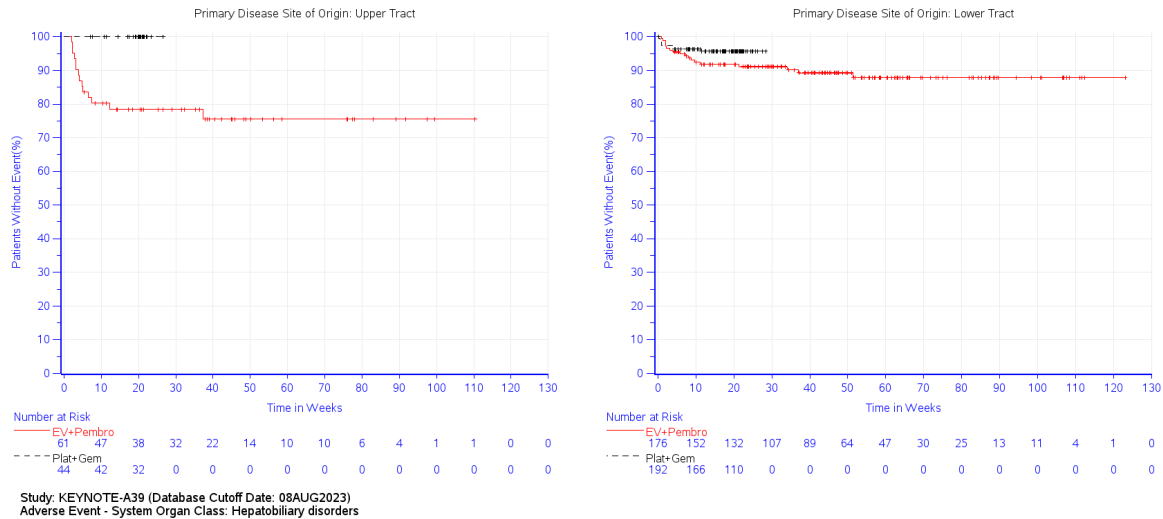


Abbildung 4G-78: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für die SOC Leber- und Gallenerkrankungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

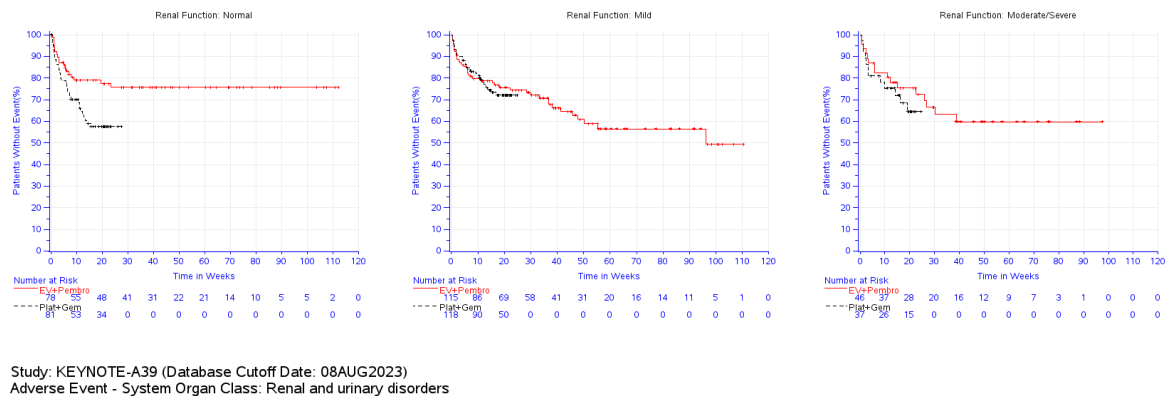


Abbildung 4G-79: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die SOC Erkrankungen der Nieren und Harnwege für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

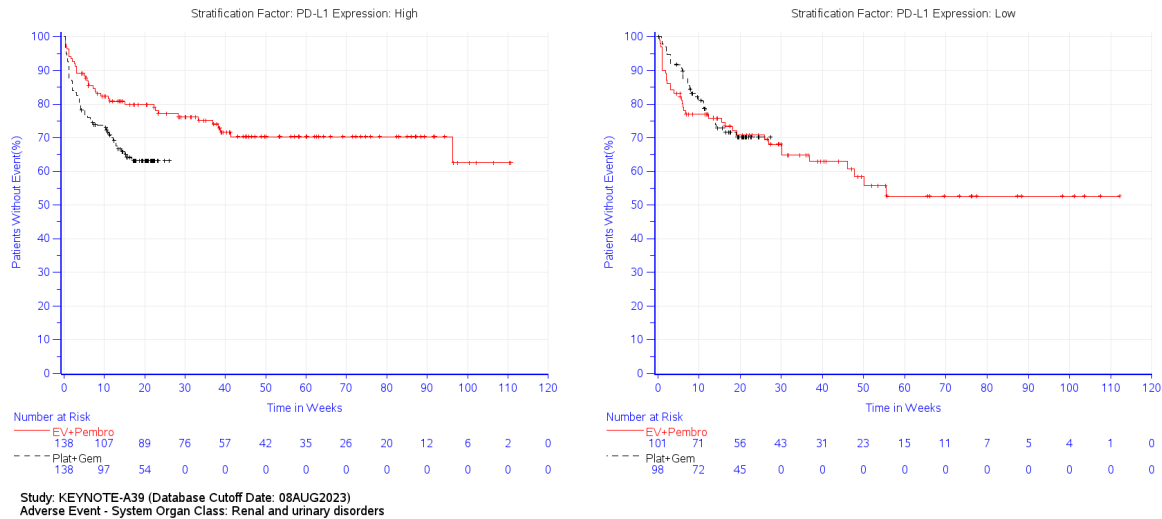


Abbildung 4G-80: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für die SOC Erkrankungen der Nieren und Harnwege für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

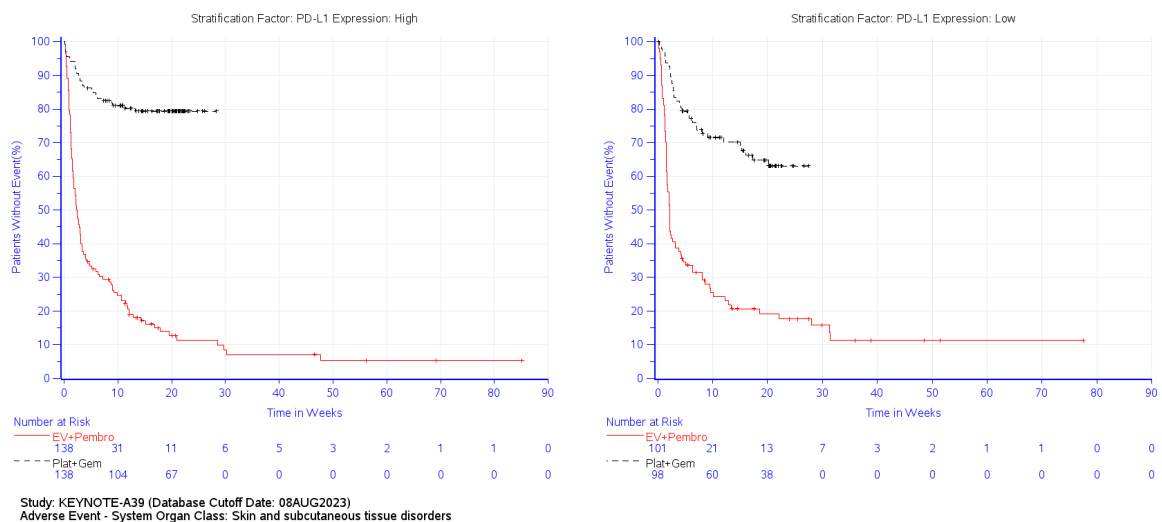


Abbildung 4G-81: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für die SOC Erkrankungen der Haut und des Unterhautgewebes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

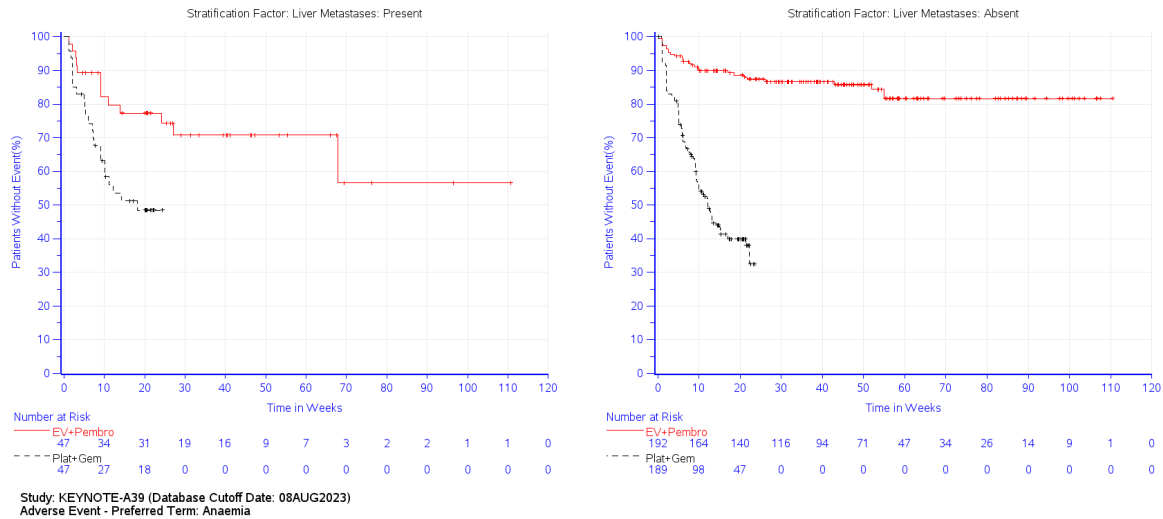


Abbildung 4G-82: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Anämie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

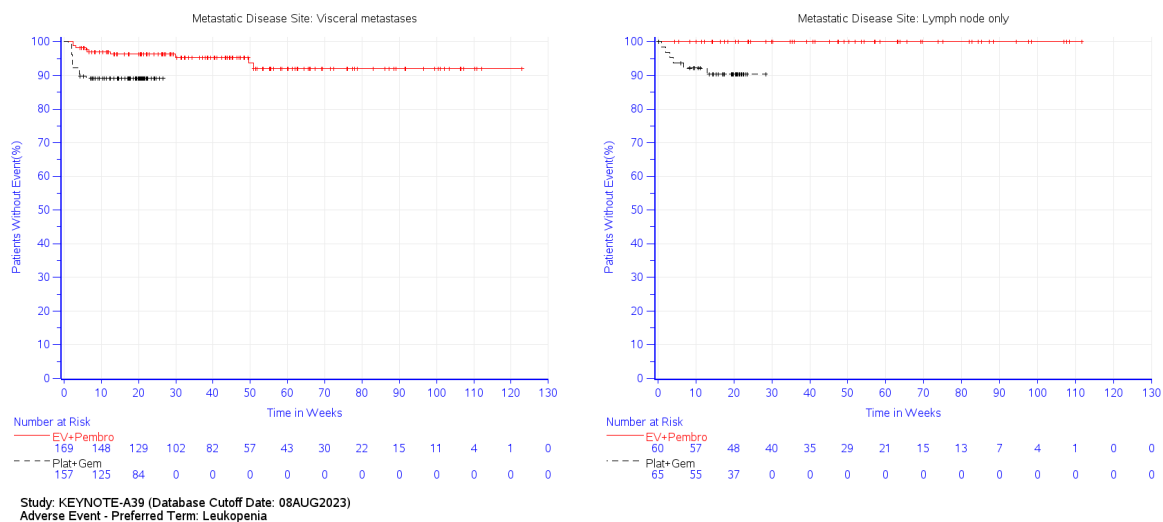


Abbildung 4G-83: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Leukopenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

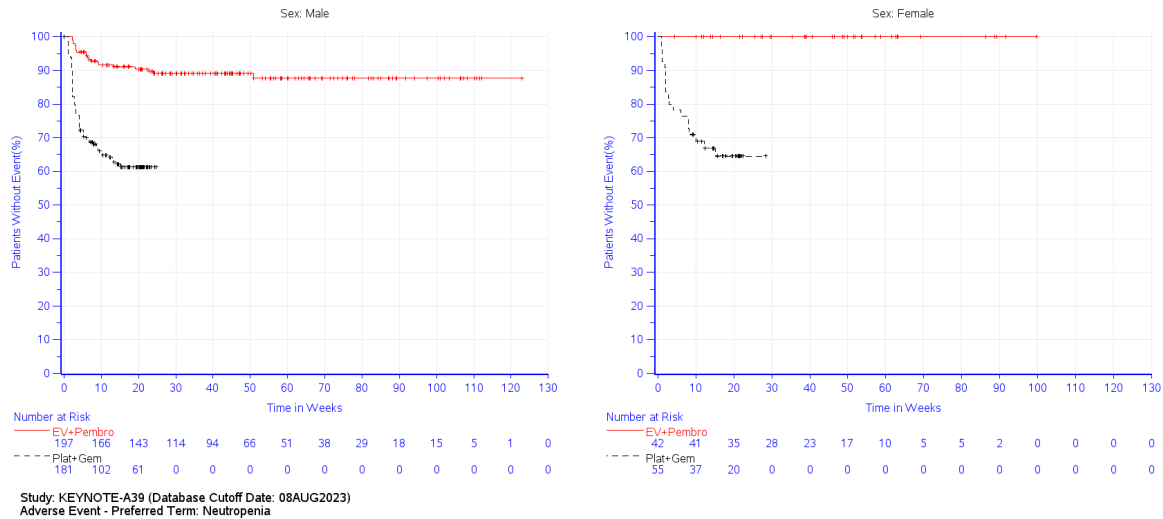


Abbildung 4G-84: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Neutropenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

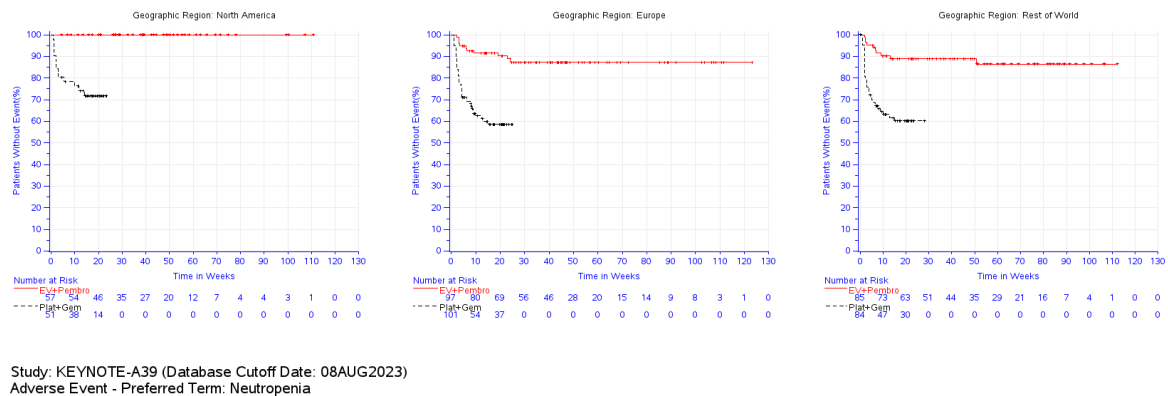


Abbildung 4G-85: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Neutropenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

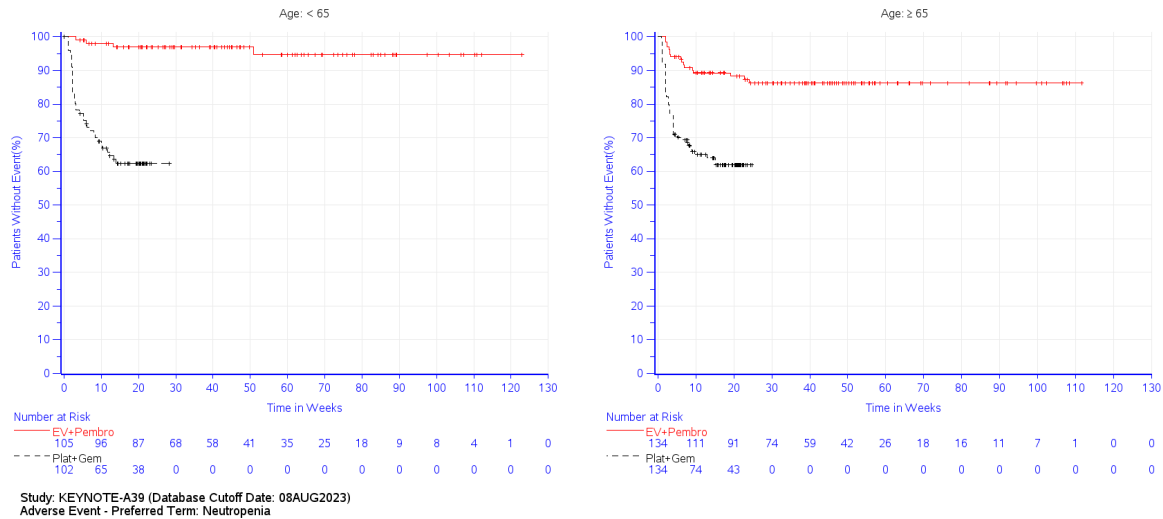


Abbildung 4G-86: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für den PT Neutropenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

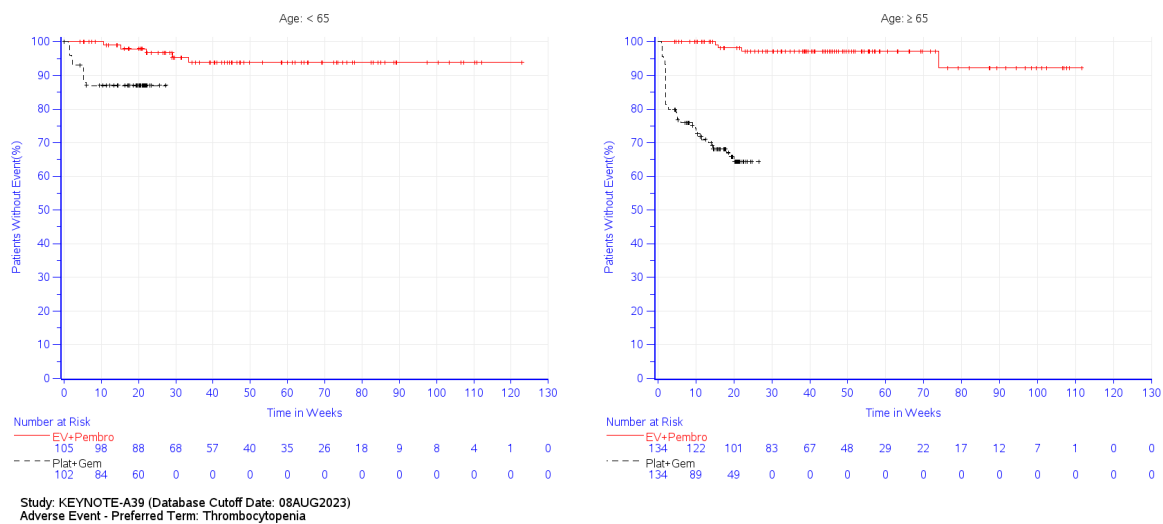


Abbildung 4G-87: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für den PT Thrombozytopenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

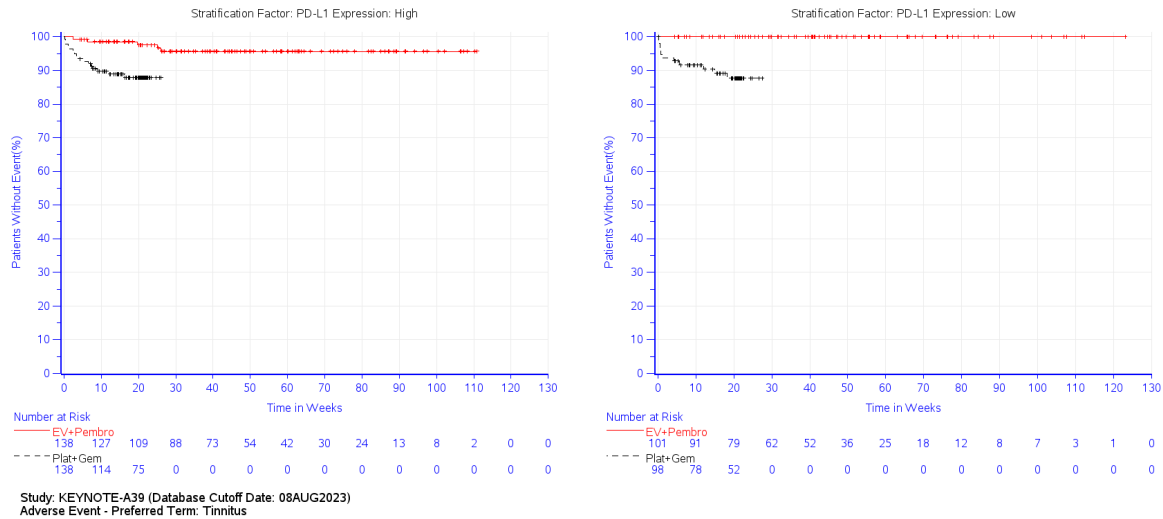


Abbildung 4G-88: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Tinnitus für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

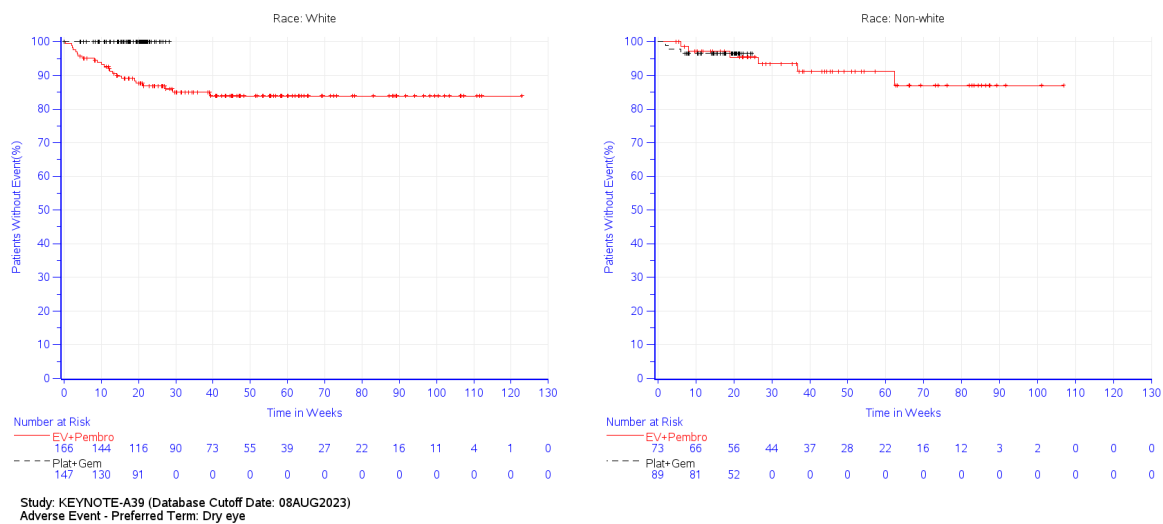


Abbildung 4G-89: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Trockenes Auge für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

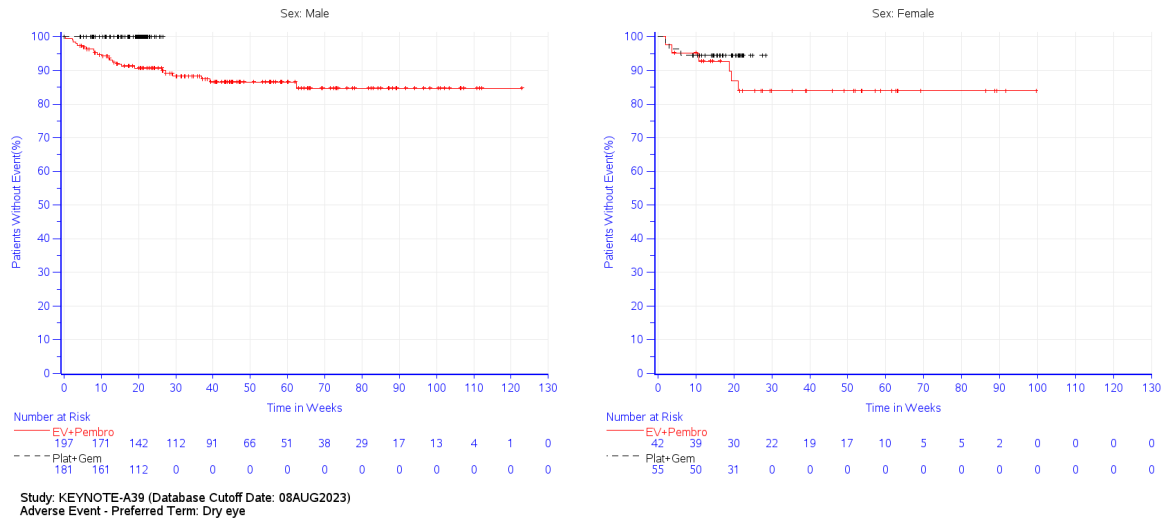


Abbildung 4G-90: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Trockenes Auge für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

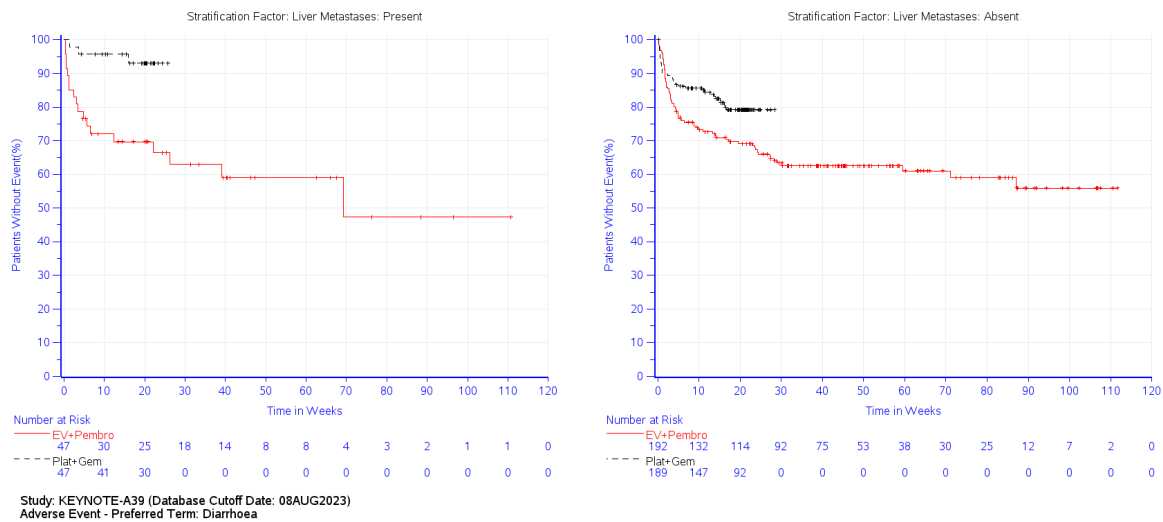


Abbildung 4G-91: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Diarrhö für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

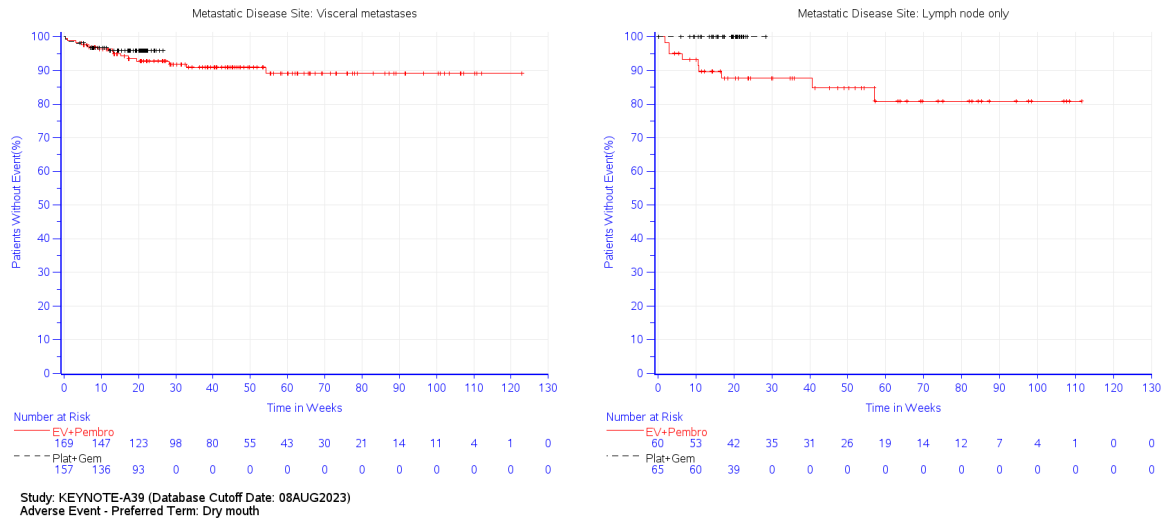


Abbildung 4G-92: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Mundtrockenheit für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

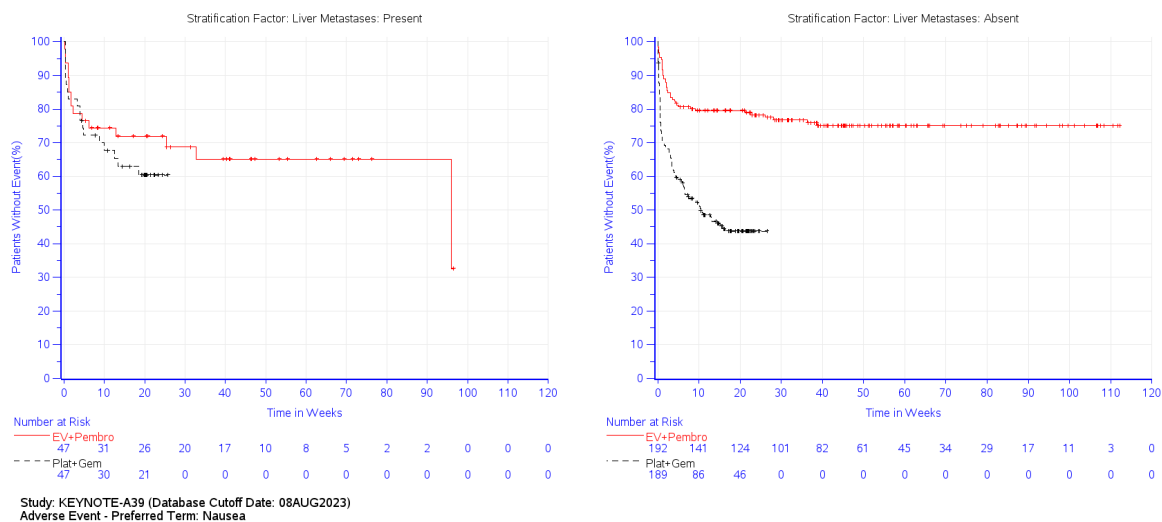


Abbildung 4G-93: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Übelkeit für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

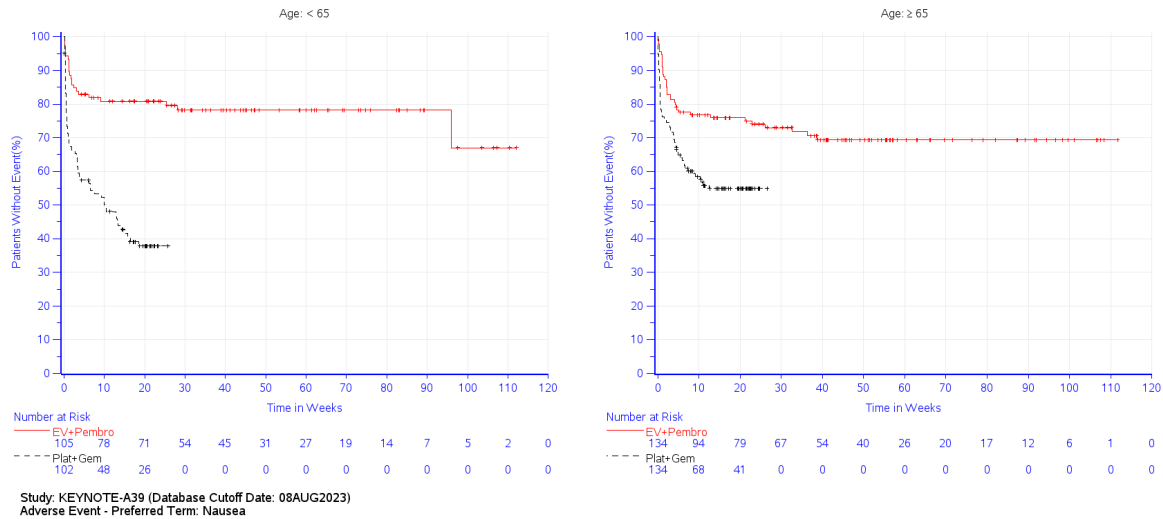


Abbildung 4G-94: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für den PT Übelkeit für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

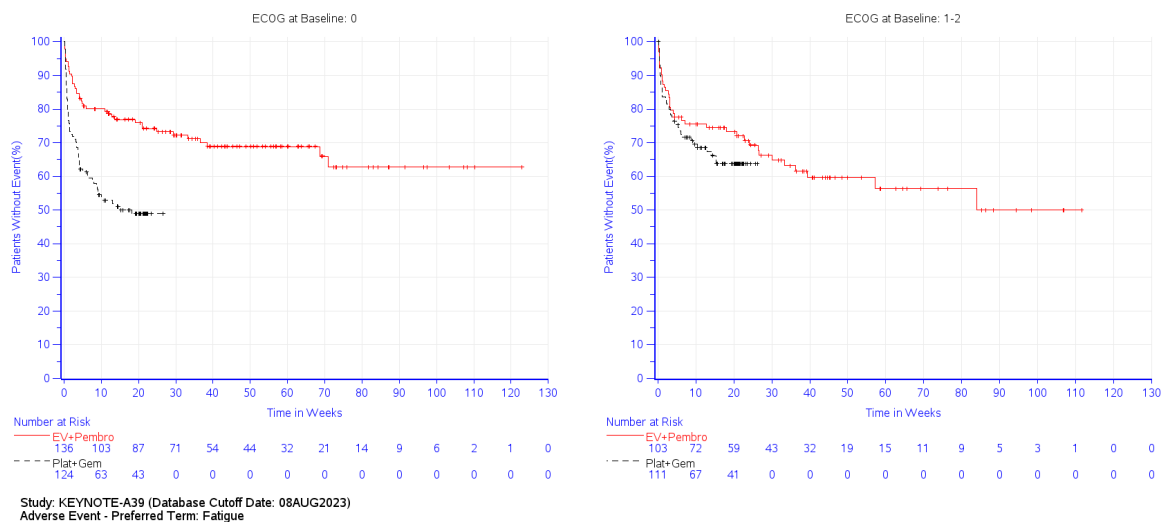


Abbildung 4G-95: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für den PT Erschöpfung für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

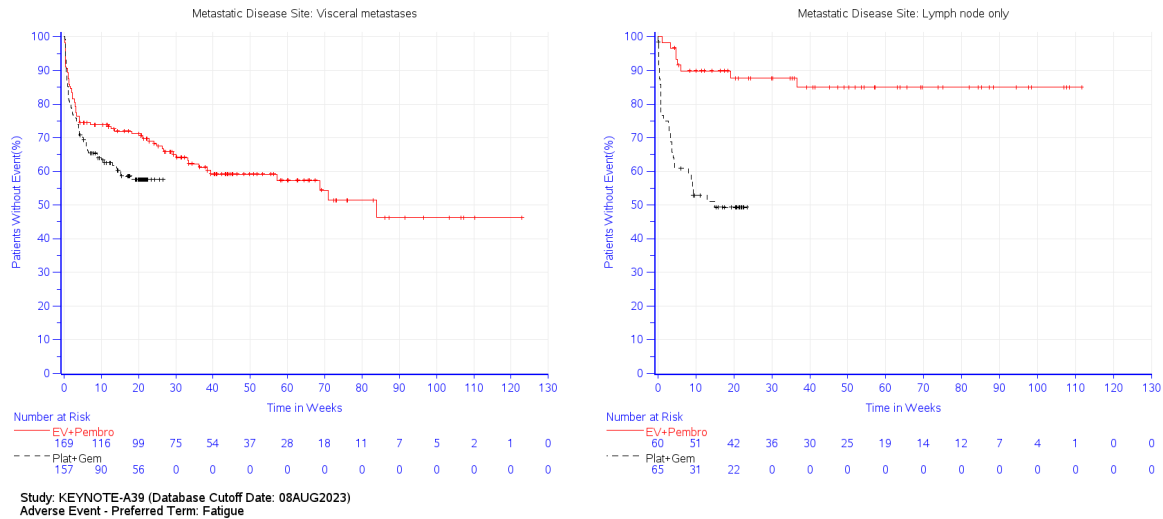


Abbildung 4G-96: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Erschöpfung für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

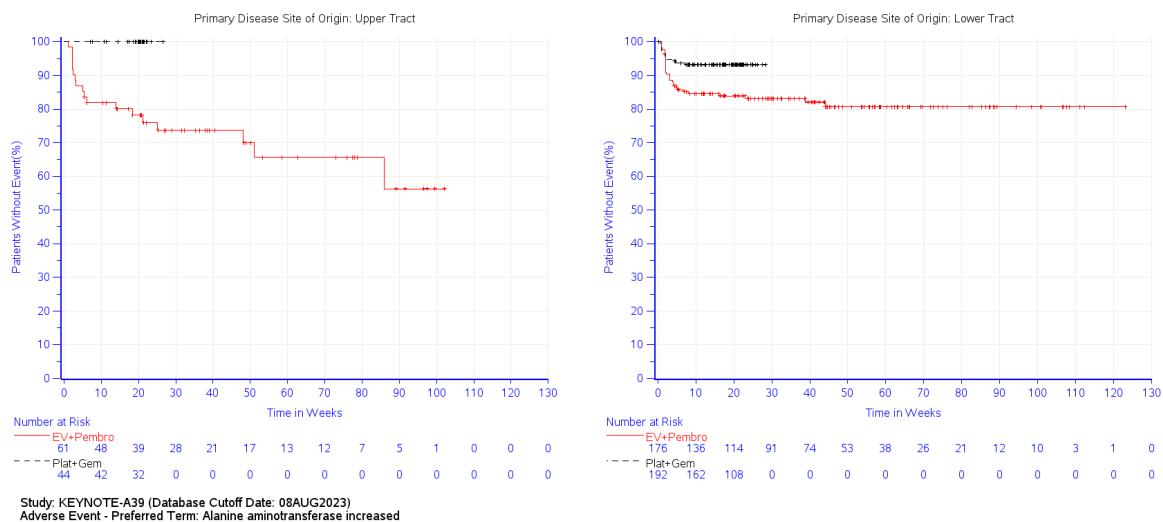


Abbildung 4G-97: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Alaninaminotransferase erhöht für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

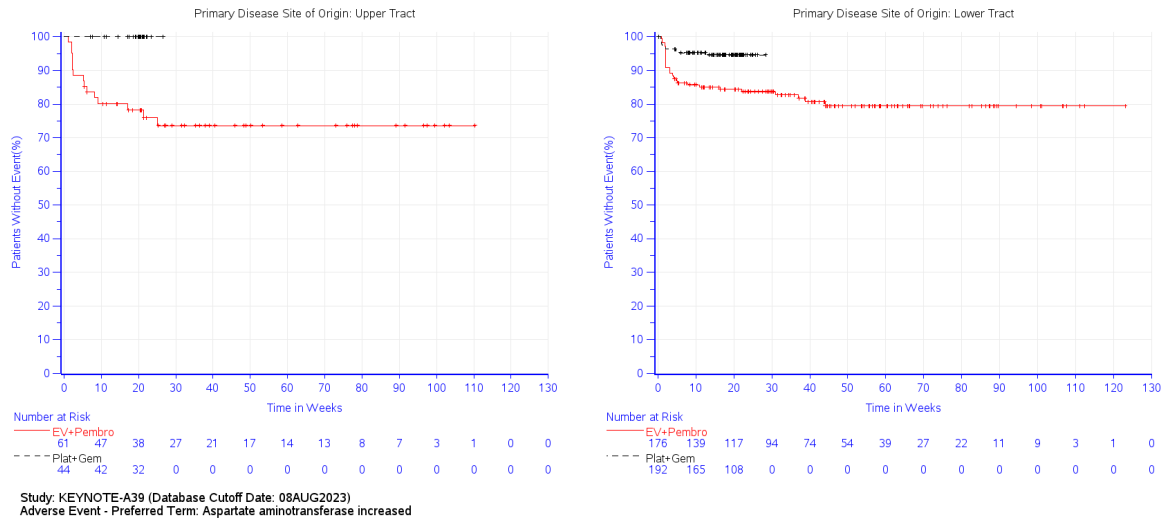


Abbildung 4G-98: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Aspartataminotransferase erhöht für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

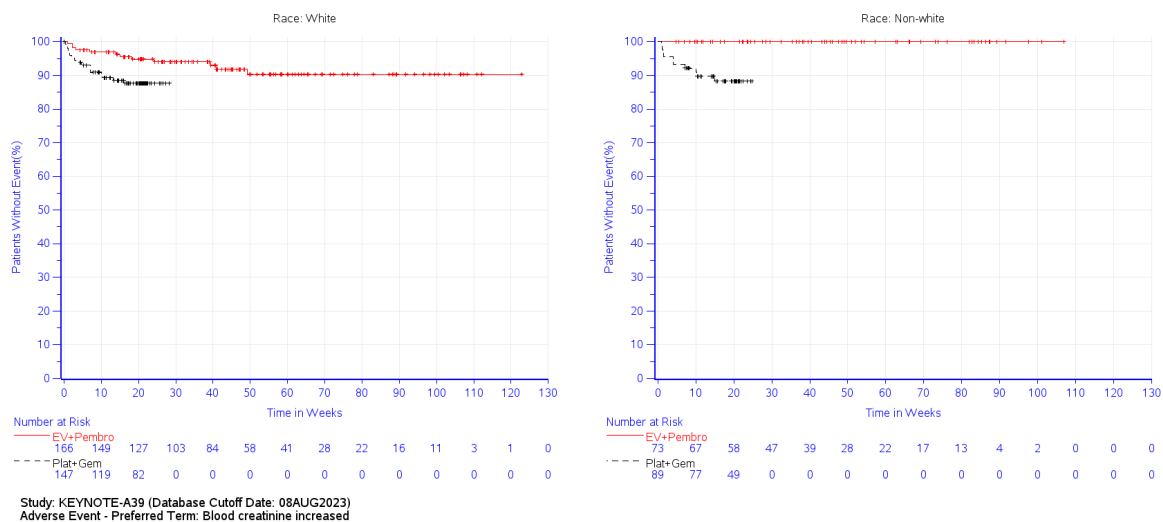
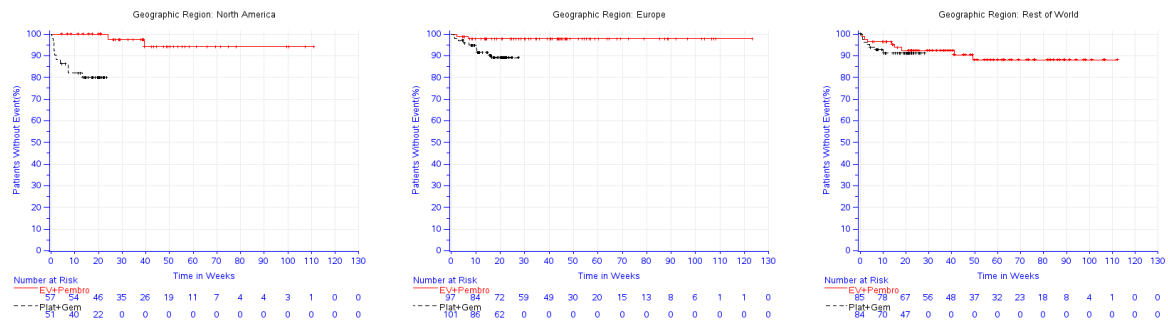
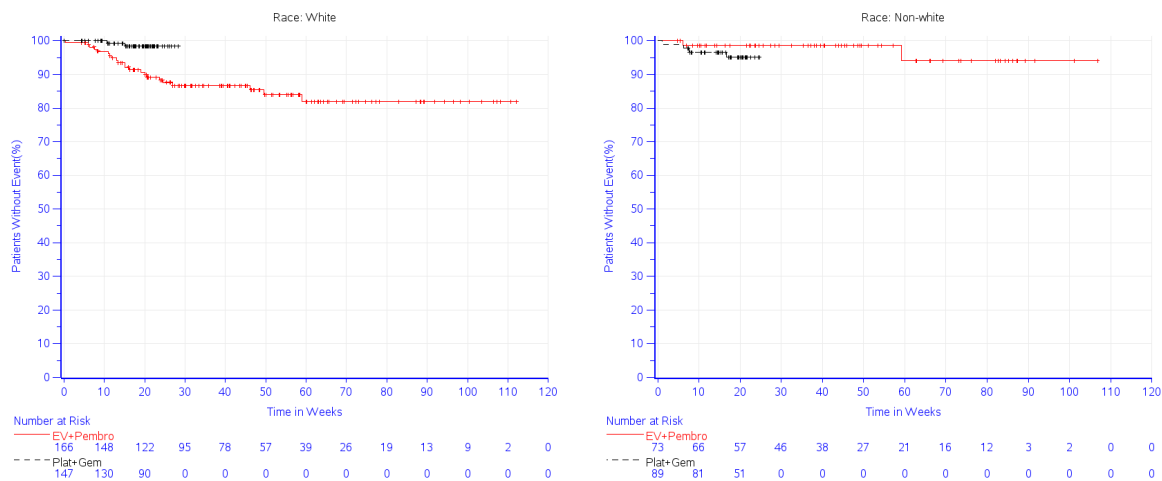


Abbildung 4G-99: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Kreatinin im Blut erhöht für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



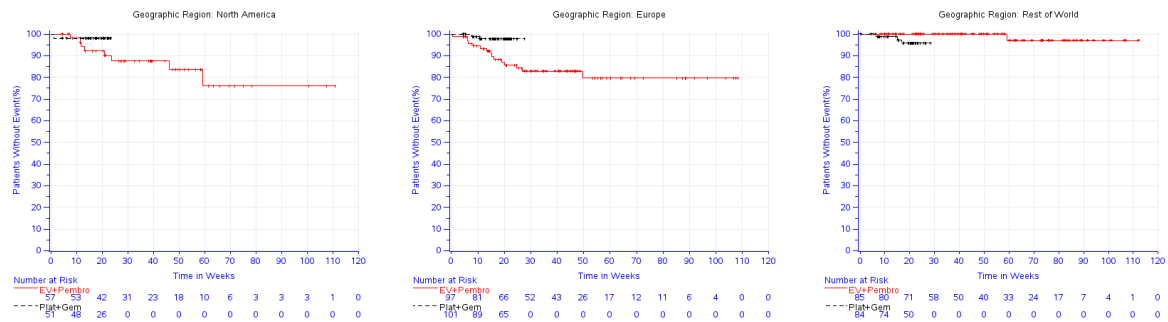
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Blood creatinine increased

Abbildung 4G-100: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Kreatinin im Blut erhöht für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



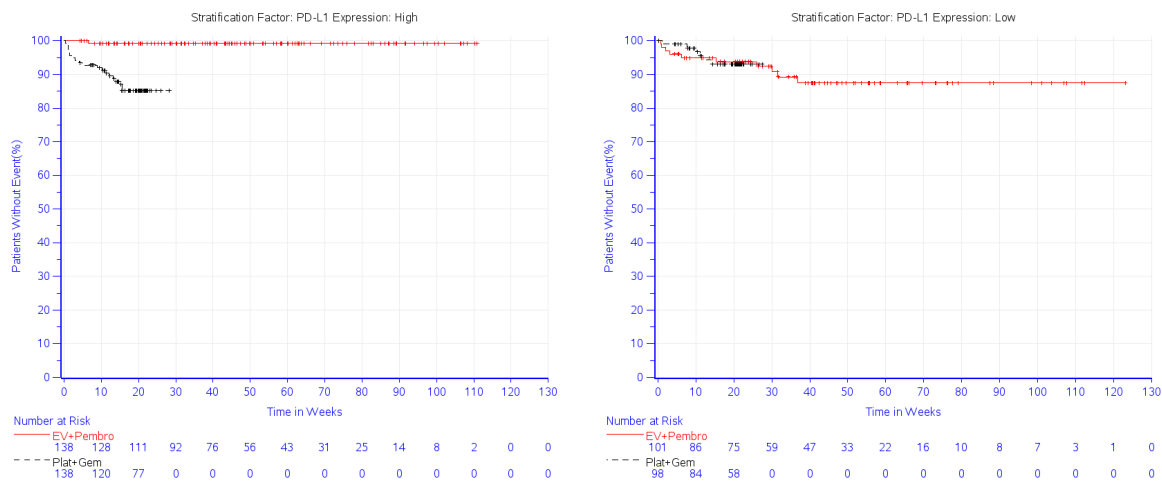
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Paraesthesia

Abbildung 4G-101: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Parästhesie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



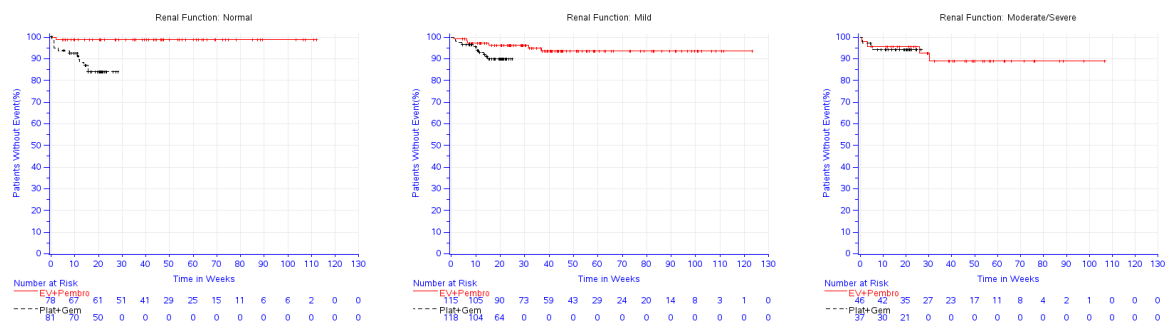
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Paraesthesia

Abbildung 4G-102: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Parästhesie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



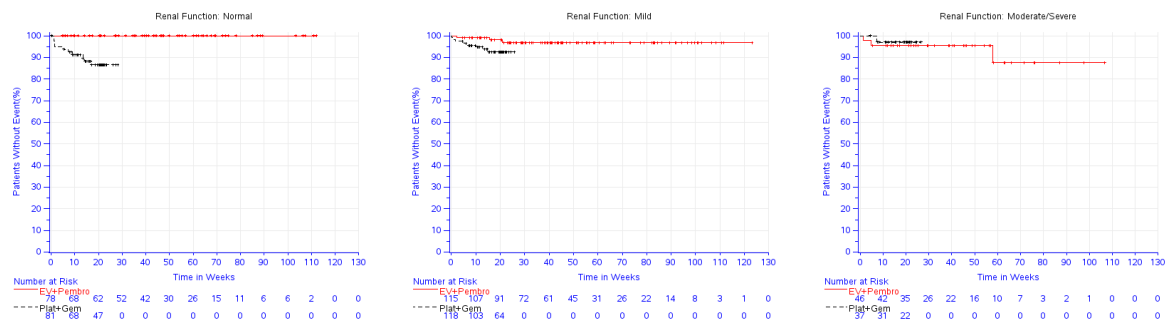
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Acute kidney injury

Abbildung 4G-103: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Akute Nierenschädigung für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Acute kidney injury

Abbildung 4G-104: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für den PT Akute Nierenschädigung für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Epistaxis

Abbildung 4G-105: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für den PT Epistaxis für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

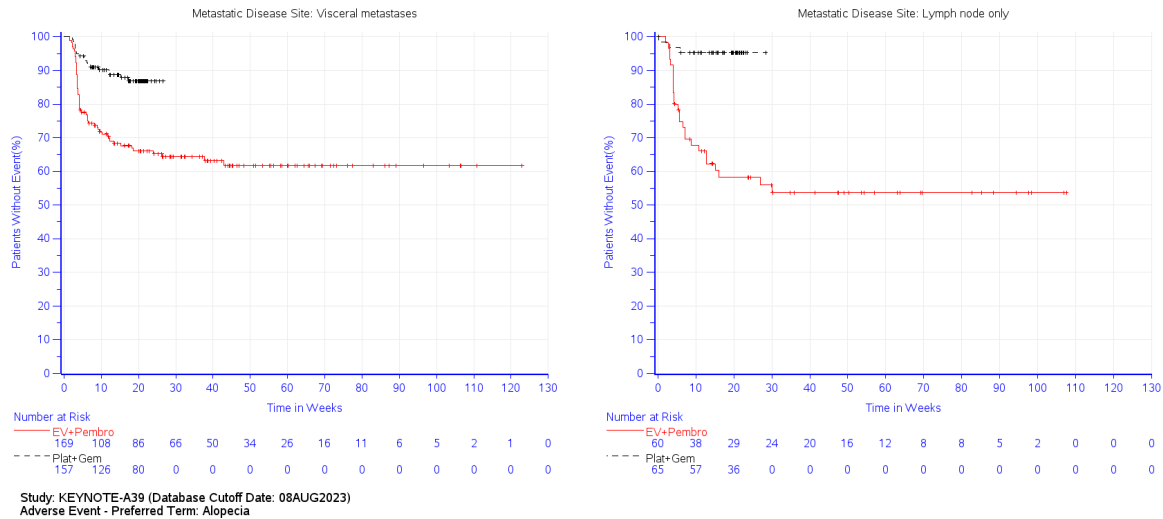


Abbildung 4G-106: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Alopecie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

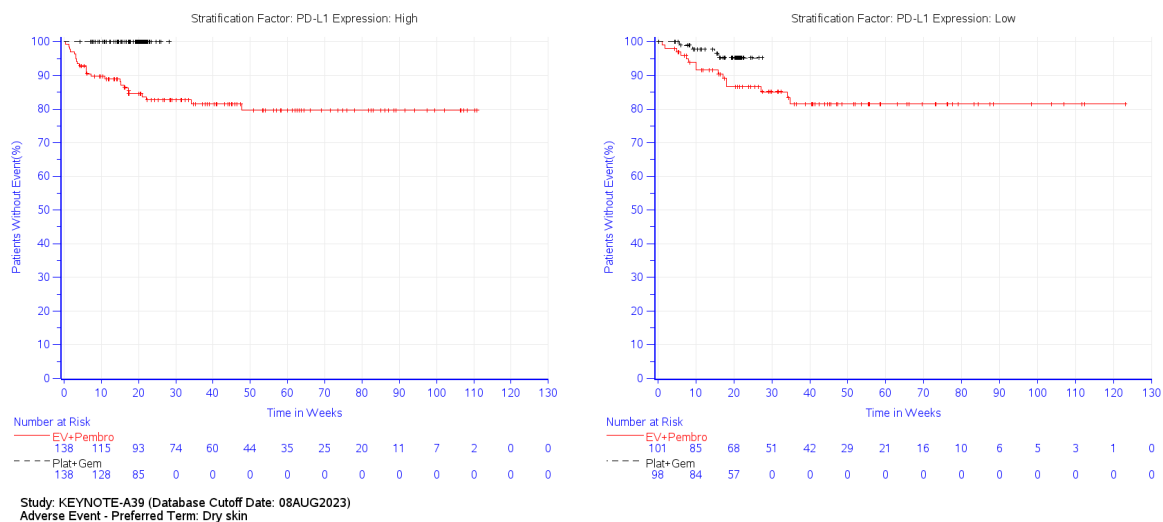


Abbildung 4G-107: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Trockene Haut für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

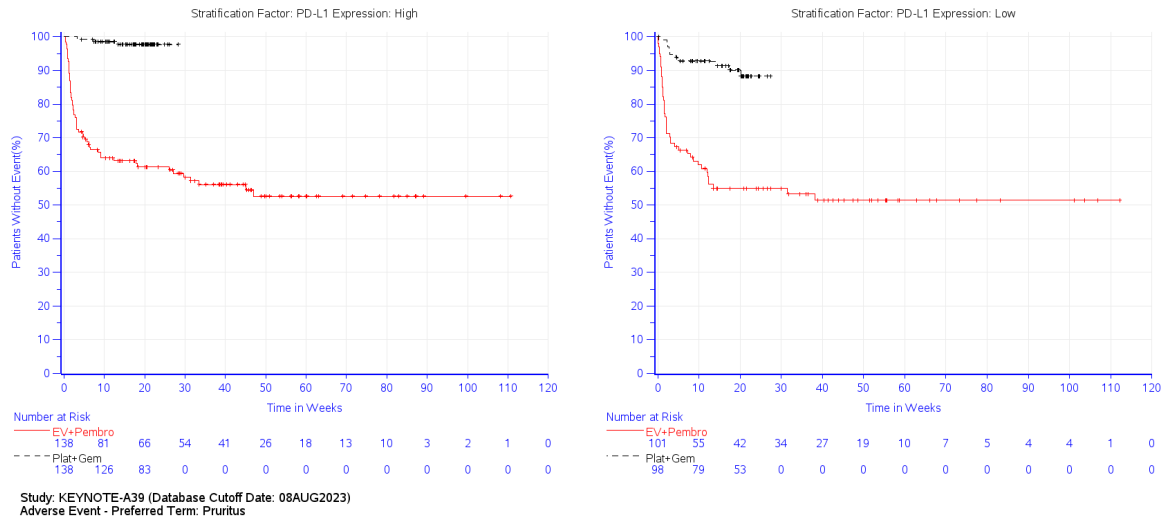


Abbildung 4G-108: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Juckreiz für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

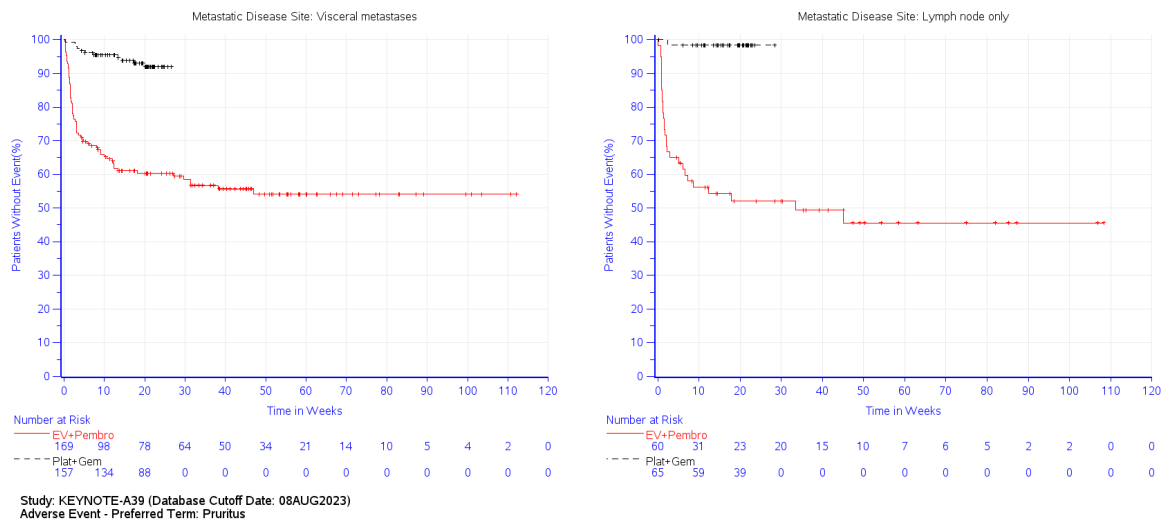


Abbildung 4G-109: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Juckreiz für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

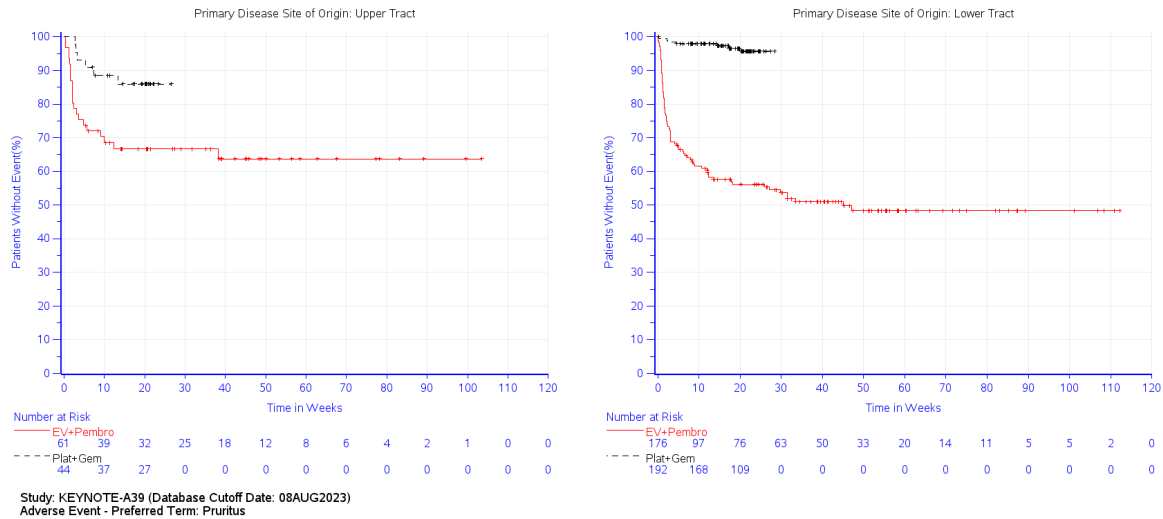


Abbildung 4G-110: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Juckreiz für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

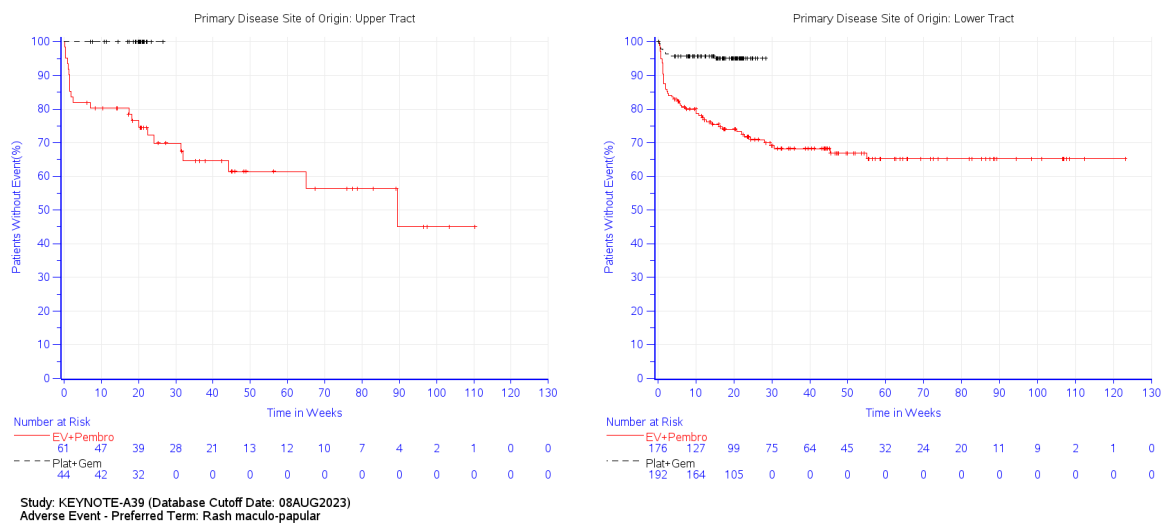


Abbildung 4G-111: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Ausschlag makulo-papuloes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

Schwerwiegende unerwünschte Ereignisse (SOC und PT)

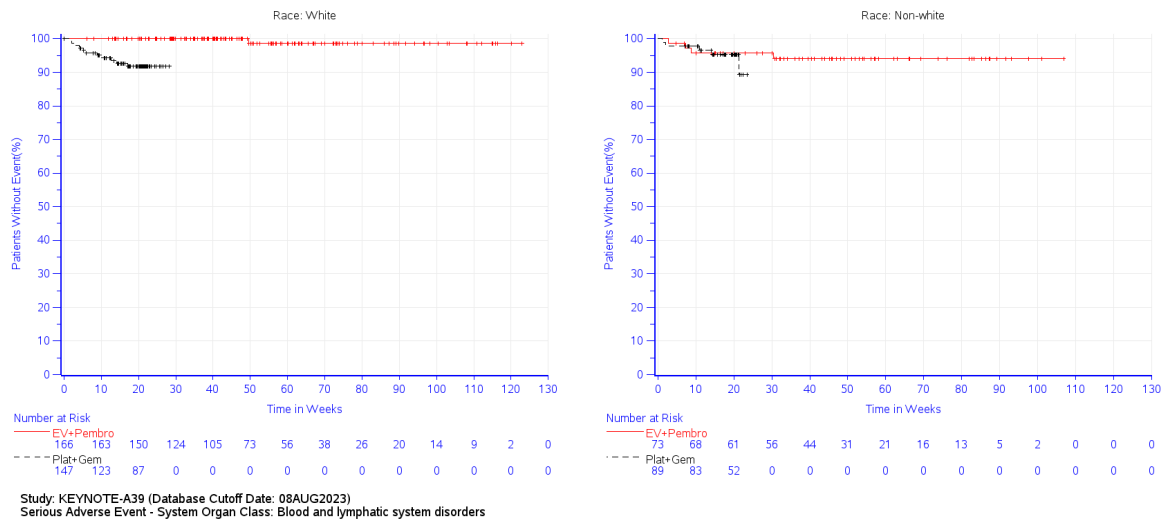


Abbildung 4G-112: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Erkrankungen des Blutes und des Lymphsystems für Schwerwiegende unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

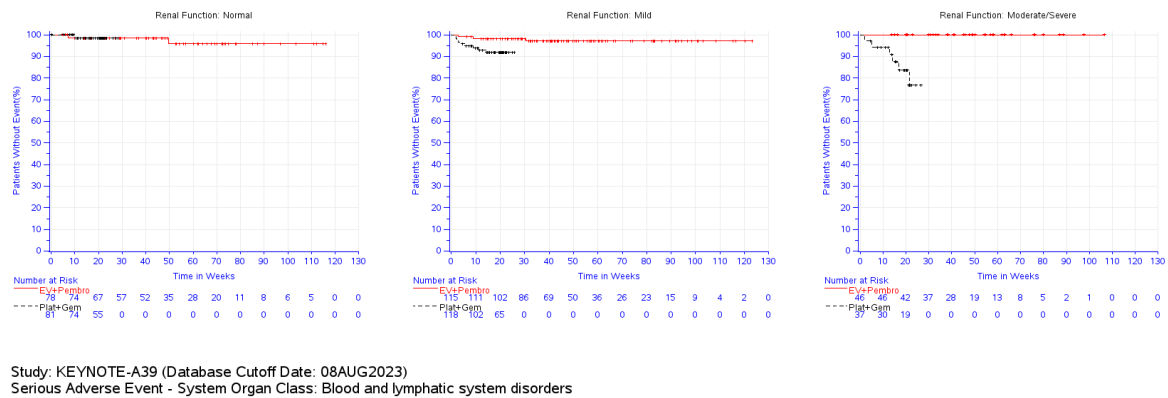


Abbildung 4G-113: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die SOC Erkrankungen des Blutes und des Lymphsystems für Schwerwiegende unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

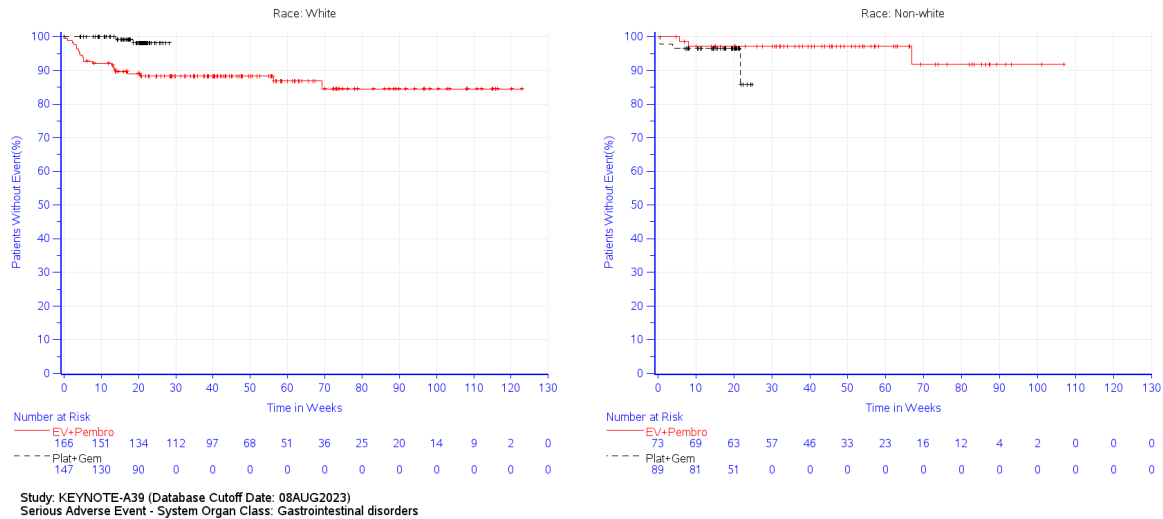


Abbildung 4G-114: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Erkrankungen des Gastrointestinaltrakts für Schwerwiegende unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

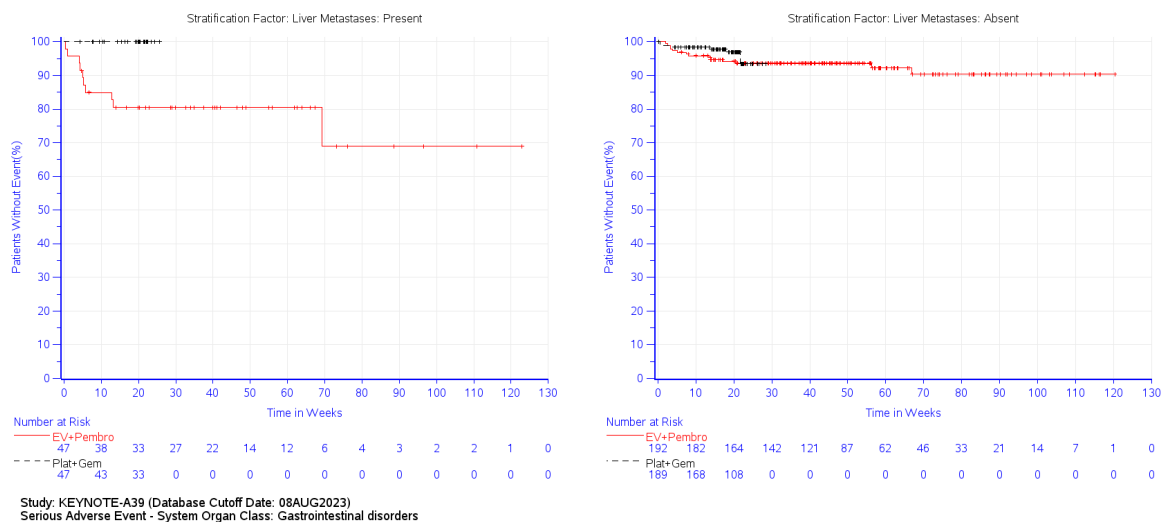


Abbildung 4G-115: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die SOC Erkrankungen des Gastrointestinaltrakts für Schwerwiegende unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT)

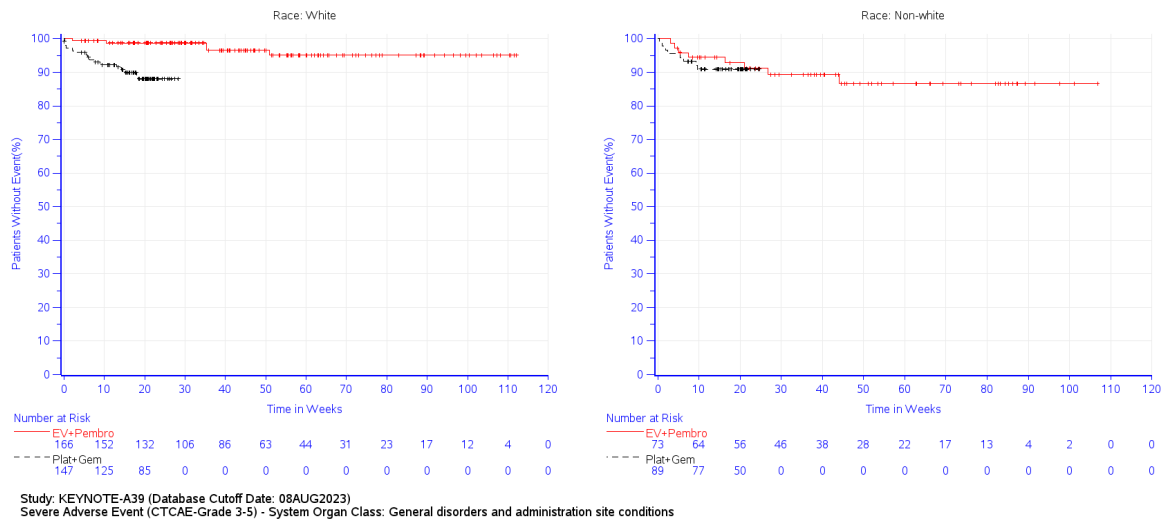


Abbildung 4G-116: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Allgemeine Erkrankungen und Beschwerden am Verabreichungsort für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

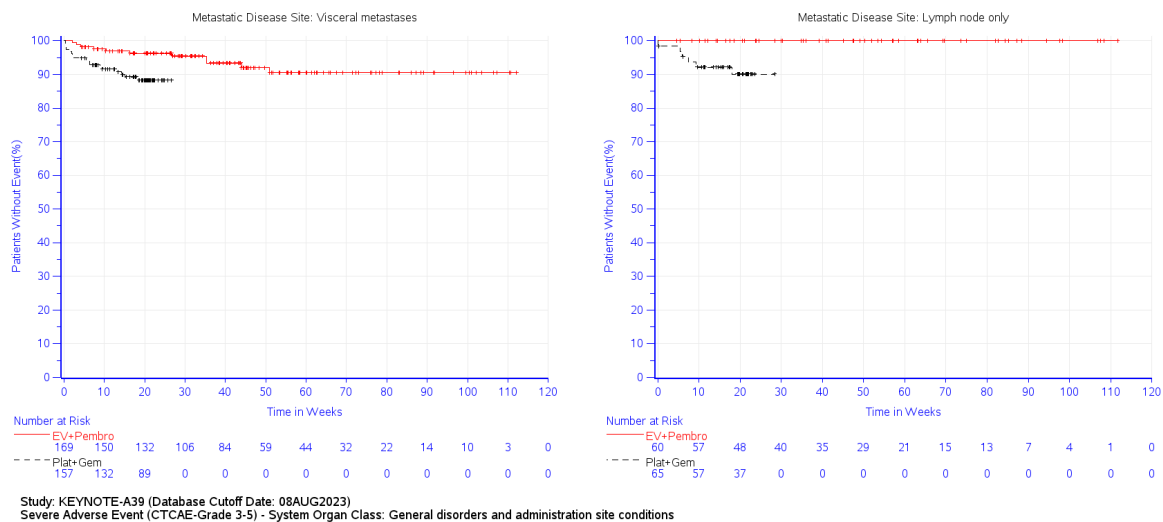


Abbildung 4G-117: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für die SOC Allgemeine Erkrankungen und Beschwerden am Verabreichungsort für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

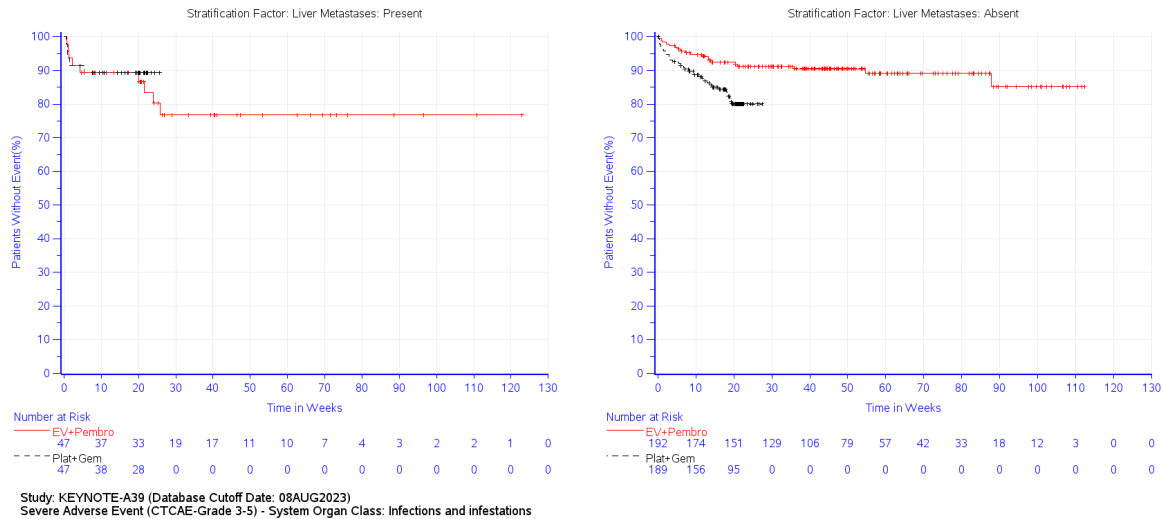


Abbildung 4G-118: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die SOC Infektionen und parasitäre Erkrankungen für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

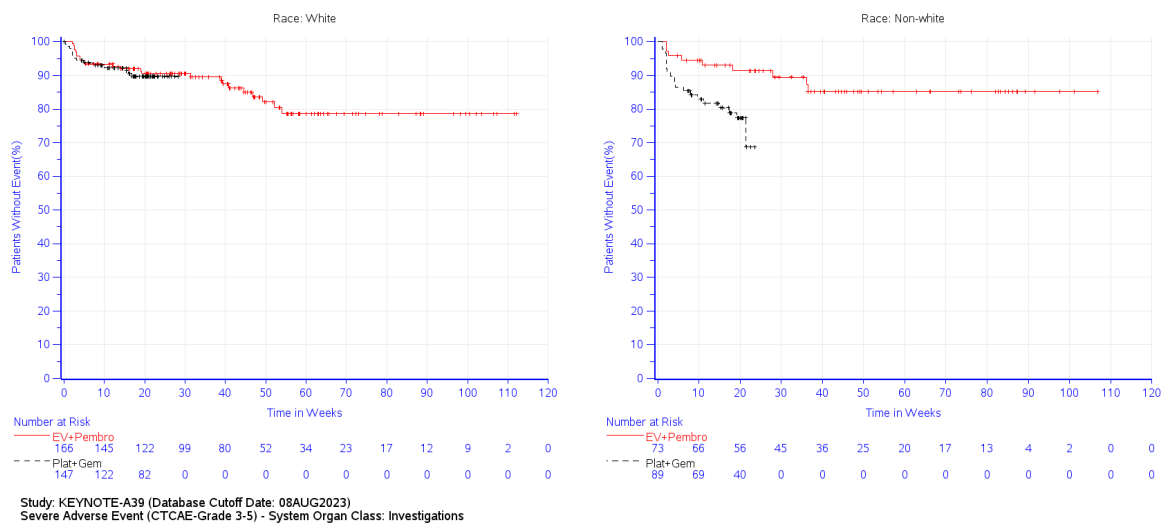


Abbildung 4G-119: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Untersuchungen für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

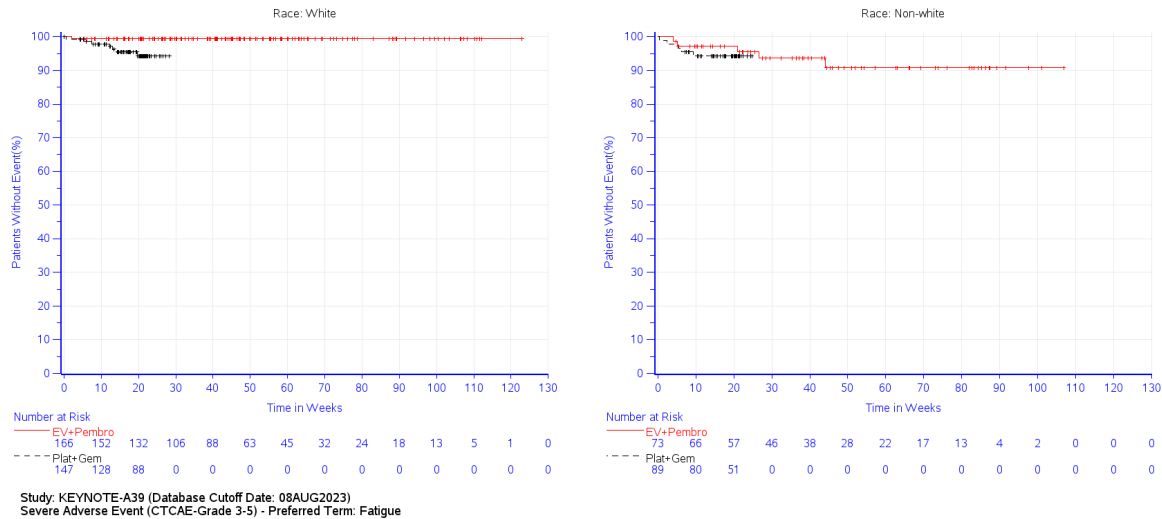


Abbildung 4G-120: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Erschöpfung für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

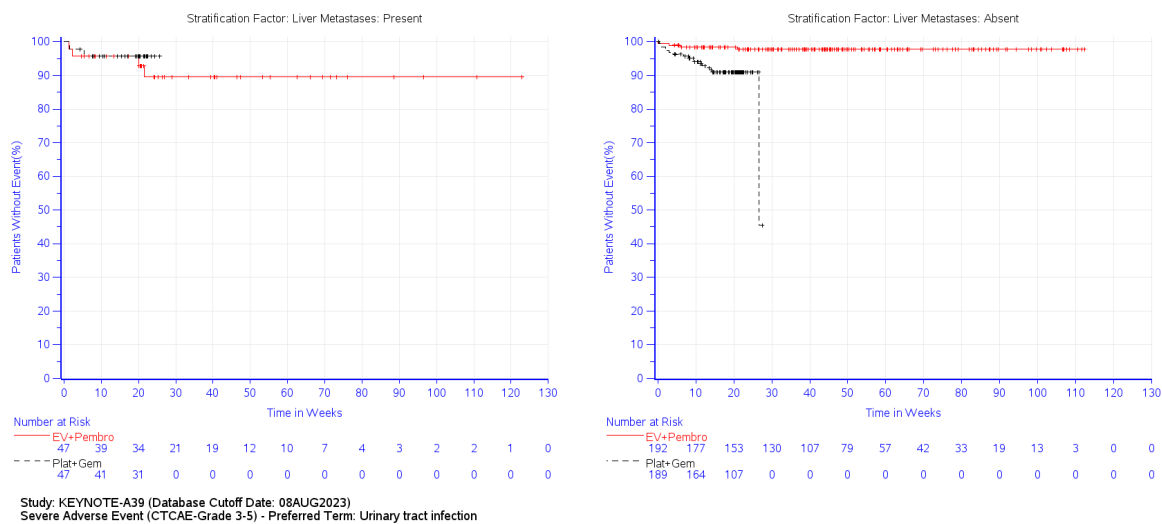


Abbildung 4G-121: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Harnwegsinfektion für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

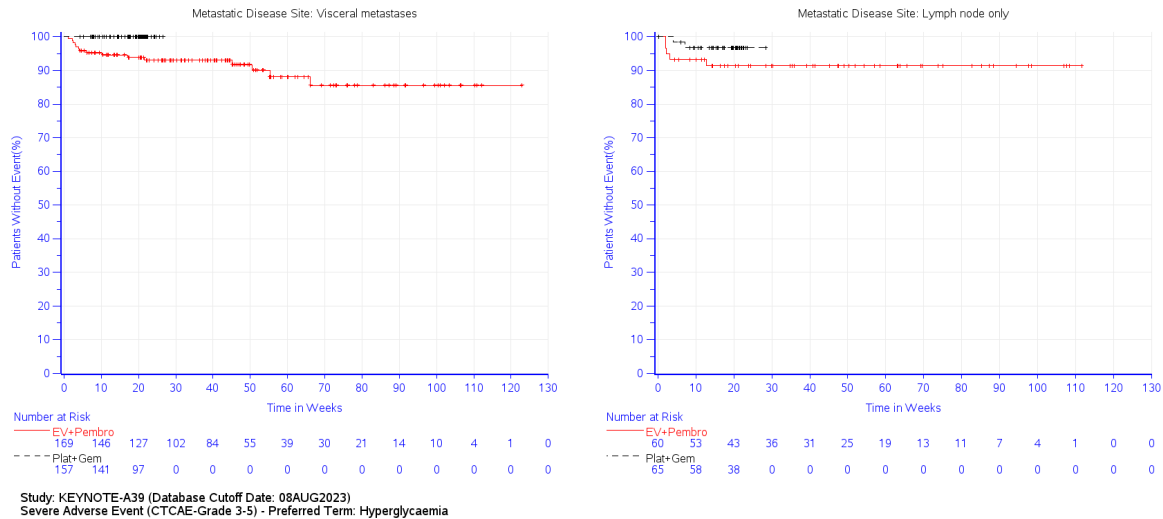


Abbildung 4G-122: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Hyperglykämie für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39 (Cisplatin geeignet)

Cisplatin ungeeignet

Morbidität

Krankheitssymptomatik und Gesundheitszustand

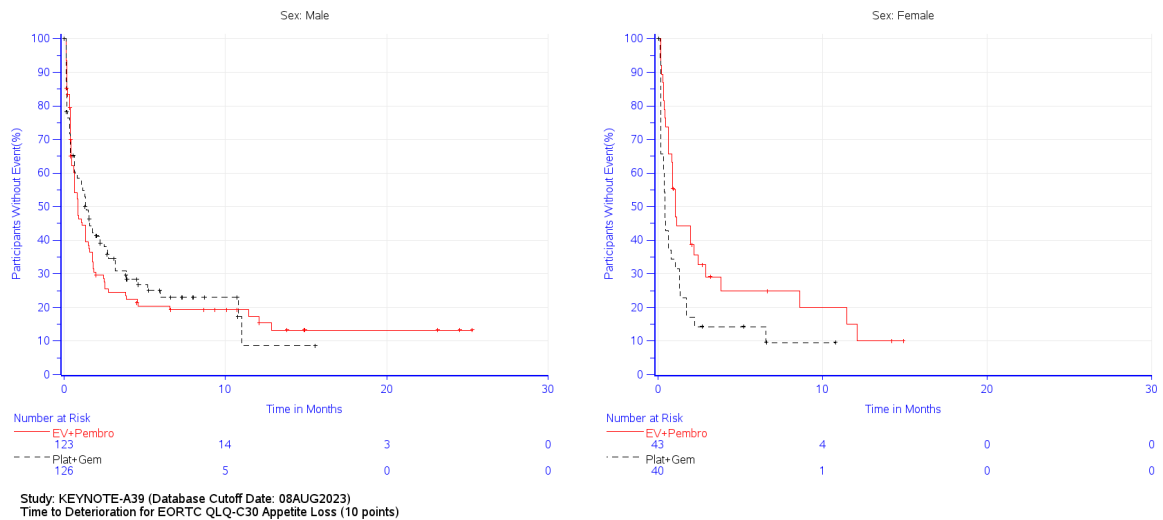


Abbildung 4G-123: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39

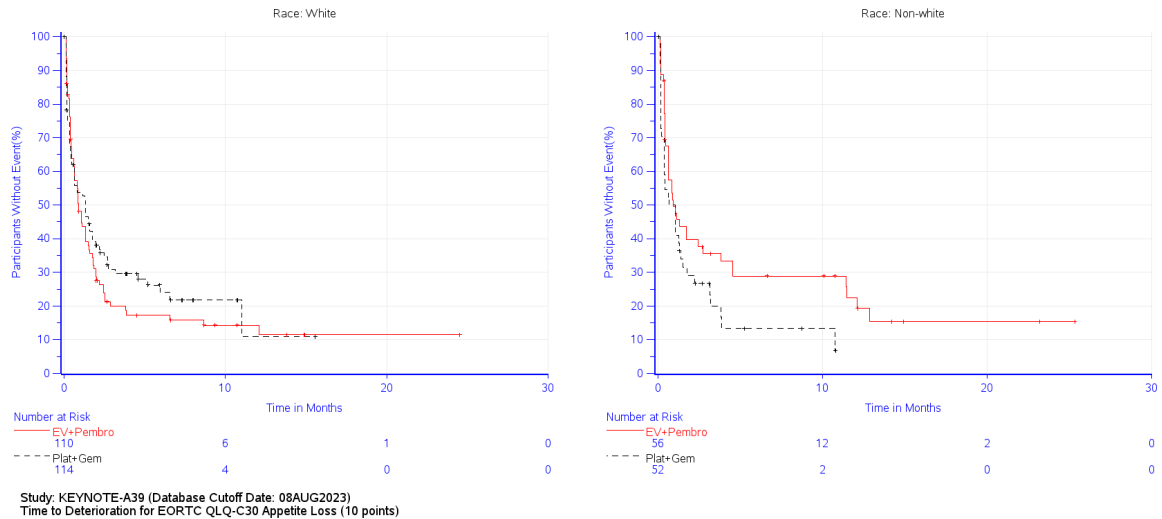


Abbildung 4G-124: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39

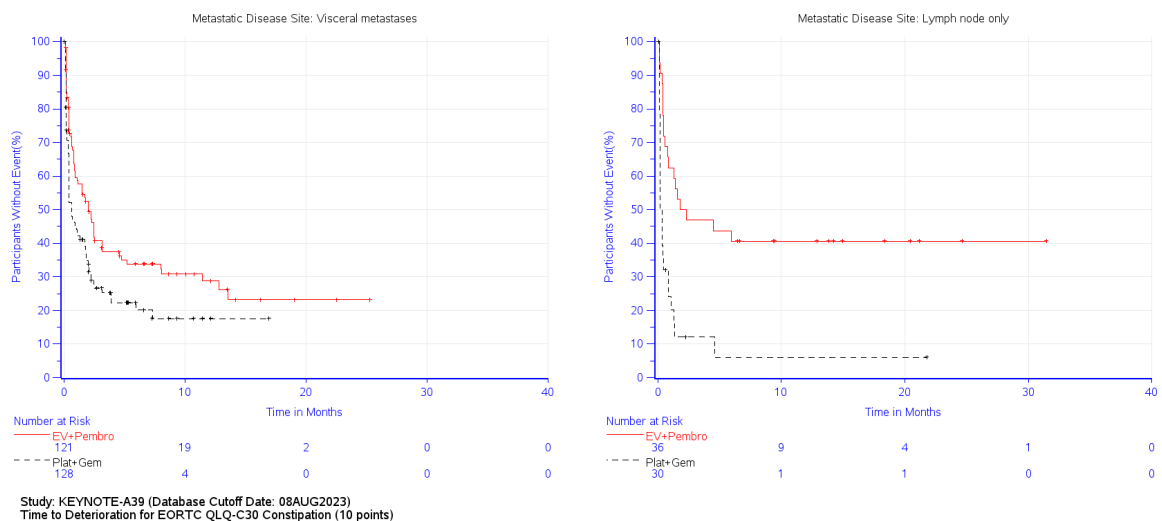


Abbildung 4G-125: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39

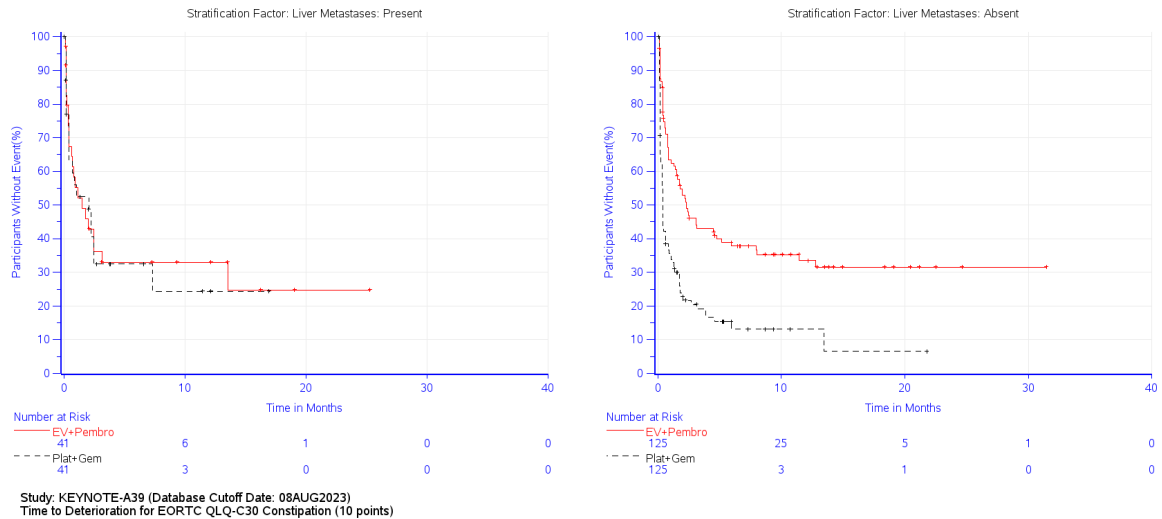


Abbildung 4G-126: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39

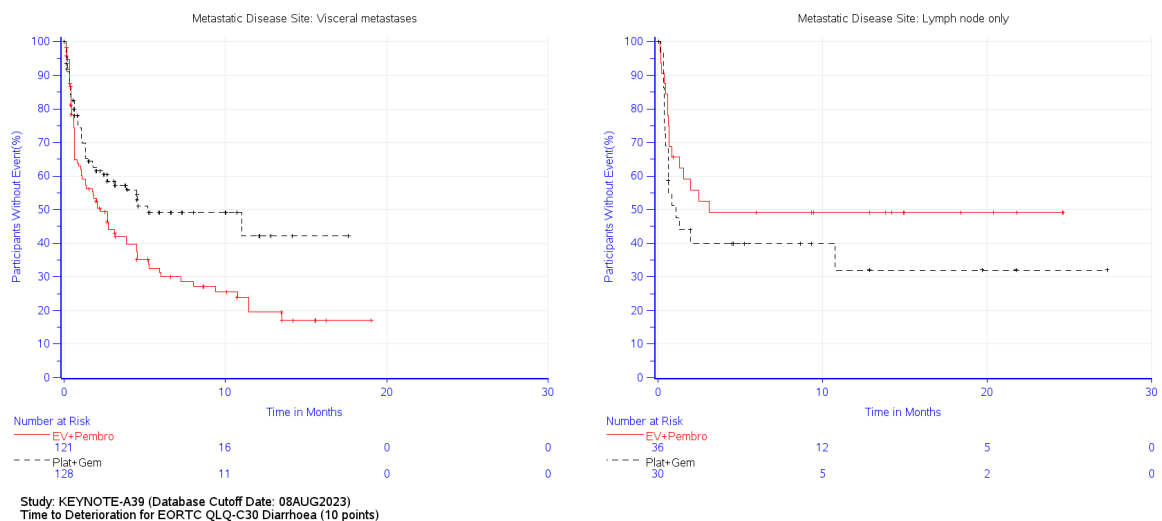


Abbildung 4G-127: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für die Symptomskala Diarrhö des EORTC QLQ-C30 der Studie KEYNOTE A39

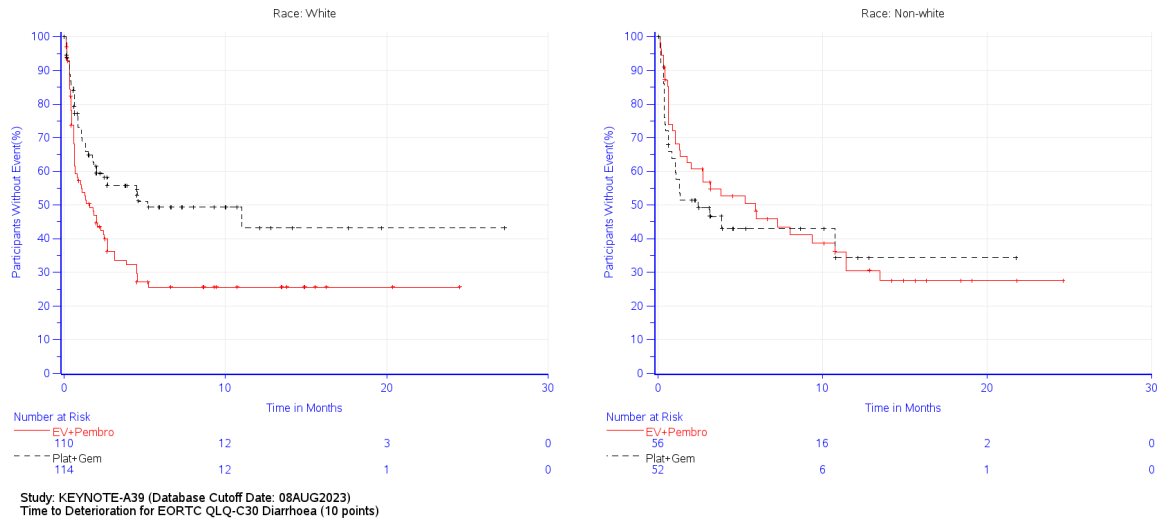


Abbildung 4G-128: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die Symptomskala Diarrhö des EORTC QLQ-C30 der Studie KEYNOTE A39

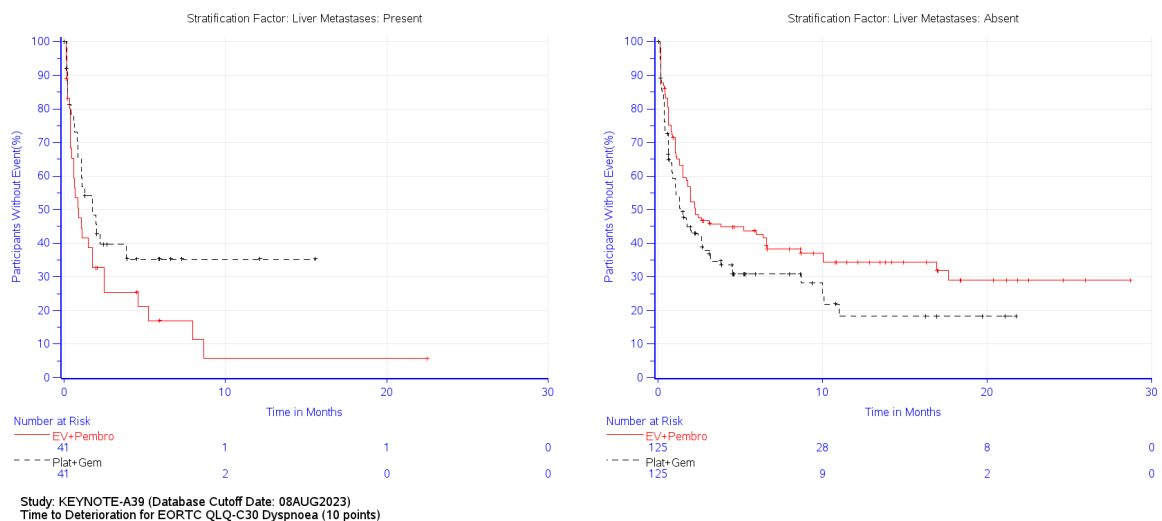


Abbildung 4G-129: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39

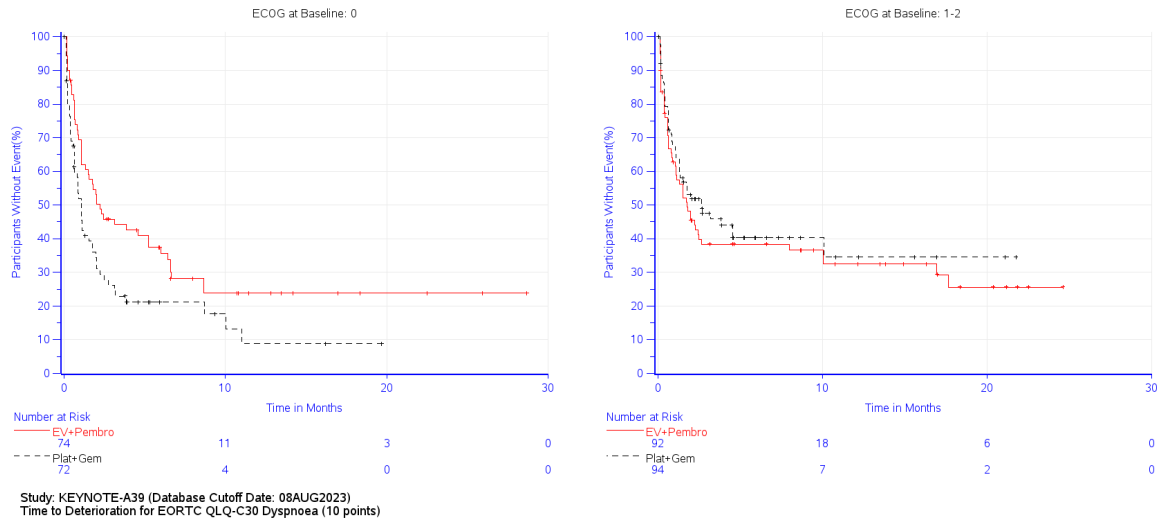


Abbildung 4G-130: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39

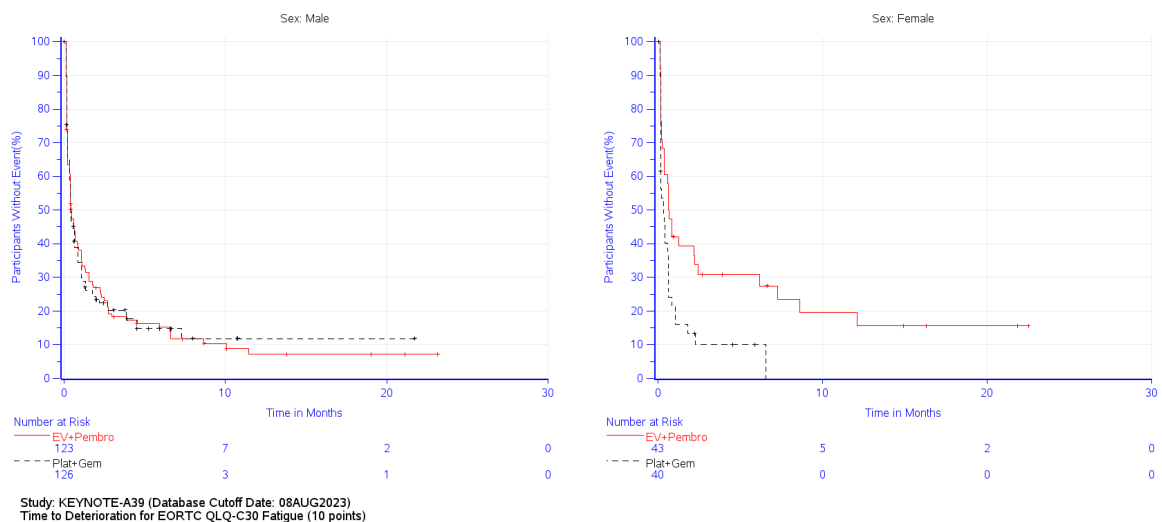


Abbildung 4G-131: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39

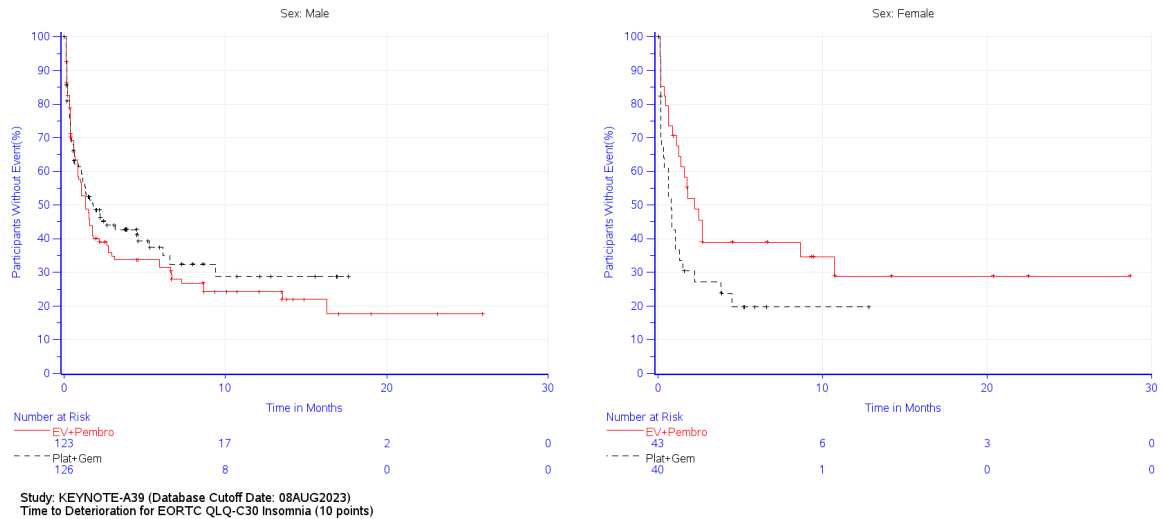


Abbildung 4G-132: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Symptomskala Schlaflosigkeit des EORTC QLQ-C30 der Studie KEYNOTE A39

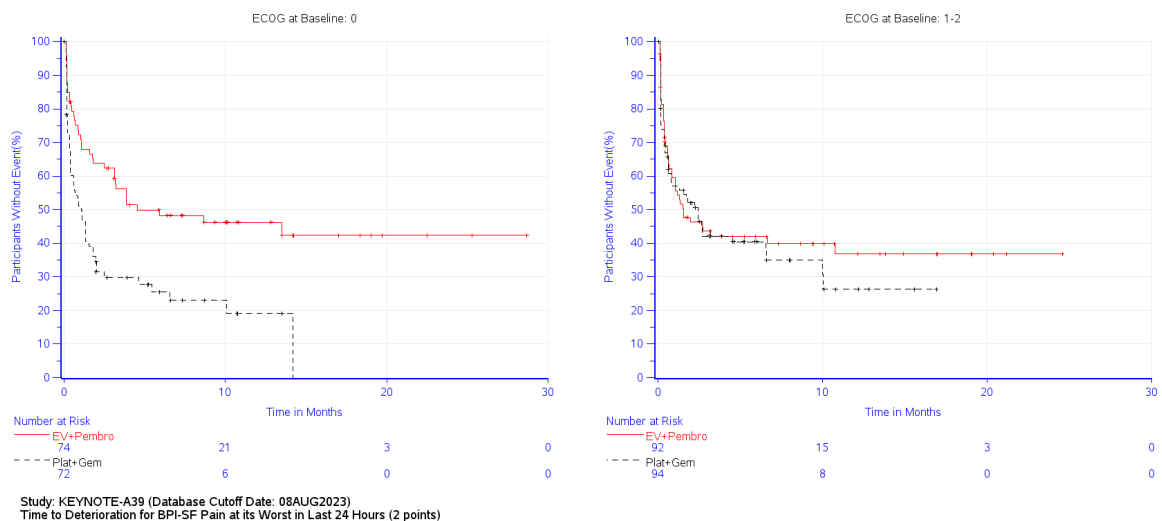


Abbildung 4G-133: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zu Baseline für die Symptomskala Stärkster Schmerz der vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39

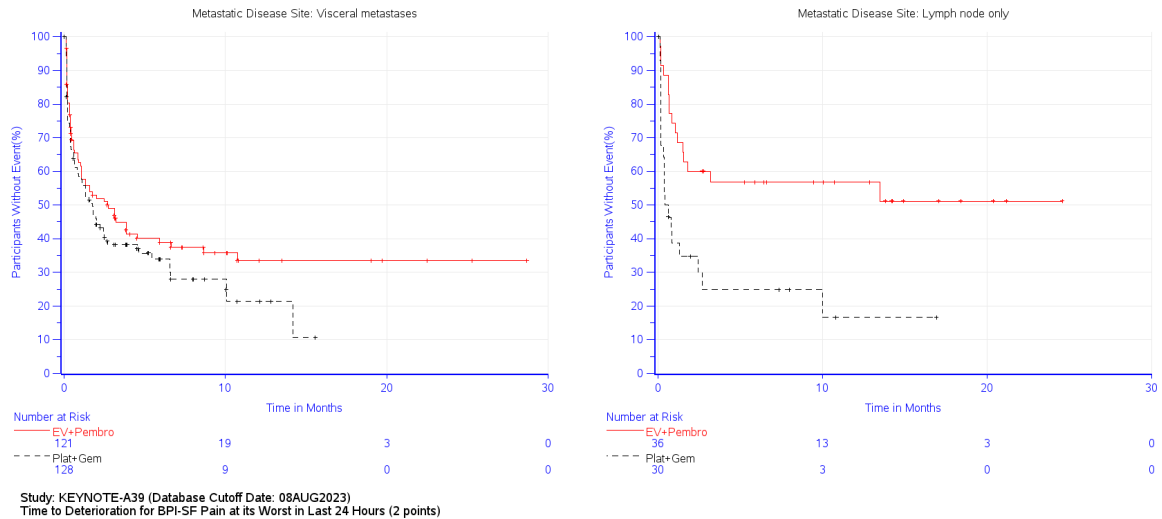


Abbildung 4G-134: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für die Symptomskala Stärkster Schmerz der vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39

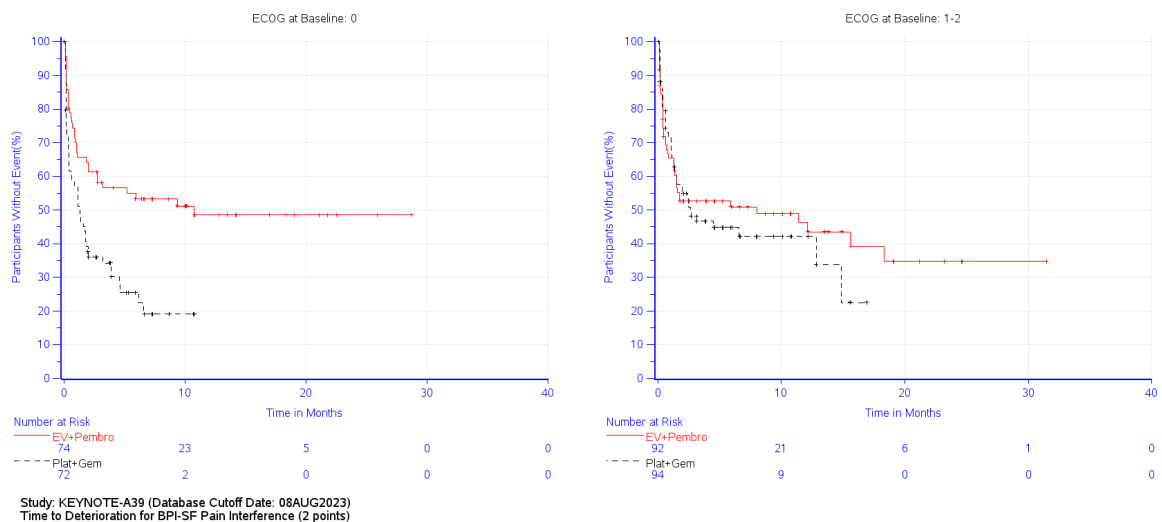


Abbildung 4G-135: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für die Symptomskala Schmerzbeeinträchtigung des BPI-SF der Studie KEYNOTE A39

Gesundheitsbezogene Lebensqualität

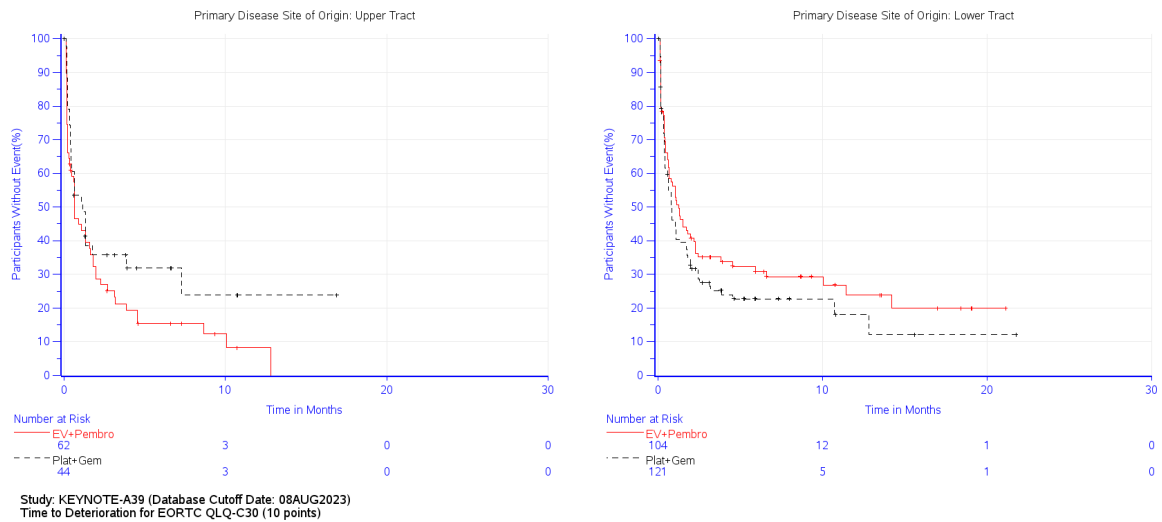


Abbildung 4G-136: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den Globalen Gesundheitsstatus des EORTC QLQ-C30 der Studie KEYNOTE A39

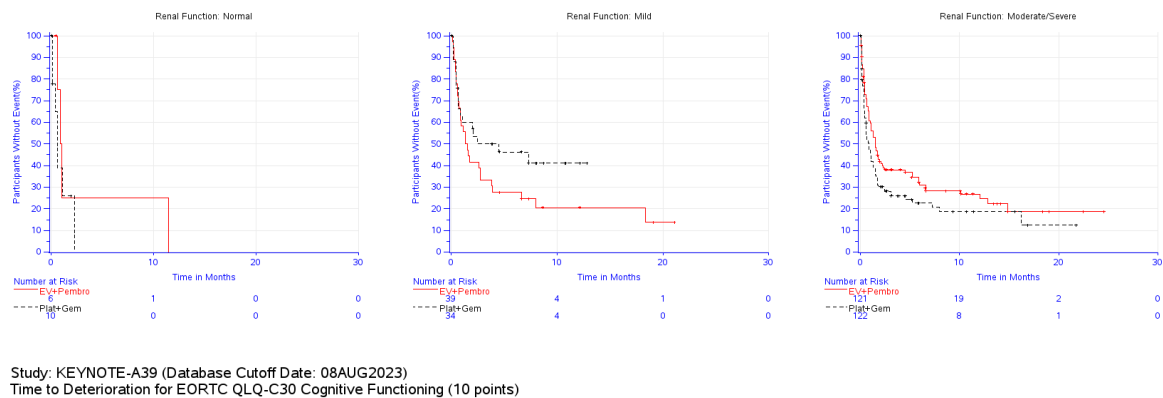


Abbildung 4G-137: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die Funktionsskala Kognitive Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

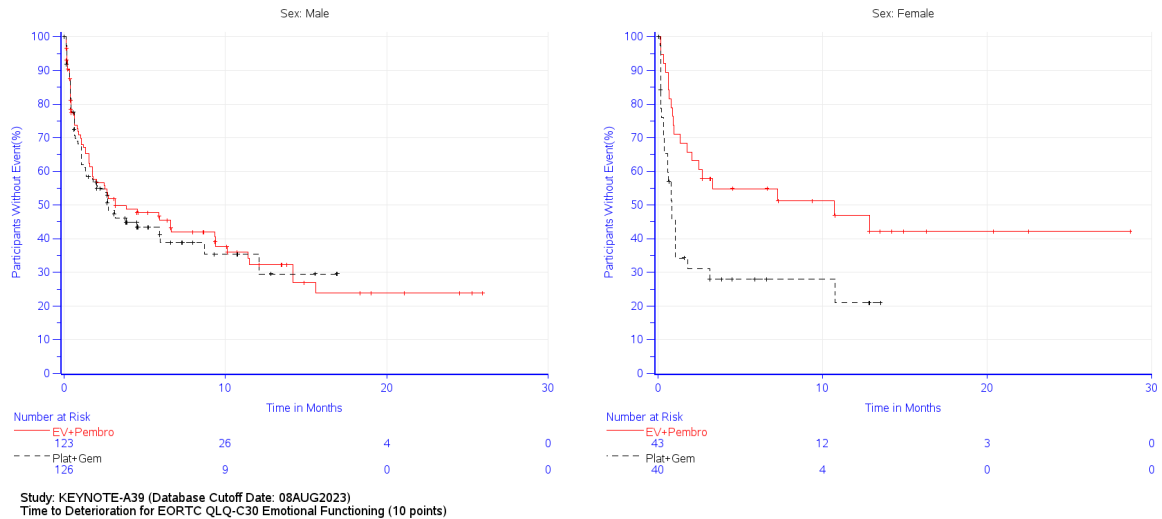


Abbildung 4G-138: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Funktionsskala Emotionale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

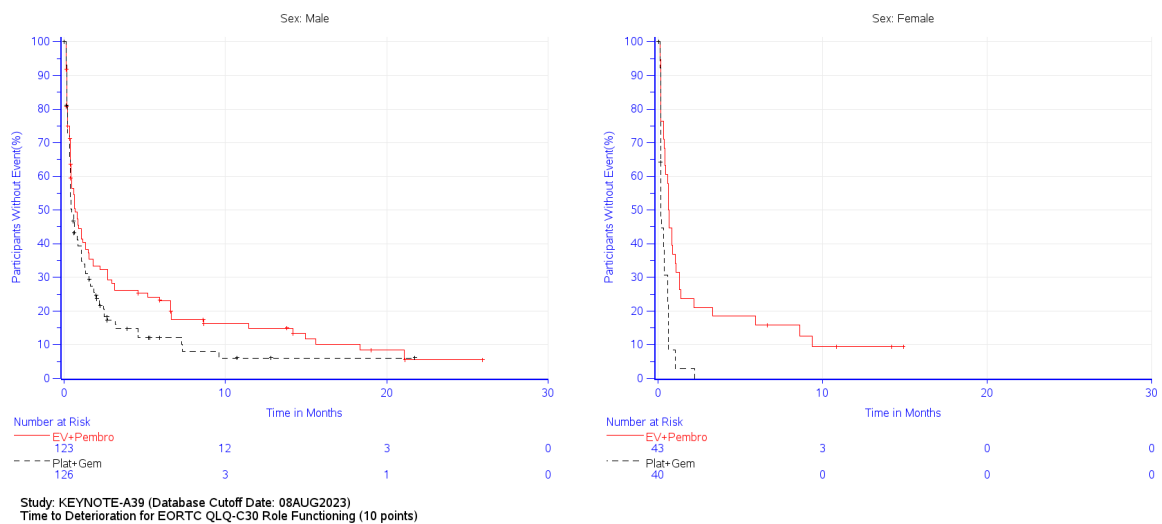


Abbildung 4G-139: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Funktionsskala Rollenfunktion des EORTC QLQ-C30 der Studie KEYNOTE A39

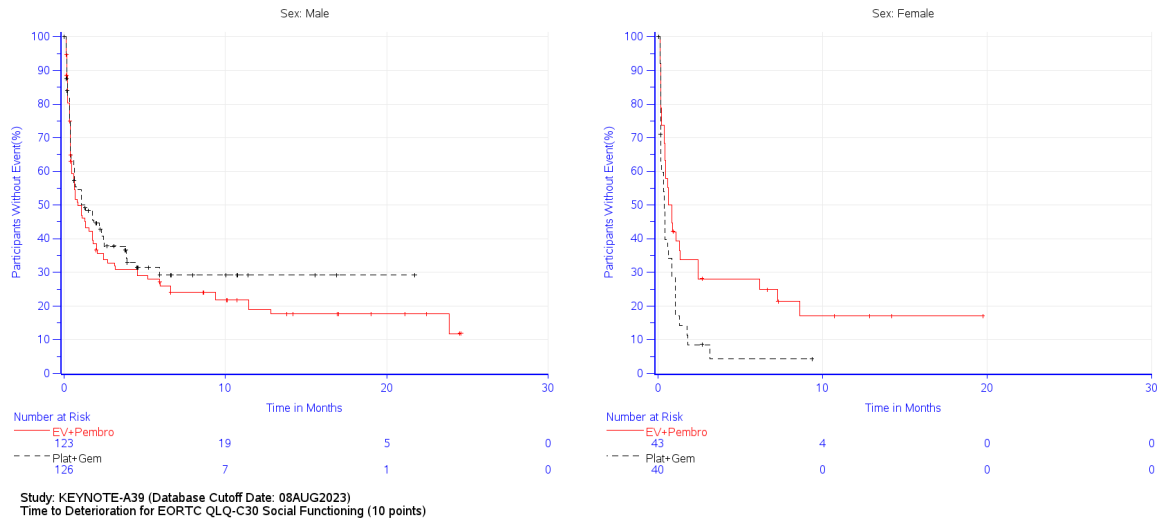


Abbildung 4G-140: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Nebenwirkungen

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

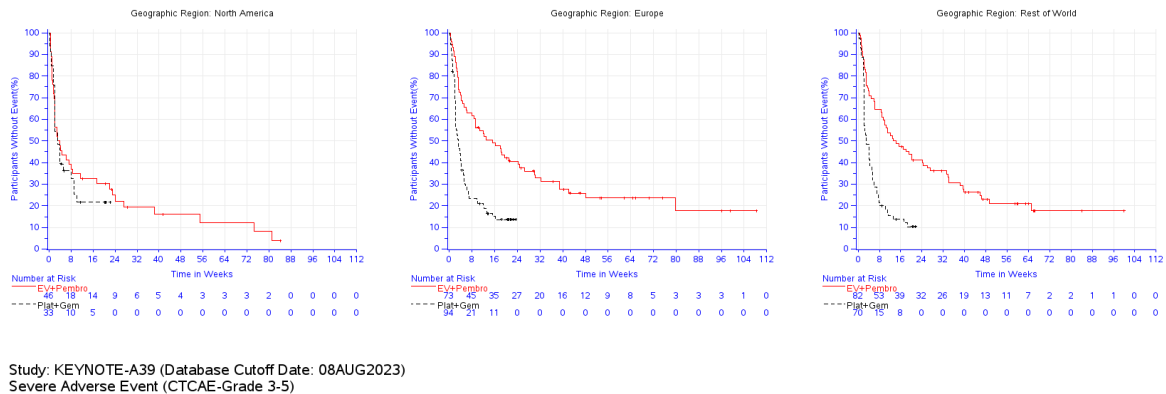


Abbildung 4G-141: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) der Studie KEYNOTE A39

Unerwünschte Ereignisse gesamt (SOC und PT)

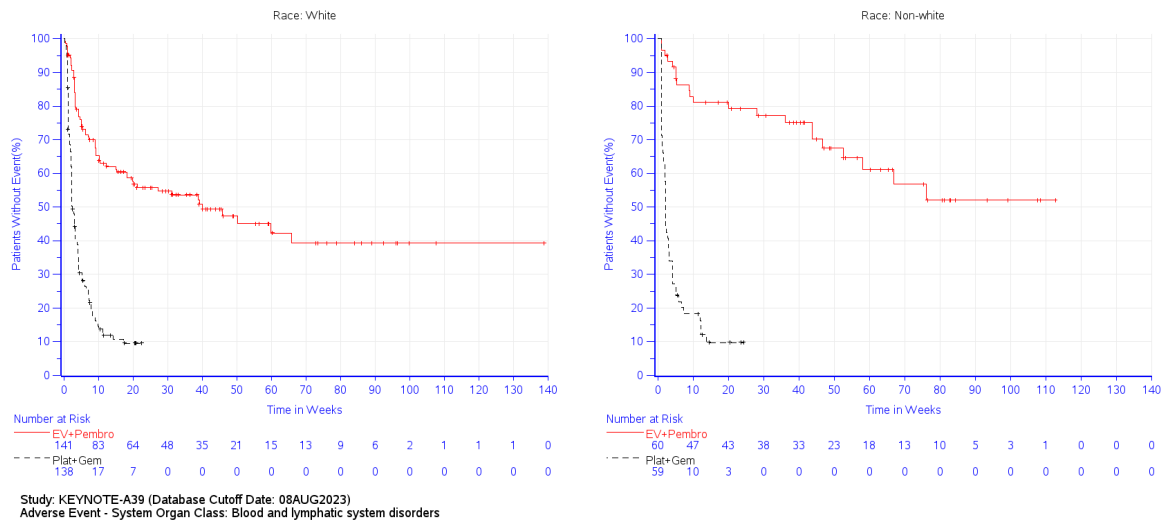


Abbildung 4G-142: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Erkrankungen des Blutes und des Lymphsystems für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

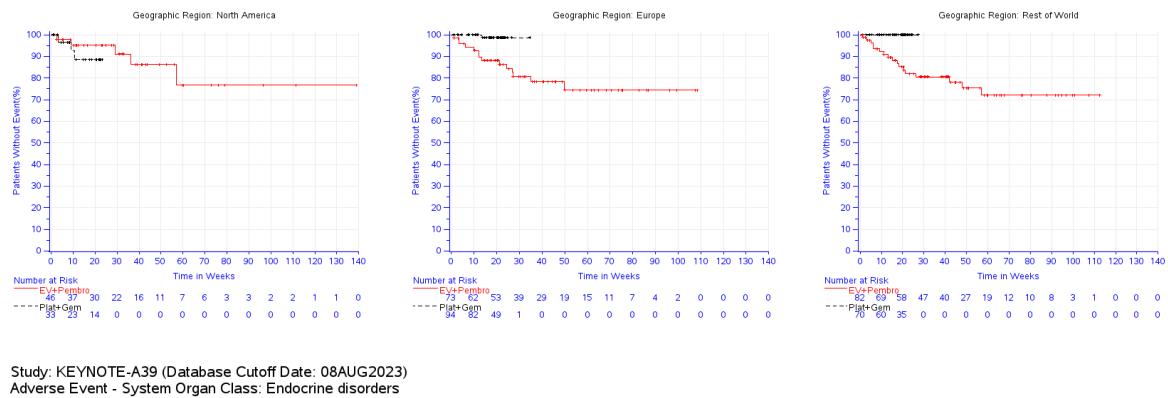


Abbildung 4G-143: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für die SOC Endokrine Erkrankungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

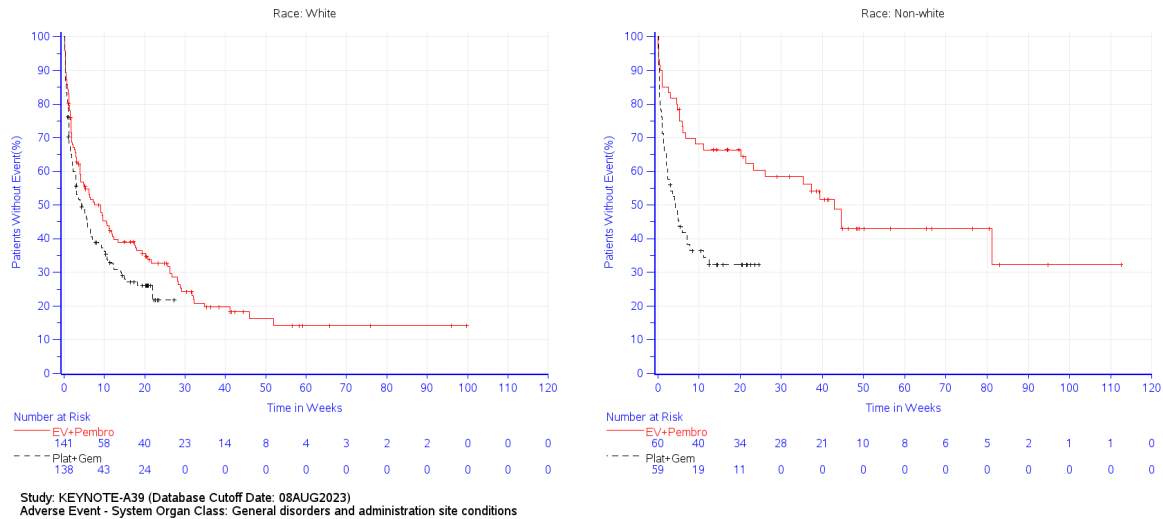


Abbildung 4G-144: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für die SOC Allgemeine Erkrankungen und Beschwerden am Verabreichungsort für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

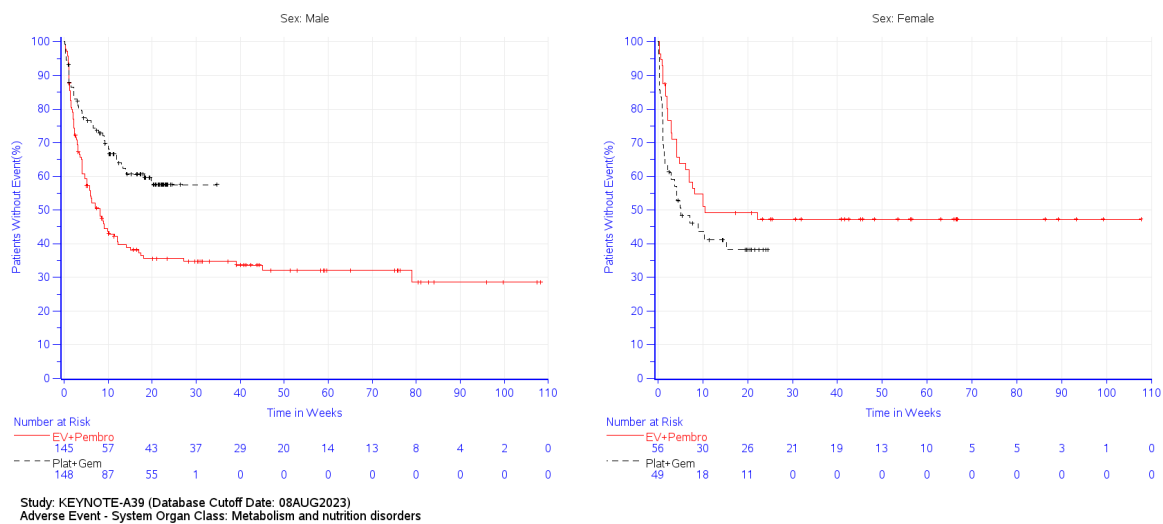
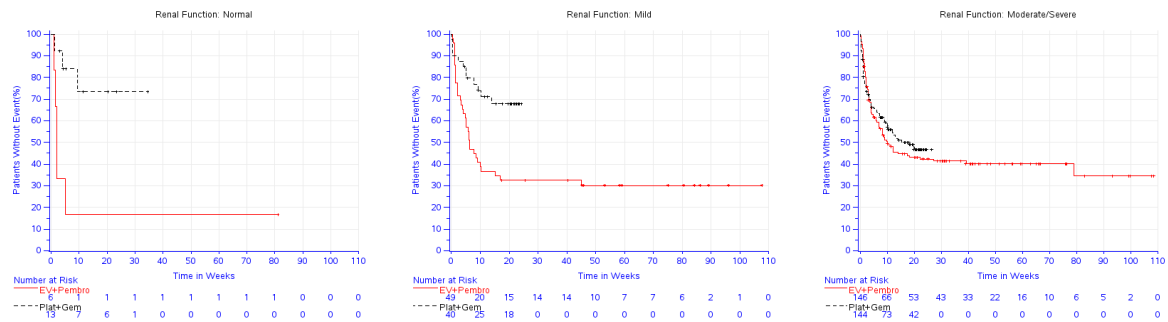


Abbildung 4G-145: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die SOC Stoffwechsel- und Ernährungsstörungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - System Organ Class: Metabolism and nutrition disorders

Abbildung 4G-146: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die SOC Stoffwechsel- und Ernährungsstörungen für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

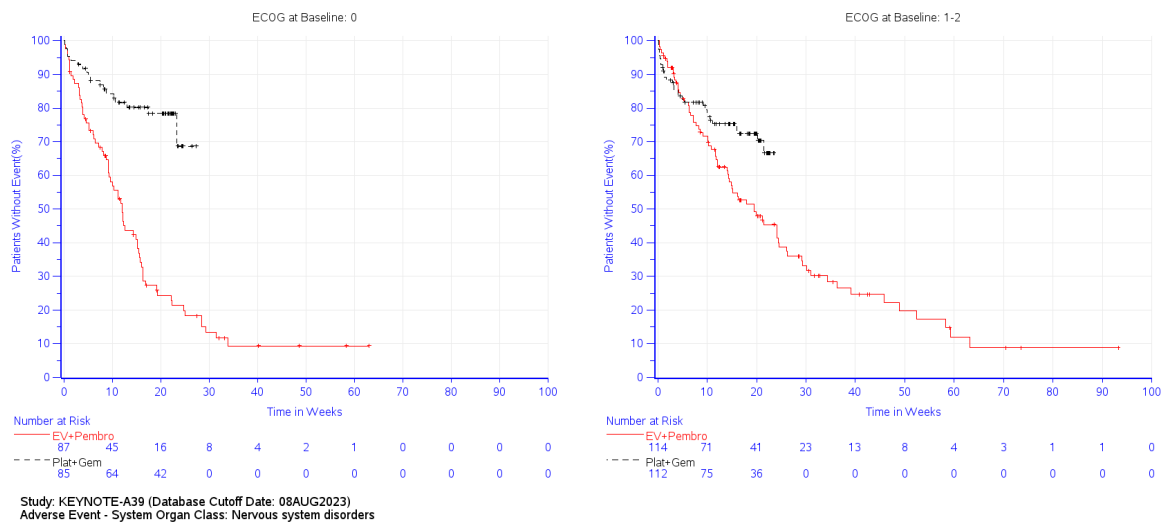
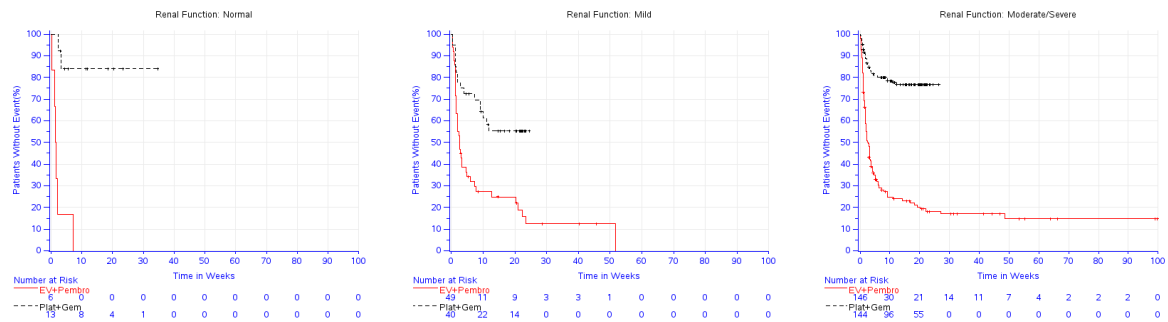
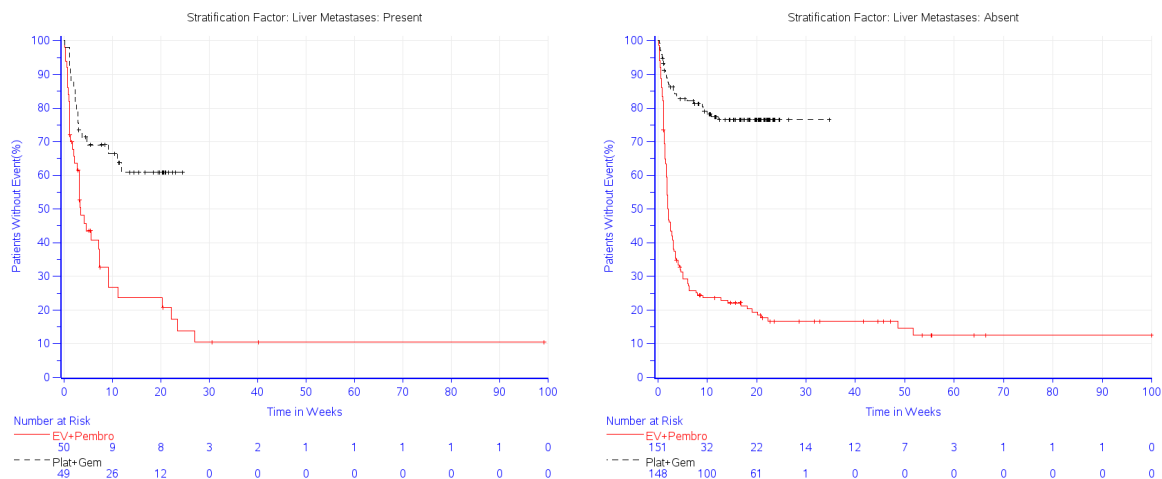


Abbildung 4G-147: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für die SOC Erkrankungen des Nervensystems für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39



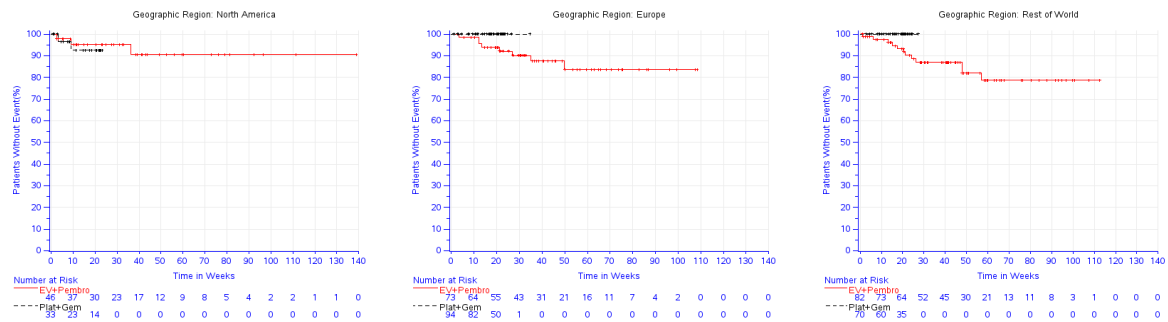
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - System Organ Class: Skin and subcutaneous tissue disorders

Abbildung 4G-148: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die SOC Erkrankungen der Haut und des Unterhautgewebes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39



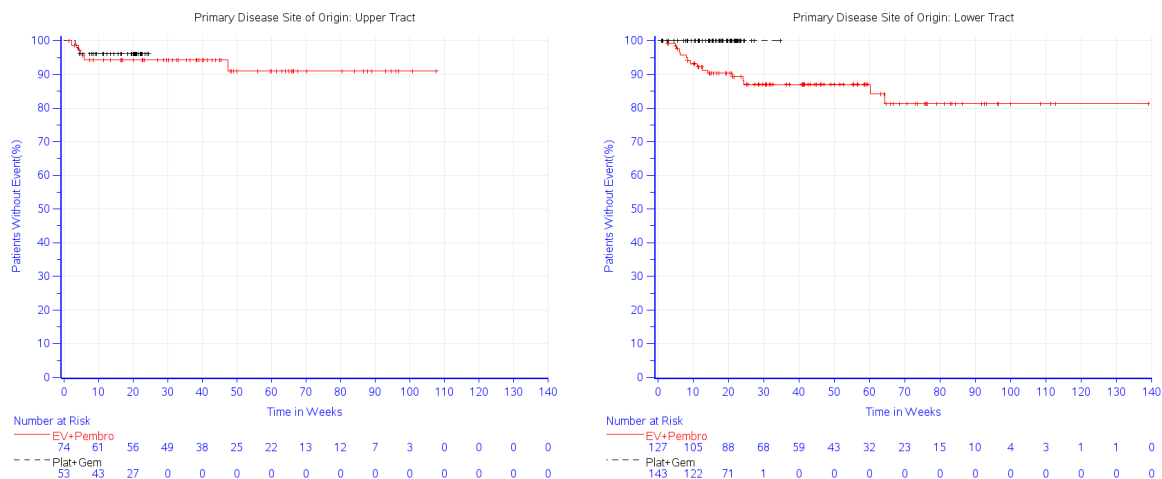
Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - System Organ Class: Skin and subcutaneous tissue disorders

Abbildung 4G-149: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die SOC Erkrankungen der Haut und des Unterhautgewebes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Hypothyroidism

Abbildung 4G-150: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Hypothyreose für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39



Study: KEYNOTE-A39 (Database Cutoff Date: 08AUG2023)
Adverse Event - Preferred Term: Dry eye

Abbildung 4G-151: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Trockenes Auge für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

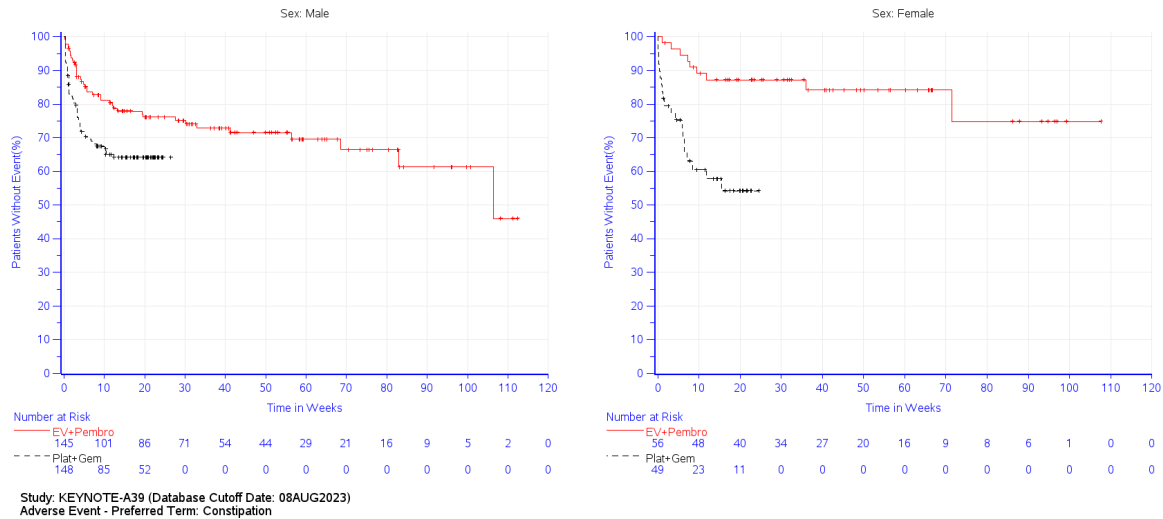


Abbildung 4G-152: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Obstipation für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

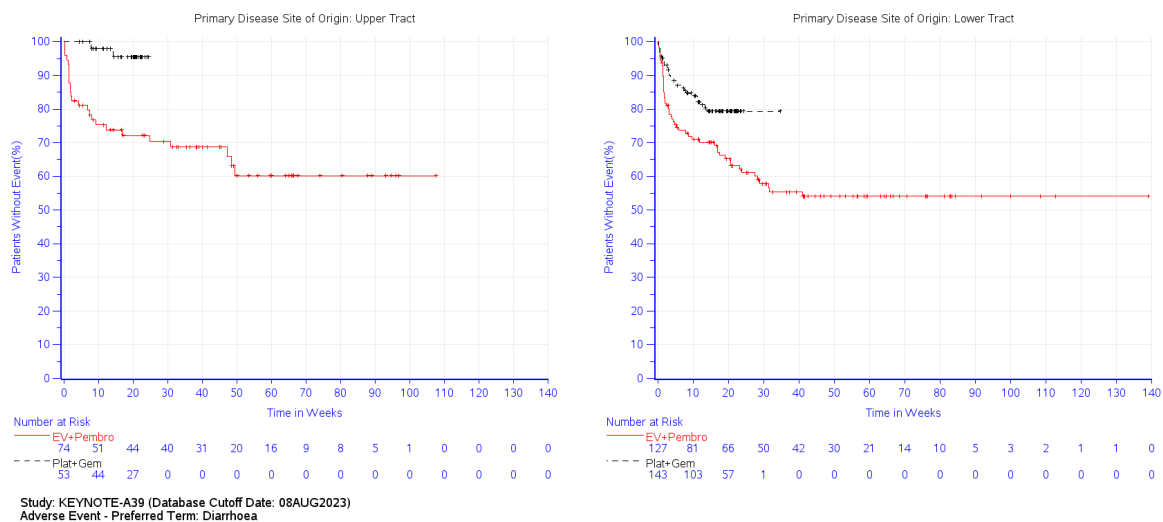


Abbildung 4G-153: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Diarrhoe für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

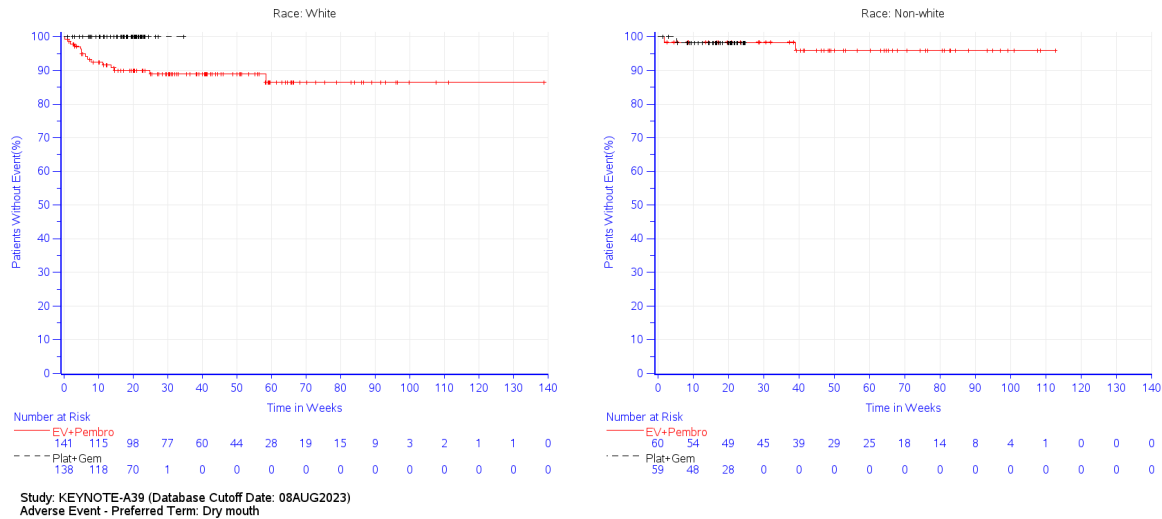


Abbildung 4G-154: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Mundtrockenheit für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

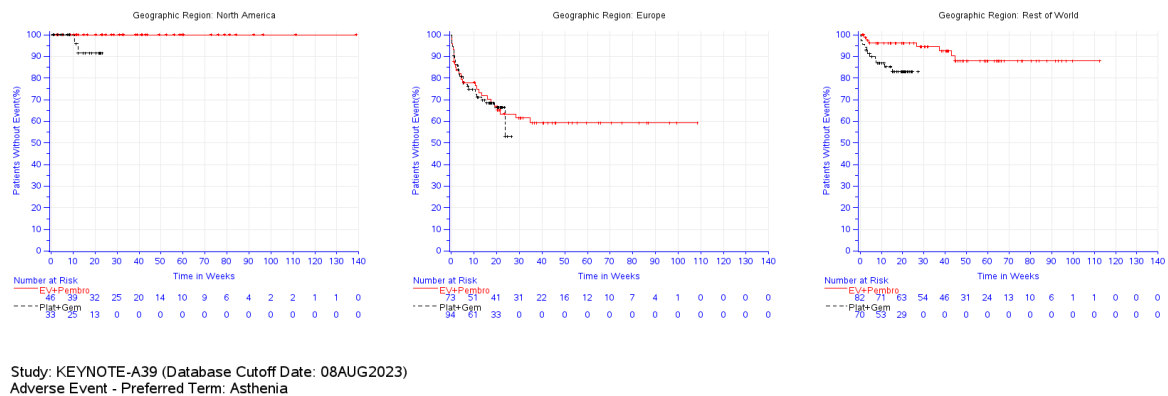


Abbildung 4G-155: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Asthenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

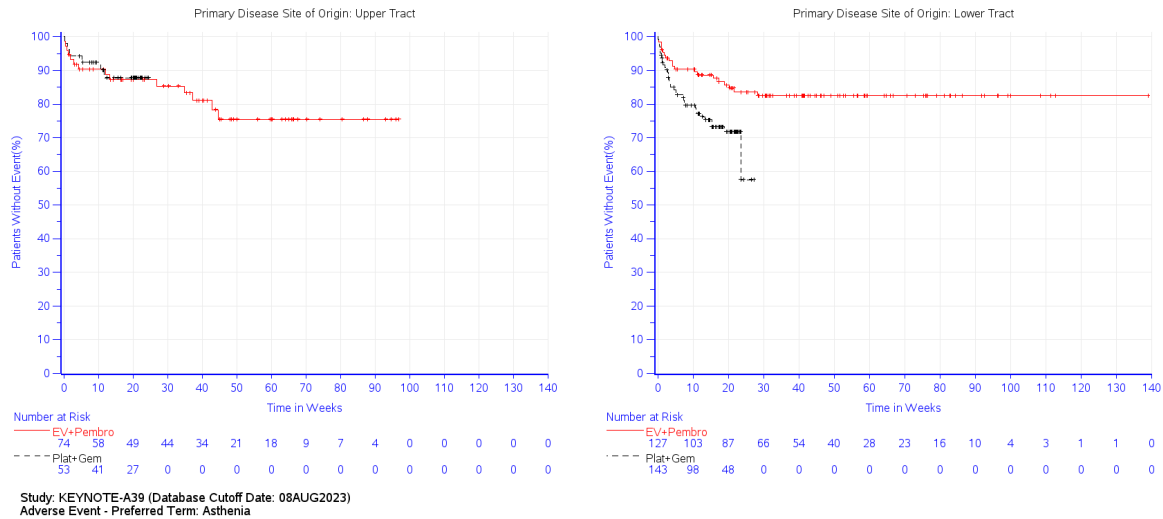


Abbildung 4G-156: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Asthenie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

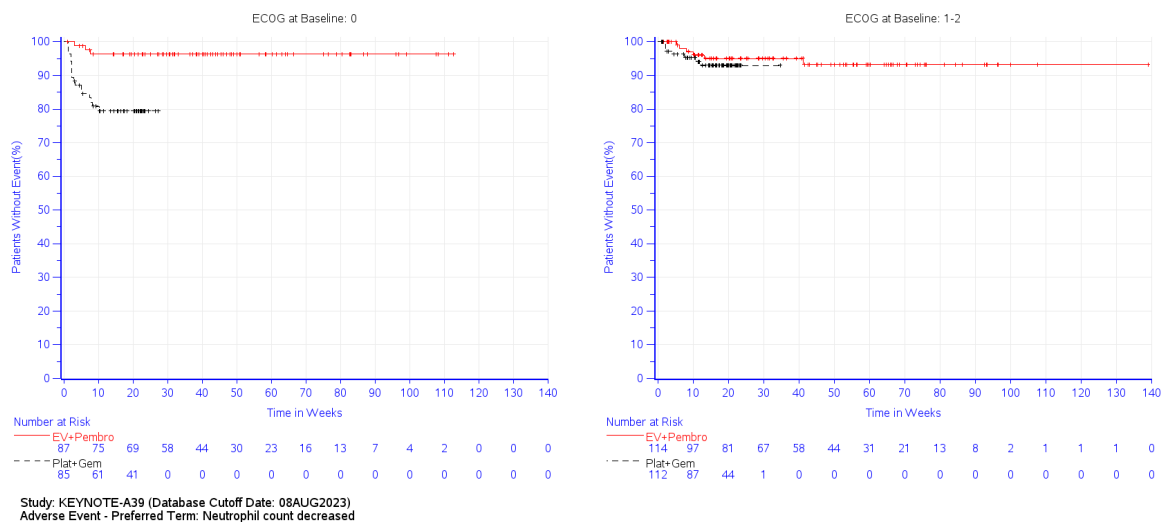


Abbildung 4G-157: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für den PT Neutrophilenzahl erniedrigt für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

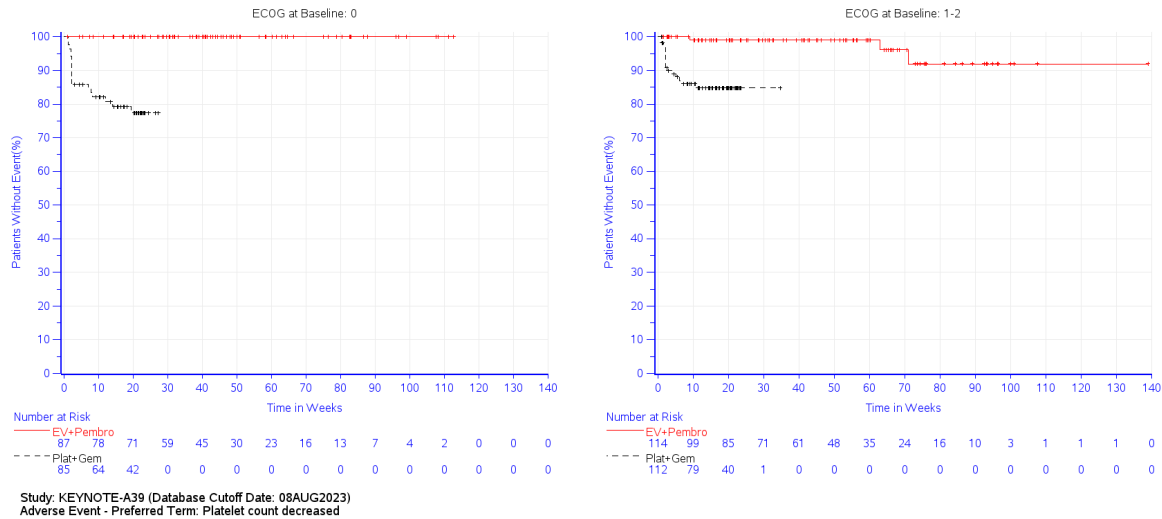


Abbildung 4G-158: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für den PT Thrombozytenzahl vermindert für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

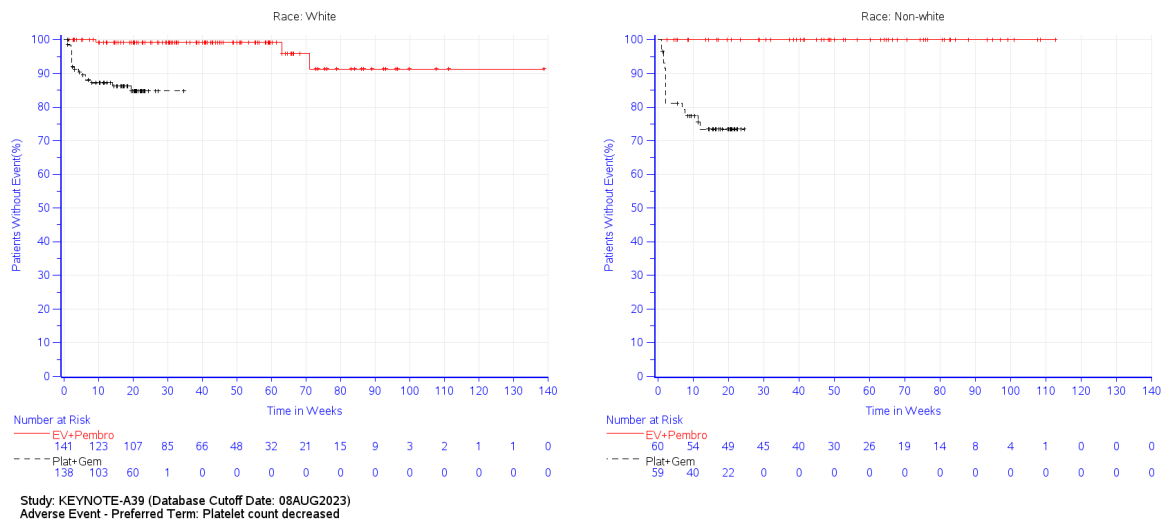


Abbildung 4G-159: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Thrombozytenzahl vermindert für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

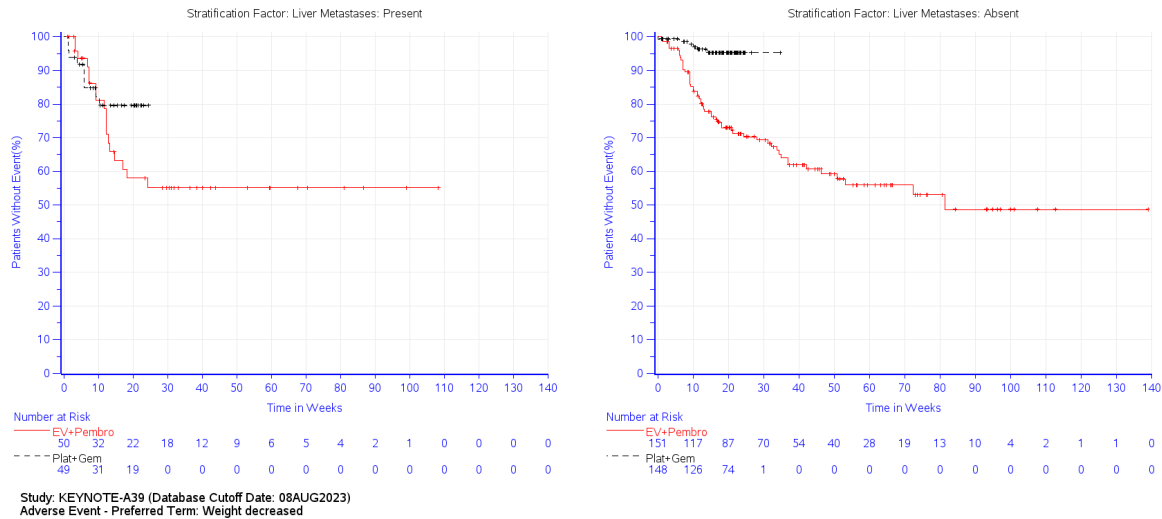


Abbildung 4G-160: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Gewicht erniedrigt für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

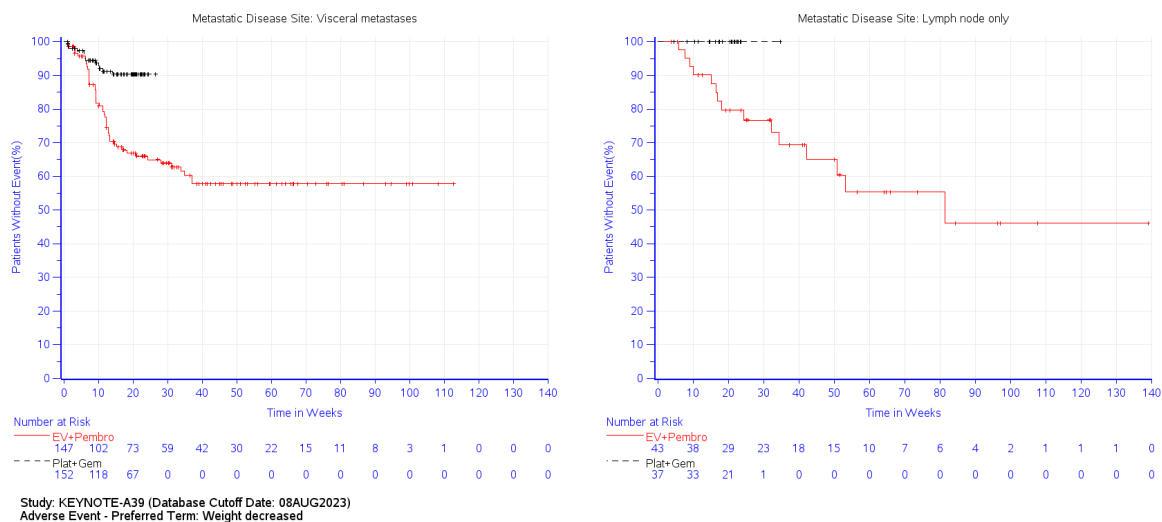


Abbildung 4G-161: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Gewicht erniedrigt für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

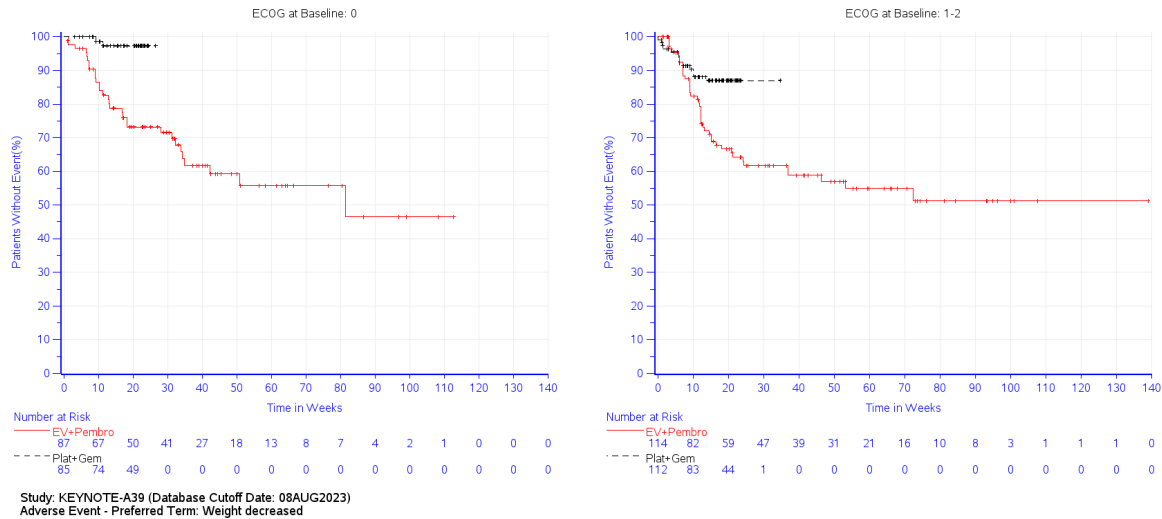


Abbildung 4G-162: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für den PT Gewicht erniedrigt für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

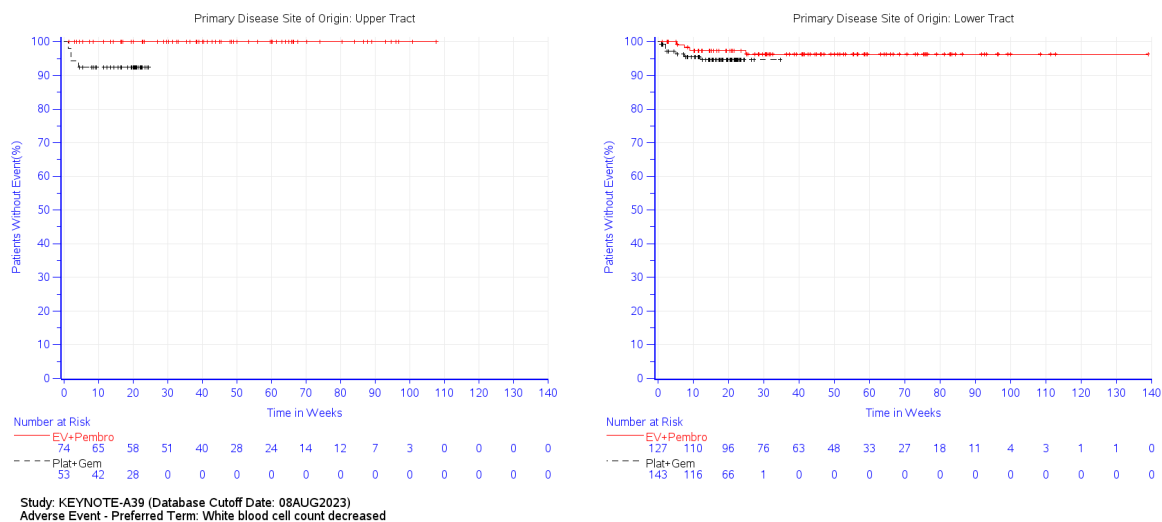


Abbildung 4G-163: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation des Primärtumors für den PT Leukozytenzahl erniedrigt für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

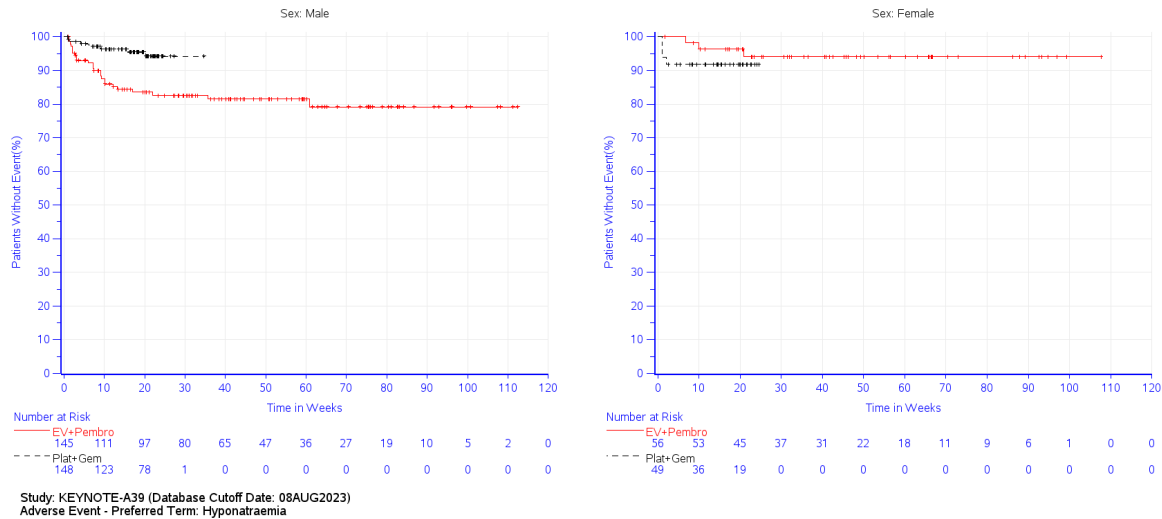


Abbildung 4G-164: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Hyponatramie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

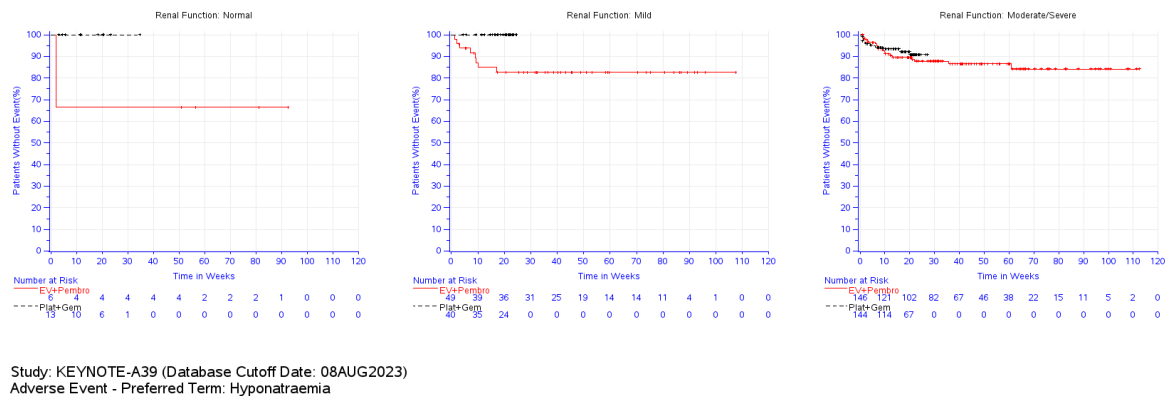


Abbildung 4G-165: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für den PT Hyponatramie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

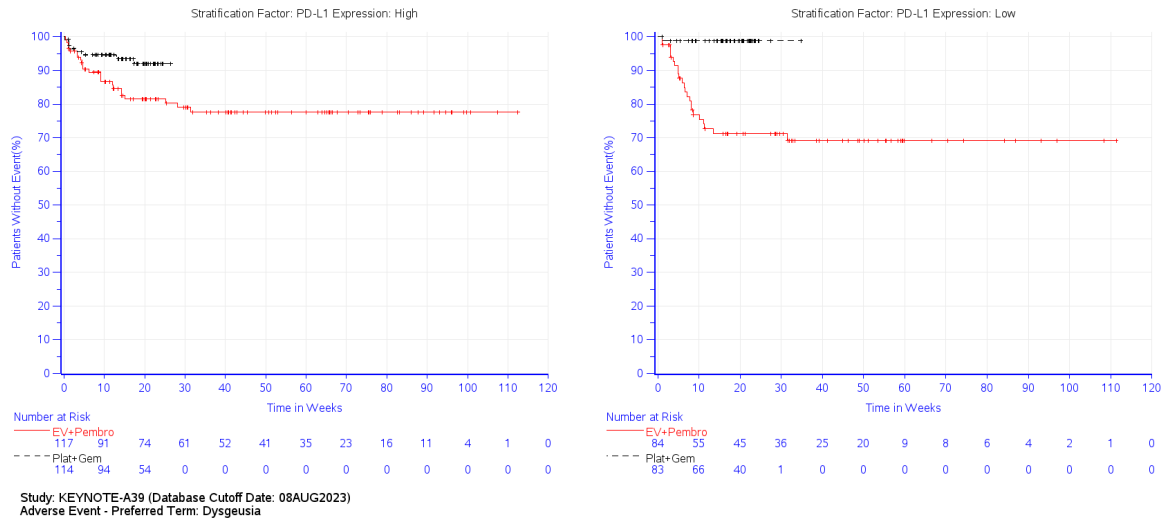


Abbildung 4G-166: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Dysgeusie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

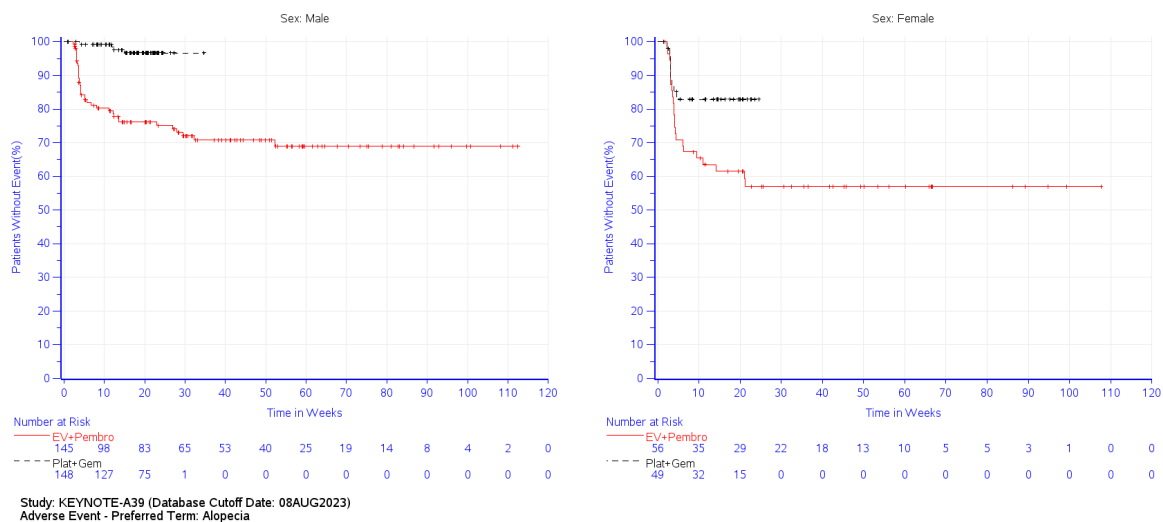


Abbildung 4G-167: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Alopecie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

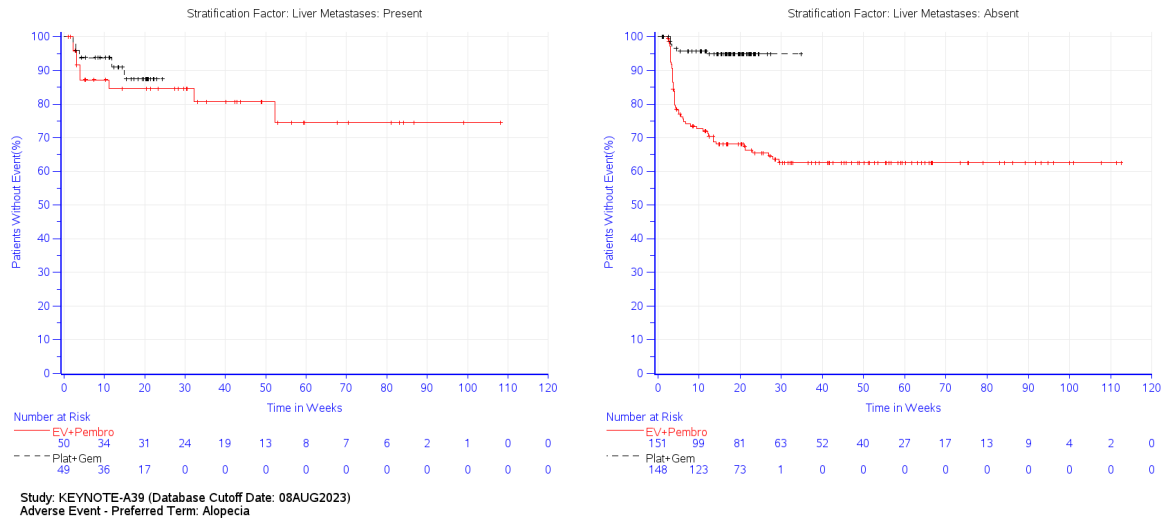


Abbildung 4G-168: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für den PT Alopecie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

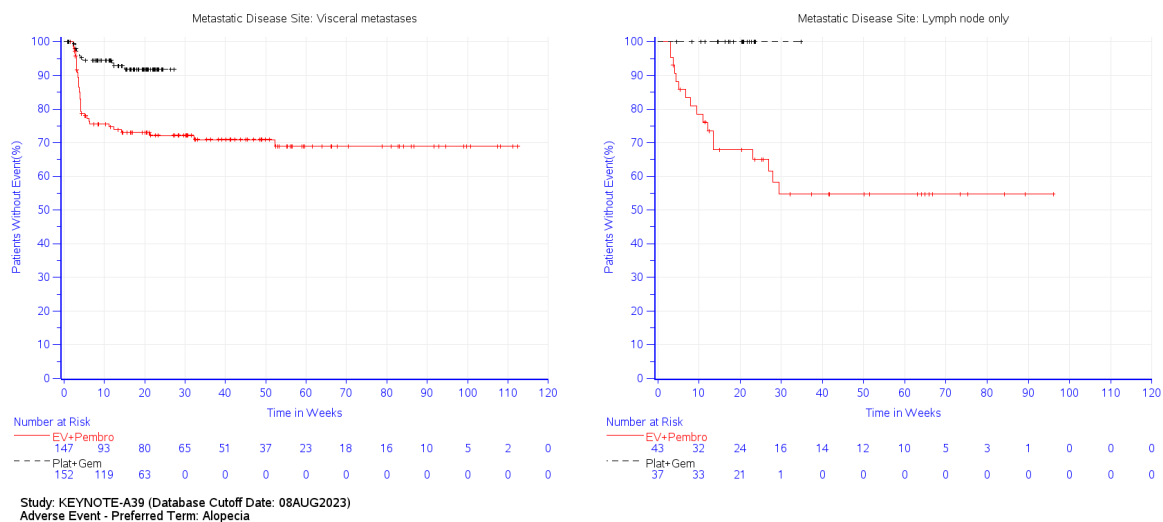


Abbildung 4G-169: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Alopecie für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

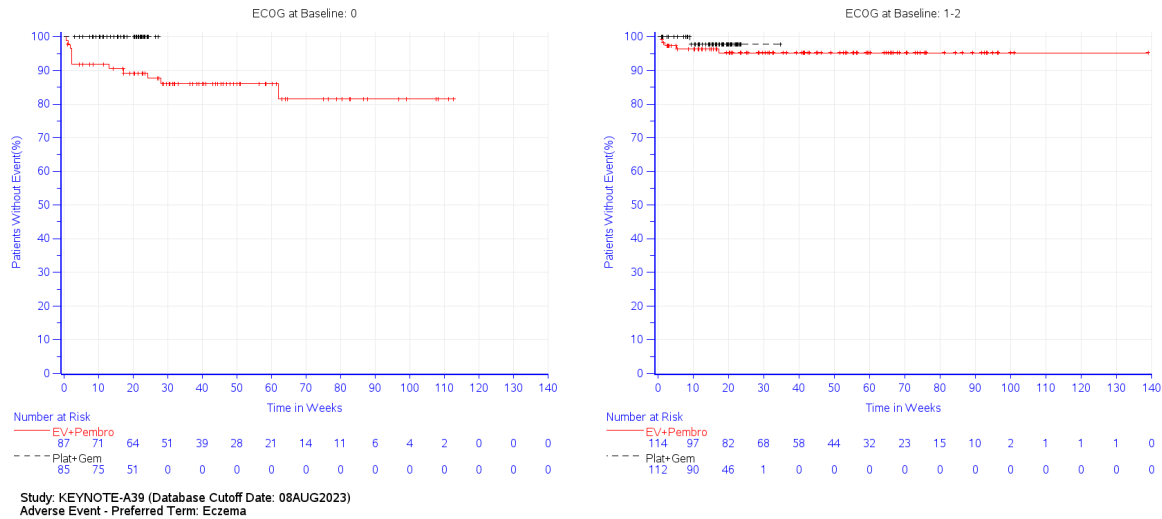


Abbildung 4G-170: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für den PT Ekzem für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

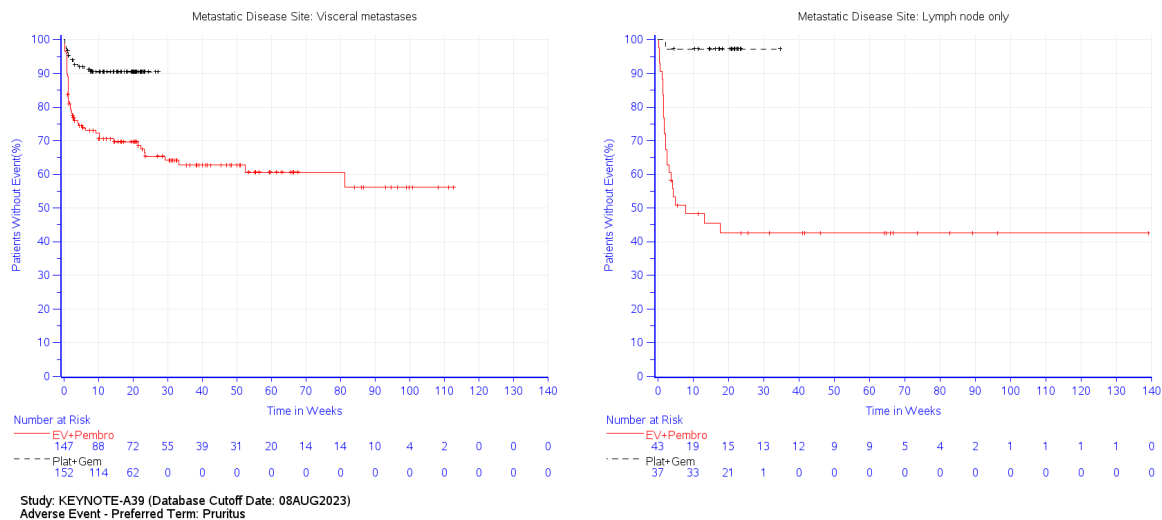


Abbildung 4G-171: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Juckreiz für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

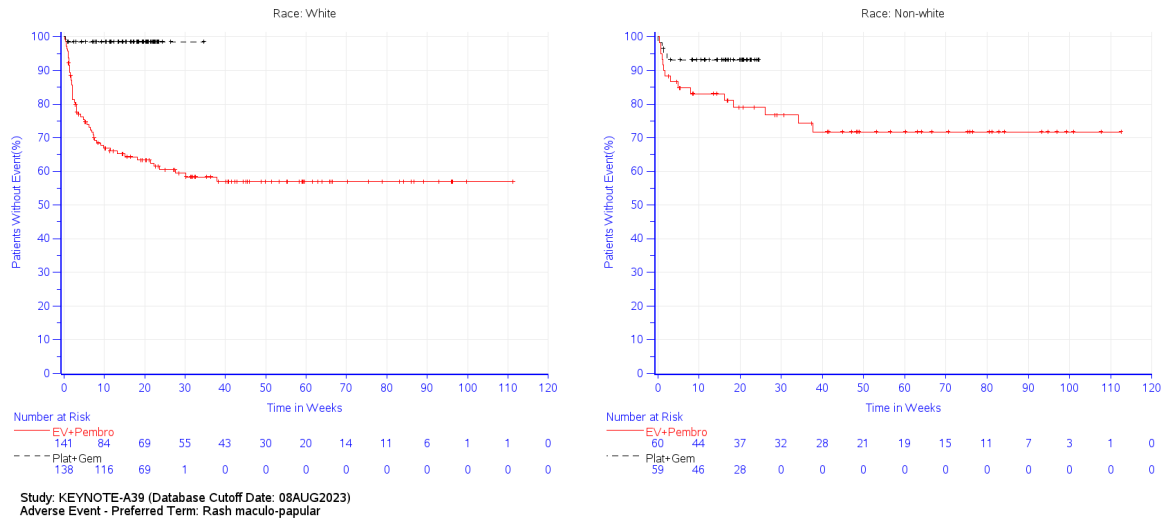


Abbildung 4G-172: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Abstammung für den PT Ausschlag makulo-papuloes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

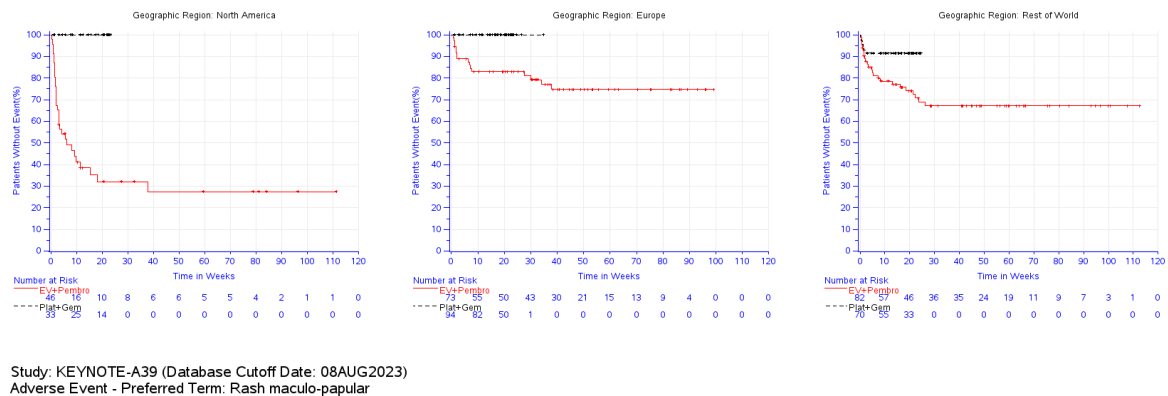


Abbildung 4G-173: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den PT Ausschlag makulo-papuloes für Unerwünschte Ereignisse gesamt (SOC und PT) der Studie KEYNOTE A39

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT)

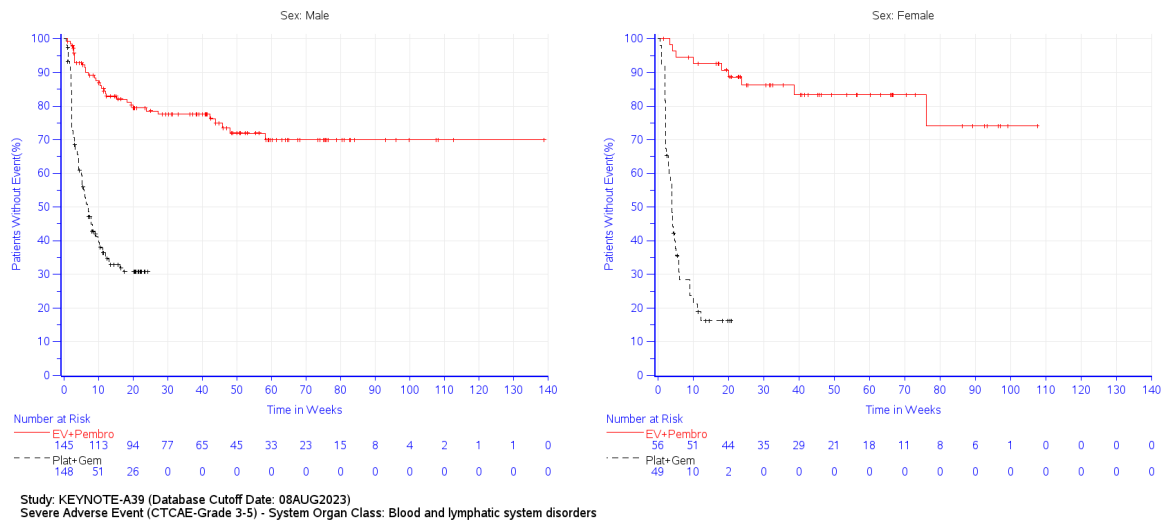


Abbildung 4G-174: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die SOC Erkrankungen des Blutes und des Lymphsystems für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

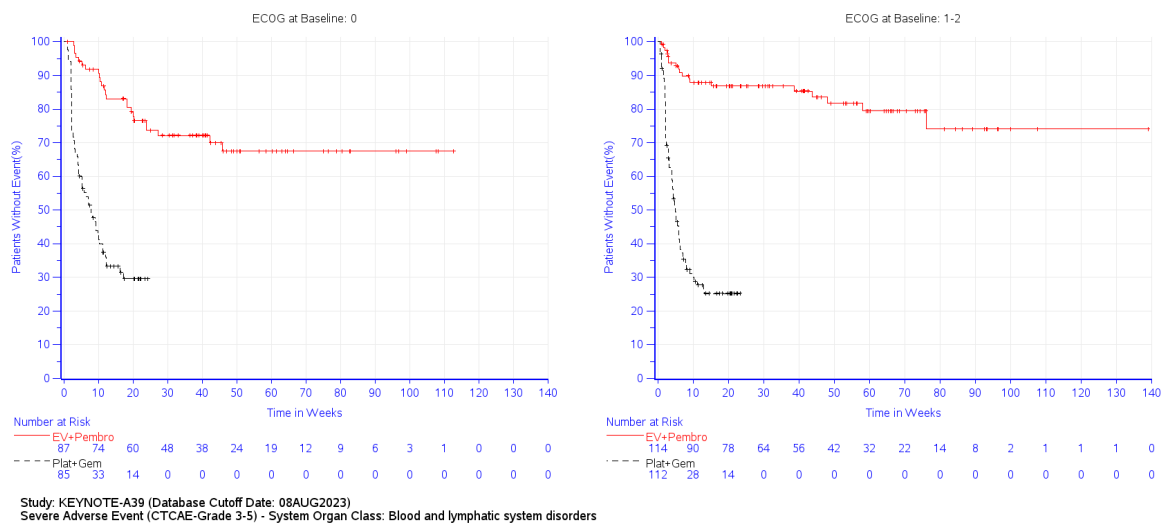


Abbildung 4G-175: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für die SOC Erkrankungen des Blutes und des Lymphsystems für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

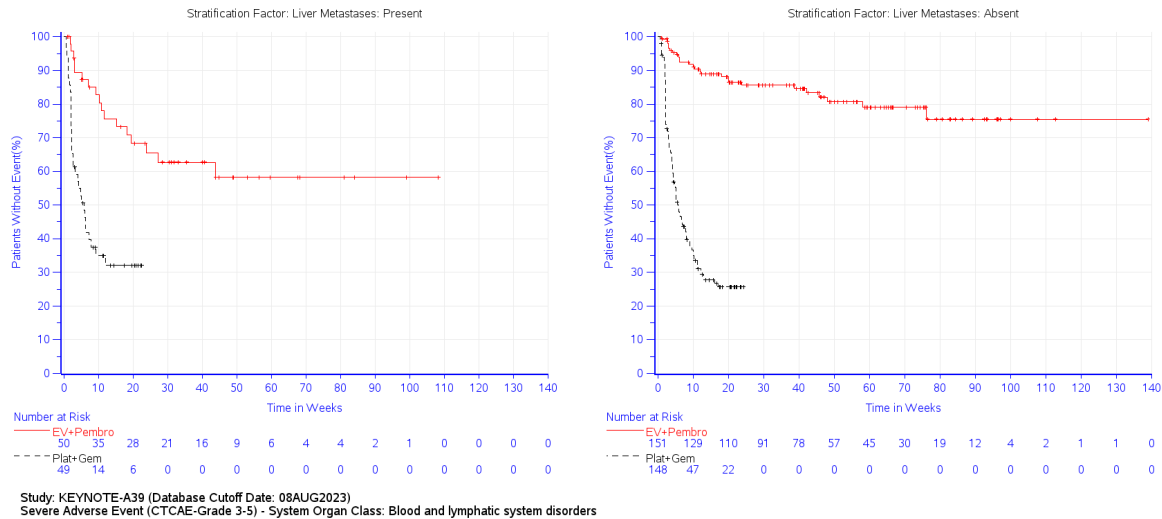


Abbildung 4G-176: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lebermetastasen für die SOC Erkrankungen des Blutes und des Lymphsystems für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

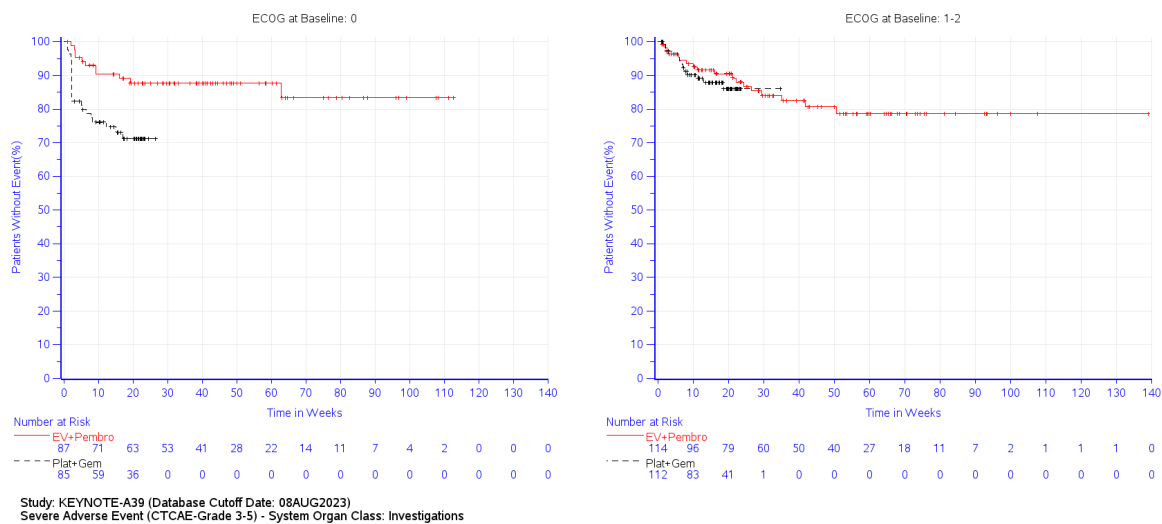


Abbildung 4G-177: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus zur Baseline für die SOC Untersuchungen für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

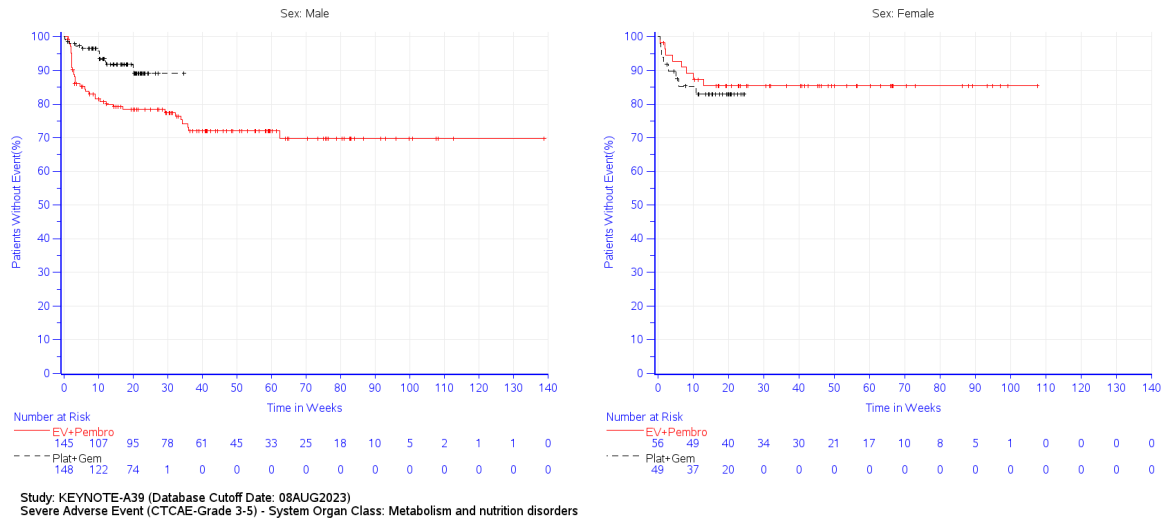


Abbildung 4G-178: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für die SOC Stoffwechsel- und Ernährungsstörungen für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

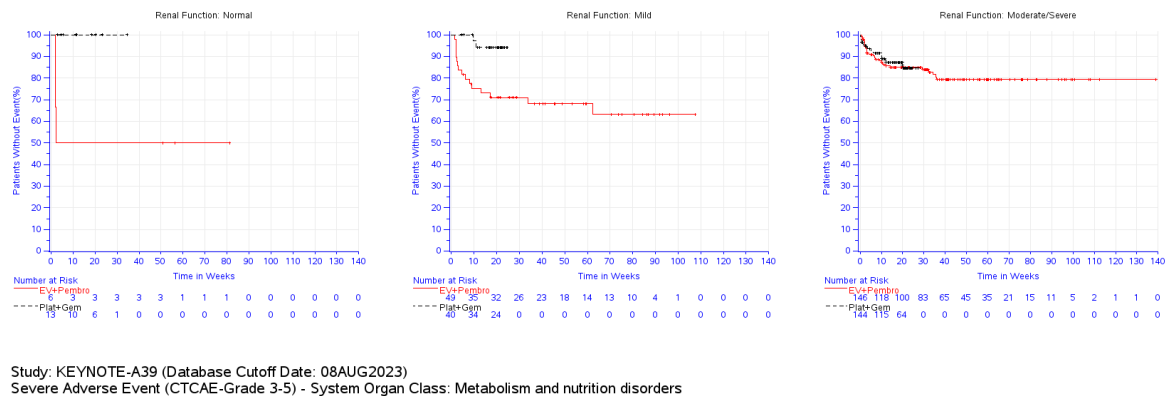


Abbildung 4G-179: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Nierenfunktion für die SOC Stoffwechsel- und Ernährungsstörungen für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

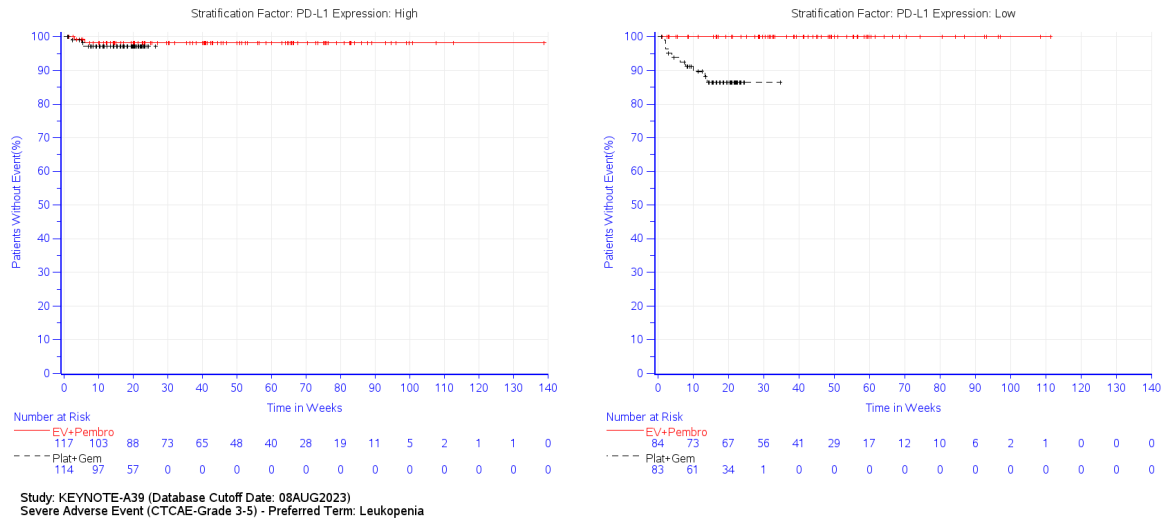


Abbildung 4G-180: Kaplan-Meier-Kurve für die Subgruppenanalyse nach PD-L1 Expression für den PT Leukopenie für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

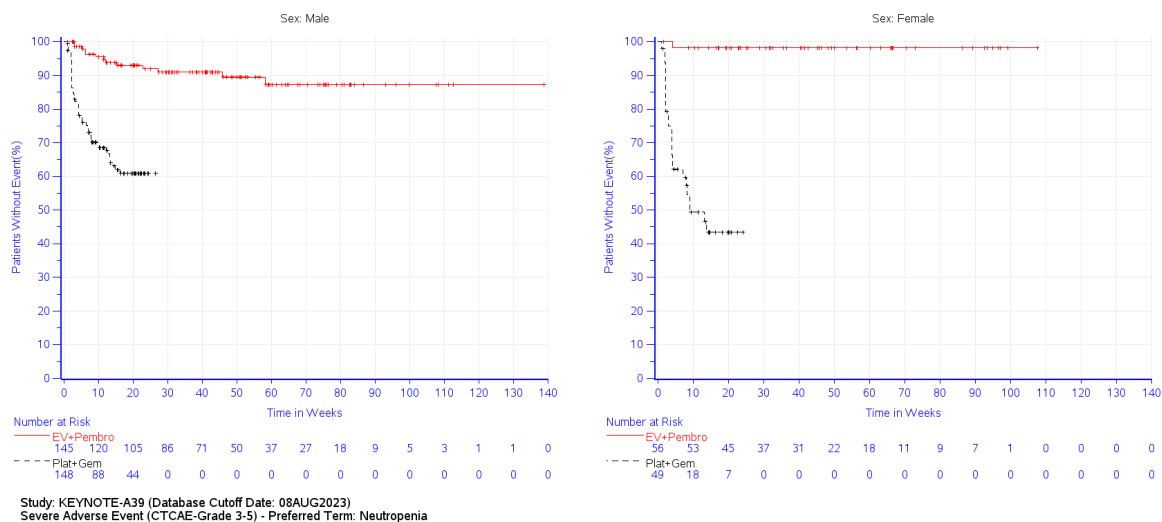


Abbildung 4G-181: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Geschlecht für den PT Neutropenie für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

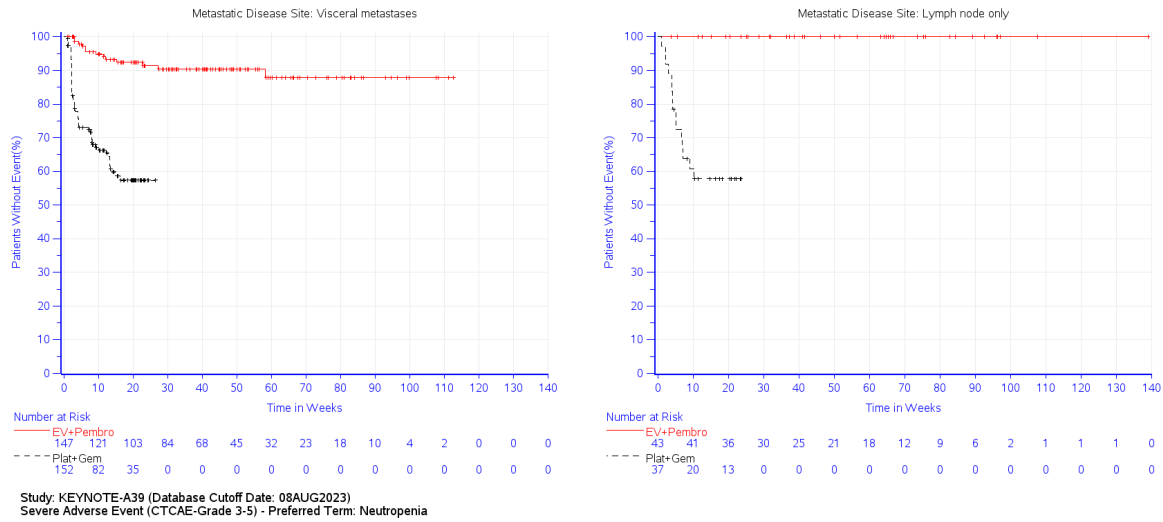


Abbildung 4G-182: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Lokalisation der Metastasierung für den PT Neutropenie für Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

Anhang 4-G7: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest ($p \geq 0,05$)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Ergebnisse der Subgruppenanalysen, für die ein nicht signifikanter Interaktionstest ($p \geq 0,05$) vorliegt, dargestellt.

Mortalität

Cisplatin geeignet

Gesamtüberleben

Tabelle 4G-45: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Overall Survival									
Age									
< 65	105	28 (26.7)	Not reached [22.8; -]	106	41 (38.7)	31.4 [17.0; -]	0.56 [0.34; 0.92]	0.022	0.737
≥ 65	135	41 (30.4)	31.5 [25.4; -]	136	69 (50.7)	16.6 [13.6; 18.4]	0.51 [0.34; 0.75]	< 0.001	
Race									
White	166	53 (31.9)	31.5 [22.8; -]	149	75 (50.3)	16.7 [15.1; 19.7]	0.50 [0.35; 0.71]	< 0.001	0.784
Non-white	74	16 (21.6)	Not reached [-; -]	93	35 (37.6)	27.5 [15.1; -]	0.58 [0.32; 1.05]	0.073	
Geographic Region									
North America	57	22 (38.6)	25.6 [21.2; -]	51	21 (41.2)	27.5 [18.4; -]	0.95 [0.51; 1.78]	0.870	0.063
Europe	98	31 (31.6)	Not reached [20.7; -]	102	55 (53.9)	13.9 [11.4; 18.4]	0.43 [0.27; 0.68]	< 0.001	
Rest of World	85	16 (18.8)	Not reached [-; -]	89	34 (38.2)	19.3 [15.3; -]	0.40 [0.22; 0.73]	0.003	
Sex									
Male	198	54 (27.3)	31.5 [26.1; -]	185	83 (44.9)	18.4 [16.6; -]	0.54 [0.38; 0.76]	< 0.001	0.863
Female	42	15 (35.7)	22.8 [19.2; -]	57	27 (47.4)	15.1 [11.6; -]	0.60 [0.31; 1.16]	0.128	
ECOG at Baseline									
0	136	28 (20.6)	Not reached [-; -]	128	50 (39.1)	22.1 [16.6; -]	0.47 [0.29; 0.75]	0.001	0.507
1-2	104	41 (39.4)	25.6 [21.2; -]	113	60 (53.1)	16.4 [12.3; 18.4]	0.59 [0.39; 0.88]	0.010	
Primary Disease Site of Origin									
Upper Tract	61	18 (29.5)	Not reached [22.8; -]	49	17 (34.7)	21.1 [15.1; -]	0.77 [0.39; 1.54]	0.460	0.307
Lower Tract	177	50 (28.2)	31.5 [25.4; -]	193	93 (48.2)	17.7 [15.1; 22.1]	0.49 [0.35; 0.69]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Overall Survival									
Stratification Factor: Liver Metastases									
Present	48	20 (41.7)	25.6 [13.8; -]	48	28 (58.3)	15.1 [10.4; 21.1]	0.61 [0.34; 1.10]	0.101	0.621
Absent	192	49 (25.5)	Not reached [25.4; -]	194	82 (42.3)	18.4 [16.6; -]	0.51 [0.36; 0.73]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	139	41 (29.5)	31.5 [25.4; -]	140	61 (43.6)	18.4 [15.3; -]	0.59 [0.39; 0.87]	0.009	0.501
Low	101	28 (27.7)	Not reached [22.3; -]	102	49 (48.0)	16.6 [15.1; 27.5]	0.47 [0.30; 0.76]	0.002	
Metastatic Disease Site									
Visceral metastases	170	53 (31.2)	31.5 [25.4; -]	161	81 (50.3)	16.7 [15.1; 19.3]	0.54 [0.38; 0.77]	< 0.001	0.590
Lymph node only	60	13 (21.7)	Not reached [21.2; -]	67	25 (37.3)	27.5 [13.7; -]	0.46 [0.24; 0.91]	0.025	
Renal Function									
Normal	78	22 (28.2)	26.1 [22.3; -]	82	37 (45.1)	18.4 [13.1; -]	0.51 [0.30; 0.88]	0.015	0.990
Mild	116	31 (26.7)	Not reached [25.4; -]	122	56 (45.9)	18.4 [15.1; 27.5]	0.55 [0.35; 0.86]	0.008	
Moderate/Severe	46	16 (34.8)	31.5 [14.5; -]	38	17 (44.7)	16.7 [11.6; -]	0.58 [0.28; 1.19]	0.135	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: intention-to-treat population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization using Wald confidence interval. Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1									

Cisplatin ungeeignet

Tabelle 4G-46: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Overall Survival									
Age									
< 65	39	11 (28.2)	Not reached [19.1; -]	29	17 (58.6)	12.2 [9.6; -]	0.26 [0.11; 0.63]	0.003	0.120
≥ 65	163	53 (32.5)	Not reached [20.2; -]	173	99 (57.2)	13.3 [10.7; 16.1]	0.47 [0.33; 0.65]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Overall Survival	N ^b	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	142	51 (35.9)	Not reached [19.9; -]	141	87 (61.7)	12.9 [10.7; 15.5]	0.43 [0.30; 0.62]	< 0.001	0.442
Non-white	60	13 (21.7)	Not reached [-; -]	61	29 (47.5)	15.0 [10.0; -]	0.35 [0.18; 0.69]	0.003	
Geographic Region									
North America	46	18 (39.1)	19.9 [18.4; -]	34	21 (61.8)	13.0 [7.4; 22.0]	0.50 [0.25; 0.99]	0.046	0.591
Europe	74	25 (33.8)	Not reached [19.1; -]	95	55 (57.9)	14.6 [10.3; 17.1]	0.36 [0.21; 0.60]	< 0.001	
Rest of World	82	21 (25.6)	Not reached [-; -]	73	40 (54.8)	12.7 [9.6; 18.8]	0.41 [0.24; 0.71]	0.001	
Sex									
Male	146	47 (32.2)	Not reached [20.4; -]	151	89 (58.9)	12.7 [10.7; 16.6]	0.40 [0.28; 0.58]	< 0.001	0.895
Female	56	17 (30.4)	Not reached [19.9; -]	51	27 (52.9)	13.6 [10.3; -]	0.43 [0.23; 0.82]	0.010	
ECOG at Baseline									
0	87	16 (18.4)	Not reached [22.9; -]	87	44 (50.6)	15.5 [12.1; -]	0.25 [0.13; 0.45]	< 0.001	0.090
1-2	115	48 (41.7)	19.9 [17.7; -]	114	71 (62.3)	11.4 [7.7; 14.7]	0.51 [0.35; 0.75]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	20 (27.0)	Not reached [-; -]	55	28 (50.9)	14.3 [9.5; -]	0.41 [0.23; 0.74]	0.003	0.973
Lower Tract	128	44 (34.4)	Not reached [19.1; -]	146	87 (59.6)	12.7 [10.7; 15.9]	0.42 [0.29; 0.62]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	23 (46.0)	17.7 [13.6; -]	50	38 (76.0)	7.3 [5.8; 10.1]	0.38 [0.22; 0.66]	< 0.001	0.835
Absent	152	41 (27.0)	Not reached [22.9; -]	152	78 (51.3)	15.0 [12.7; 18.9]	0.42 [0.29; 0.62]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	38 (32.5)	Not reached [20.2; -]	115	65 (56.5)	12.5 [11.3; 17.1]	0.40 [0.26; 0.61]	< 0.001	0.847
Low	85	26 (30.6)	Not reached [19.9; -]	87	51 (58.6)	13.3 [8.3; 16.1]	0.41 [0.26; 0.66]	< 0.001	
Metastatic Disease Site									
Visceral metastases	148	55 (37.2)	22.9 [18.7; -]	157	101 (64.3)	10.7 [8.9; 12.5]	0.41 [0.29; 0.58]	< 0.001	0.782
Lymph node only	43	9 (20.9)	Not reached [-; -]	37	14 (37.8)	18.3 [13.3; -]	0.46 [0.20; 1.07]	0.072	
Renal Function									
Normal	6	2 (33.3)	Not reached [0.7; -]	13	7 (53.8)	13.0 [3.7; -]	0.49 [0.05; 5.14]	0.548	0.406
Mild	49	11 (22.4)	Not reached [22.9; -]	40	22 (55.0)	12.9 [10.3; 18.9]	0.23 [0.10; 0.51]	< 0.001	
Moderate/Severe	147	51 (34.7)	Not reached [19.1; -]	149	87 (58.4)	12.5 [10.1; 16.1]	0.48 [0.34; 0.69]	< 0.001	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: intention-to-treat population, cisplatin ineligible									

Study: KEYNOTE-A39 ^a	EV+Pembro		Plat+Gem		EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Overall Survival	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
c: From product-limit (Kaplan-Meier) method for censored data							
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization using Wald confidence interval. Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors							
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)							
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors							
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1							

Morbidität

Cisplatin geeignet

Zeit bis zur ersten Folgetherapie (oder Tod)

Tabelle 4G-47: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis zur ersten Folgetherapie oder Tod aus RCT mit dem zu bewertenden Arzneimittel(Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro		Plat+Gem		EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f		
Time to Subsequent Therapy or Death	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	105	49 (46.7)	20.9 [13.2; -]	106	68 (64.2)	8.8 [7.2; 11.3]	0.49 [0.33; 0.72]	< 0.001	0.864
≥ 65	135	64 (47.4)	17.0 [12.2; 25.4]	136	93 (68.4)	8.8 [7.5; 10.7]	0.54 [0.39; 0.74]	< 0.001	
Race									
White	166	83 (50.0)	17.0 [12.3; 25.4]	149	100 (67.1)	8.2 [7.0; 10.7]	0.55 [0.41; 0.74]	< 0.001	0.628
Non-white	74	30 (40.5)	Not reached [12.2; -]	93	61 (65.6)	8.9 [8.0; 11.3]	0.49 [0.32; 0.77]	0.002	
Geographic Region									
North America	57	38 (66.7)	12.1 [8.9; 16.2]	51	38 (74.5)	8.2 [7.1; 11.3]	0.73 [0.46; 1.15]	0.176	0.150
Europe	98	43 (43.9)	20.9 [12.2; -]	102	70 (68.6)	8.8 [6.9; 10.8]	0.46 [0.31; 0.68]	< 0.001	
Rest of World	85	32 (37.6)	Not reached [15.4; -]	89	53 (59.6)	8.8 [7.1; 15.6]	0.45 [0.29; 0.70]	< 0.001	
Sex									
Male	198	90 (45.5)	24.7 [13.2; -]	185	125 (67.6)	8.8 [7.2; 10.6]	0.49 [0.37; 0.65]	< 0.001	0.240
Female	42	23 (54.8)	13.5 [10.6; -]	57	36 (63.2)	8.9 [7.3; 13.3]	0.68 [0.39; 1.17]	0.162	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Time to Subsequent Therapy or Death	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Primary Disease Site of Origin										
Upper Tract	61	35 (57.4)	13.2 [8.6; 23.7]	49	27 (55.1)	8.9 [7.3; 17.3]	0.79 [0.46; 1.33]	0.371	0.056	
Lower Tract	177	76 (42.9)	24.7 [15.5; -]	193	134 (69.4)	8.8 [7.3; 10.4]	0.45 [0.34; 0.60]	< 0.001		
Stratification Factor: Liver Metastases										
Present	48	28 (58.3)	13.8 [8.2; 25.6]	48	34 (70.8)	8.5 [6.9; 9.2]	0.62 [0.37; 1.04]	0.071	0.426	
Absent	192	85 (44.3)	23.7 [13.5; -]	194	127 (65.5)	8.9 [7.5; 10.8]	0.50 [0.38; 0.66]	< 0.001		
Stratification Factor: PD-L1 Expression										
High	139	61 (43.9)	25.4 [12.1; -]	140	87 (62.1)	8.9 [8.0; 11.1]	0.56 [0.40; 0.78]	< 0.001	0.669	
Low	101	52 (51.5)	15.4 [12.6; 24.7]	102	74 (72.5)	7.8 [6.9; 10.7]	0.49 [0.34; 0.69]	< 0.001		
Metastatic Disease Site										
Visceral metastases	170	86 (50.6)	15.5 [12.2; 25.4]	161	114 (70.8)	8.3 [7.1; 9.1]	0.51 [0.39; 0.68]	< 0.001	0.621	
Lymph node only	60	23 (38.3)	Not reached [12.8; -]	67	40 (59.7)	9.4 [7.1; 15.8]	0.51 [0.31; 0.86]	0.011		
Renal Function										
Normal	78	36 (46.2)	20.9 [13.0; -]	82	53 (64.6)	10.8 [8.3; 16.0]	0.53 [0.34; 0.82]	0.004	0.879	
Mild	116	55 (47.4)	17.8 [11.6; -]	122	84 (68.9)	8.2 [7.0; 9.3]	0.53 [0.38; 0.75]	< 0.001		
Moderate/Severe	46	22 (47.8)	25.4 [9.2; -]	38	24 (63.2)	8.5 [5.5; 15.8]	0.52 [0.29; 0.95]	0.034		
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: intention-to-treat population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization using Wald confidence interval. Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1</p>										

Krankheitssymptomatik und Gesundheitszustand

Tabelle 4G-48: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Fatigue									
Sex									
Male	174	136 (78.2)	0.4 [0.4; 0.6]	147	119 (81.0)	0.4 [0.4; 0.6]	0.87 [0.68; 1.12]	0.286	0.249
Female	36	33 (91.7)	0.5 [0.2; 1.8]	42	38 (90.5)	0.2 [0.2; 0.4]	0.53 [0.32; 0.89]	0.017	
Geographic Region									
North America	49	40 (81.6)	0.4 [0.2; 0.7]	42	38 (90.5)	0.4 [0.2; 0.4]	0.69 [0.43; 1.10]	0.117	0.295
Europe	80	65 (81.3)	0.4 [0.2; 0.7]	73	61 (83.6)	0.3 [0.2; 0.4]	0.67 [0.47; 0.96]	0.029	
Rest of World	81	64 (79.0)	0.6 [0.4; 1.1]	74	58 (78.4)	0.7 [0.4; 1.0]	0.94 [0.66; 1.35]	0.745	
ECOG at Baseline									
0	117	100 (85.5)	0.4 [0.4; 0.6]	97	86 (88.7)	0.4 [0.2; 0.4]	0.75 [0.56; 1.00]	0.054	0.432
1-2	93	69 (74.2)	0.5 [0.4; 0.9]	91	70 (76.9)	0.6 [0.4; 0.8]	0.85 [0.61; 1.21]	0.371	
Race									
White	140	110 (78.6)	0.4 [0.4; 0.7]	115	98 (85.2)	0.4 [0.4; 0.4]	0.70 [0.53; 0.93]	0.014	0.115
Non-white	70	59 (84.3)	0.4 [0.4; 0.6]	74	59 (79.7)	0.4 [0.2; 0.9]	0.97 [0.67; 1.40]	0.862	
Metastatic Disease Site									
Visceral metastases	148	115 (77.7)	0.4 [0.4; 0.7]	130	104 (80.0)	0.4 [0.4; 0.6]	0.79 [0.60; 1.04]	0.092	0.917
Lymph node only	55	47 (85.5)	0.4 [0.2; 0.7]	49	45 (91.8)	0.4 [0.2; 0.6]	0.75 [0.49; 1.15]	0.182	
Primary Disease Site of Origin									
Upper Tract	54	46 (85.2)	0.4 [0.4; 0.6]	37	29 (78.4)	0.4 [0.2; 0.7]	1.08 [0.65; 1.80]	0.755	0.388
Lower Tract	154	122 (79.2)	0.5 [0.4; 0.7]	152	128 (84.2)	0.4 [0.4; 0.6]	0.74 [0.58; 0.96]	0.022	
Renal Function									
Normal	68	52 (76.5)	0.6 [0.4; 2.0]	60	49 (81.7)	0.3 [0.2; 0.6]	0.60 [0.41; 0.90]	0.013	0.279
Mild	101	83 (82.2)	0.4 [0.4; 0.6]	96	81 (84.4)	0.4 [0.4; 0.6]	0.99 [0.72; 1.36]	0.945	
Moderate/Severe	41	34 (82.9)	0.4 [0.2; 1.1]	33	27 (81.8)	0.5 [0.2; 0.7]	0.83 [0.48; 1.43]	0.493	
Stratification Factor: Liver Metastases									
Present	38	30 (78.9)	0.4 [0.2; 0.7]	34	26 (76.5)	0.4 [0.3; 1.3]	1.11 [0.65; 1.90]	0.692	0.226
Absent	172	139 (80.8)	0.5 [0.4; 0.6]	155	131 (84.5)	0.4 [0.4; 0.6]	0.75 [0.59; 0.96]	0.021	
Stratification Factor: PD-L1 Expression									

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Fatigue									
High	122	102 (83.6)	0.5 [0.4; 0.7]	112	97 (86.6)	0.4 [0.4; 0.6]	0.76 [0.57; 1.01]	0.059	0.783
Low	88	67 (76.1)	0.4 [0.4; 0.6]	77	60 (77.9)	0.4 [0.2; 0.7]	0.87 [0.61; 1.24]	0.450	

a: Database Cutoff Date: 08AUG2023
b: Number of participants: PRO full-analysis-set population, cisplatin eligible
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome

Tabelle 4G-49: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Nausea and Vomiting									
Age									
< 65	94	56 (59.6)	3.8 [1.3; 8.6]	84	64 (76.2)	0.4 [0.2; 0.7]	0.48 [0.33; 0.70]	< 0.001	0.300
≥ 65	116	75 (64.7)	1.5 [0.6; 4.5]	105	78 (74.3)	0.6 [0.4; 1.1]	0.61 [0.44; 0.84]	0.003	
Sex									
Male	174	104 (59.8)	3.1 [1.3; 5.9]	147	106 (72.1)	0.6 [0.4; 0.9]	0.54 [0.41; 0.71]	< 0.001	0.754
Female	36	27 (75.0)	0.6 [0.4; 2.0]	42	36 (85.7)	0.4 [0.2; 0.9]	0.55 [0.33; 0.93]	0.024	
Geographic Region									
North America	49	32 (65.3)	1.3 [0.6; 7.3]	42	34 (81.0)	0.4 [0.2; 0.9]	0.53 [0.32; 0.88]	0.014	0.192
Europe	80	47 (58.8)	3.8 [1.1; 13.5]	73	56 (76.7)	0.4 [0.2; 1.1]	0.42 [0.28; 0.62]	< 0.001	
Rest of World	81	52 (64.2)	1.7 [0.6; 5.3]	74	52 (70.3)	0.6 [0.4; 2.0]	0.68 [0.46; 1.00]	0.049	
ECOG at Baseline									
0	117	73 (62.4)	2.8 [1.1; 5.3]	97	76 (78.4)	0.4 [0.2; 0.7]	0.48 [0.34; 0.67]	< 0.001	0.301
1-2	93	58 (62.4)	1.5 [0.7; 6.6]	91	65 (71.4)	0.7 [0.4; 1.5]	0.57 [0.40; 0.83]	0.003	
Race									
White	140	85 (60.7)	2.8 [1.1; 6.6]	115	87 (75.7)	0.4 [0.4; 0.8]	0.49 [0.36; 0.67]	< 0.001	0.381
Non-white	70	46 (65.7)	1.5 [0.6; 5.9]	74	55 (74.3)	0.6 [0.2; 1.4]	0.64 [0.43; 0.96]	0.030	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Nausea and Vomiting	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Metastatic Disease Site									
Visceral metastases	148	96 (64.9)	1.7 [0.8; 4.5]	130	92 (70.8)	0.6 [0.4; 0.9]	0.62 [0.46; 0.83]	0.001	0.115
Lymph node only	55	31 (56.4)	2.0 [1.1; -]	49	42 (85.7)	0.4 [0.2; 0.9]	0.42 [0.26; 0.68]	< 0.001	
Renal Function									
Normal	68	45 (66.2)	1.5 [0.7; 5.2]	60	47 (78.3)	0.4 [0.2; 0.8]	0.49 [0.32; 0.75]	0.001	0.208
Mild	101	61 (60.4)	3.8 [1.1; 5.9]	96	75 (78.1)	0.4 [0.3; 0.9]	0.46 [0.33; 0.66]	< 0.001	
Moderate/Severe	41	25 (61.0)	2.0 [0.4; 16.4]	33	20 (60.6)	1.6 [0.2; -]	0.83 [0.45; 1.53]	0.549	
Stratification Factor: PD-L1 Expression									
High	122	77 (63.1)	2.0 [1.1; 5.9]	112	92 (82.1)	0.4 [0.3; 0.6]	0.47 [0.34; 0.64]	< 0.001	0.111
Low	88	54 (61.4)	2.1 [0.8; 6.6]	77	50 (64.9)	0.8 [0.4; 1.6]	0.69 [0.47; 1.02]	0.062	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-50: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerzen des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	94	57 (60.6)	1.6 [0.6; 7.3]	84	57 (67.9)	0.9 [0.4; 1.7]	0.80 [0.55; 1.17]	0.249	0.074
≥ 65	116	90 (77.6)	0.6 [0.4; 0.9]	105	73 (69.5)	1.1 [0.6; 1.5]	1.18 [0.86; 1.61]	0.314	
Sex									
Male	174	122 (70.1)	0.7 [0.5; 1.3]	147	98 (66.7)	0.9 [0.6; 1.4]	0.99 [0.76; 1.30]	0.963	0.731
Female	36	25 (69.4)	0.6 [0.4; 7.3]	42	32 (76.2)	1.4 [0.4; 1.8]	0.86 [0.50; 1.47]	0.579	
Geographic Region									
North America	49	35 (71.4)	0.5 [0.4; 1.6]	42	30 (71.4)	0.7 [0.4; 1.4]	1.11 [0.66; 1.84]	0.700	0.718

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Pain	Europe	80 58 (72.5)	0.9 [0.6; 3.2]	73 48 (65.8)	1.1 [0.4; 1.8]	0.80 [0.54; 1.19]	0.269		
	Rest of World	81 54 (66.7)	0.5 [0.4; 1.3]	74 52 (70.3)	1.2 [0.6; 1.8]	1.05 [0.71; 1.54]	0.806		
ECOG at Baseline									
0	117	87 (74.4)	0.8 [0.6; 1.3]	97	71 (73.2)	1.1 [0.6; 1.7]	0.92 [0.67; 1.27]	0.608	0.756
1-2	93	60 (64.5)	0.5 [0.4; 1.4]	91	58 (63.7)	1.1 [0.5; 1.5]	1.03 [0.71; 1.49]	0.879	
Race									
White	140	99 (70.7)	0.7 [0.5; 1.3]	115	75 (65.2)	1.1 [0.6; 1.4]	1.03 [0.76; 1.40]	0.850	0.568
Non-white	70	48 (68.6)	0.6 [0.4; 4.5]	74	55 (74.3)	1.3 [0.6; 1.7]	0.84 [0.56; 1.25]	0.381	
Metastatic Disease Site									
Visceral metastases	148	98 (66.2)	0.6 [0.5; 1.3]	130	86 (66.2)	1.1 [0.7; 1.6]	0.96 [0.72; 1.29]	0.798	0.969
Lymph node only	55	42 (76.4)	0.7 [0.4; 2.5]	49	38 (77.6)	0.7 [0.4; 1.7]	0.90 [0.57; 1.42]	0.655	
Primary Disease Site of Origin									
Upper Tract	54	35 (64.8)	0.6 [0.4; 6.6]	37	28 (75.7)	1.3 [0.4; 2.6]	1.02 [0.60; 1.72]	0.944	0.971
Lower Tract	154	111 (72.1)	0.8 [0.5; 1.3]	152	102 (67.1)	1.1 [0.6; 1.4]	0.97 [0.74; 1.28]	0.845	
Renal Function									
Normal	68	46 (67.6)	0.9 [0.5; 6.7]	60	42 (70.0)	1.1 [0.6; 1.5]	0.80 [0.52; 1.23]	0.312	0.279
Mild	101	76 (75.2)	0.6 [0.4; 1.3]	96	66 (68.8)	1.3 [0.6; 1.8]	1.16 [0.83; 1.62]	0.395	
Moderate/Severe	41	25 (61.0)	0.4 [0.4; 5.3]	33	22 (66.7)	0.6 [0.4; 1.6]	1.04 [0.58; 1.87]	0.883	
Stratification Factor: Liver Metastases									
Present	38	24 (63.2)	0.6 [0.4; 1.7]	34	22 (64.7)	1.3 [0.4; 3.1]	1.06 [0.59; 1.92]	0.842	0.895
Absent	172	123 (71.5)	0.7 [0.5; 1.3]	155	108 (69.7)	1.1 [0.6; 1.6]	0.95 [0.73; 1.24]	0.715	
Stratification Factor: PD-L1 Expression									
High	122	91 (74.6)	0.6 [0.4; 1.3]	112	83 (74.1)	0.9 [0.5; 1.6]	0.98 [0.72; 1.32]	0.873	0.779
Low	88	56 (63.6)	0.8 [0.5; 2.5]	77	47 (61.0)	1.1 [0.6; 1.8]	0.96 [0.64; 1.43]	0.836	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-51: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Dyspnoea	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	94	59 (62.8)	3.8 [1.6; 8.0]	84	45 (53.6)	3.1 [1.8; -]	1.06 [0.71; 1.58]	0.778	0.598
≥ 65	116	75 (64.7)	2.0 [1.1; 4.5]	105	62 (59.0)	1.8 [1.1; 4.5]	0.97 [0.69; 1.36]	0.844	
Sex									
Male	174	114 (65.5)	2.7 [1.6; 4.6]	147	82 (55.8)	2.4 [1.5; 4.5]	1.01 [0.76; 1.35]	0.928	0.727
Female	36	20 (55.6)	1.6 [0.6; -]	42	25 (59.5)	2.0 [1.4; 5.3]	1.06 [0.58; 1.92]	0.855	
ECOG at Baseline									
0	117	73 (62.4)	2.4 [1.6; 6.6]	97	59 (60.8)	1.8 [1.3; 5.2]	0.85 [0.60; 1.22]	0.382	0.206
1-2	93	61 (65.6)	2.0 [0.9; 5.2]	91	47 (51.6)	2.7 [1.5; 5.3]	1.21 [0.82; 1.77]	0.341	
Race									
White	140	86 (61.4)	2.4 [1.3; 6.6]	115	67 (58.3)	1.8 [1.3; 3.1]	0.84 [0.61; 1.16]	0.296	0.116
Non-white	70	48 (68.6)	2.2 [0.8; 4.6]	74	40 (54.1)	3.9 [1.8; 5.3]	1.34 [0.87; 2.05]	0.182	
Metastatic Disease Site									
Visceral metastases	148	96 (64.9)	2.0 [1.1; 5.2]	130	69 (53.1)	2.4 [1.8; 4.6]	1.14 [0.83; 1.56]	0.423	0.167
Lymph node only	55	33 (60.0)	2.7 [1.8; 10.1]	49	31 (63.3)	1.8 [0.9; 5.9]	0.77 [0.47; 1.27]	0.304	
Primary Disease Site of Origin									
Upper Tract	54	43 (79.6)	1.4 [0.9; 3.2]	37	21 (56.8)	2.2 [1.1; -]	1.61 [0.94; 2.74]	0.083	0.055
Lower Tract	154	89 (57.8)	2.7 [1.8; 8.6]	152	86 (56.6)	2.0 [1.6; 3.9]	0.85 [0.63; 1.15]	0.297	
Renal Function									
Normal	68	39 (57.4)	5.9 [2.0; 11.4]	60	30 (50.0)	2.0 [1.3; -]	0.82 [0.50; 1.34]	0.419	0.703
Mild	101	71 (70.3)	1.9 [1.1; 4.5]	96	59 (61.5)	2.2 [1.5; 3.9]	1.10 [0.77; 1.56]	0.612	
Moderate/Severe	41	24 (58.5)	0.9 [0.6; -]	33	18 (54.5)	4.0 [1.1; -]	1.13 [0.60; 2.14]	0.701	
Stratification Factor: Liver Metastases									
Present	38	23 (60.5)	1.0 [0.4; -]	34	19 (55.9)	2.4 [1.1; -]	1.30 [0.70; 2.42]	0.404	0.397
Absent	172	111 (64.5)	2.7 [1.6; 5.2]	155	88 (56.8)	2.0 [1.6; 4.0]	0.94 [0.71; 1.25]	0.673	
Stratification Factor: PD-L1 Expression									
High	122	78 (63.9)	2.4 [1.5; 5.9]	112	65 (58.0)	2.5 [1.5; 4.6]	0.99 [0.71; 1.38]	0.947	0.973
Low	88	56 (63.6)	2.0 [1.1; 5.9]	77	42 (54.5)	1.8 [1.3; 6.6]	1.01 [0.67; 1.51]	0.977	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Dyspnoea									
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Tabelle 4G-52: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schlaflosigkeit des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Insomnia									
Age									
< 65	94	57 (60.6)	3.2 [1.1; 6.6]	84	54 (64.3)	2.0 [0.7; 5.2]	0.74 [0.50; 1.08]	0.115	0.556
≥ 65	116	68 (58.6)	1.3 [0.7; 5.3]	105	59 (56.2)	2.0 [0.8; 6.0]	0.93 [0.65; 1.32]	0.676	
Sex									
Male	174	101 (58.0)	2.4 [1.1; 5.2]	147	86 (58.5)	1.5 [0.9; 5.2]	0.85 [0.63; 1.13]	0.257	0.784
Female	36	24 (66.7)	0.9 [0.4; 10.1]	42	27 (64.3)	2.5 [0.4; 5.2]	0.91 [0.51; 1.59]	0.730	
Geographic Region									
North America	49	29 (59.2)	1.1 [0.6; 7.4]	42	29 (69.0)	1.5 [0.4; 5.2]	0.73 [0.42; 1.25]	0.248	0.811
Europe	80	48 (60.0)	2.7 [1.1; 6.6]	73	41 (56.2)	2.0 [0.7; 6.6]	0.81 [0.53; 1.24]	0.334	
Rest of World	81	48 (59.3)	1.3 [0.6; 10.1]	74	43 (58.1)	2.5 [0.8; 6.0]	0.98 [0.64; 1.48]	0.909	
ECOG at Baseline									
0	117	77 (65.8)	1.6 [0.9; 3.8]	97	60 (61.9)	2.0 [0.6; 6.0]	0.92 [0.65; 1.30]	0.650	0.340
1-2	93	48 (51.6)	2.7 [0.9; 10.1]	91	53 (58.2)	2.0 [0.9; 3.9]	0.75 [0.51; 1.12]	0.163	
Race									
White	140	80 (57.1)	2.4 [0.9; 5.2]	115	66 (57.4)	2.5 [0.9; 5.2]	0.86 [0.62; 1.19]	0.364	0.882
Non-white	70	45 (64.3)	1.1 [0.7; 8.0]	74	47 (63.5)	1.3 [0.4; 5.2]	0.79 [0.52; 1.20]	0.266	
Metastatic Disease Site									
Visceral metastases	148	85 (57.4)	2.3 [0.9; 7.4]	130	75 (57.7)	2.7 [1.1; 6.0]	0.86 [0.62; 1.17]	0.331	0.621

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Insomnia	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Lymph node only	55	35 (63.6)	1.2 [0.6; 5.3]	49	33 (67.3)	0.9 [0.4; 2.0]	0.78 [0.48; 1.27]	0.326	
Primary Disease Site of Origin									
Upper Tract	54	32 (59.3)	3.2 [0.7; 10.8]	37	22 (59.5)	3.9 [0.7; 14.2]	1.14 [0.64; 2.04]	0.649	0.402
Lower Tract	154	92 (59.7)	1.7 [0.9; 5.2]	152	91 (59.9)	2.0 [0.8; 3.1]	0.80 [0.60; 1.08]	0.144	
Renal Function									
Normal	68	41 (60.3)	1.3 [0.9; 8.6]	60	38 (63.3)	1.9 [0.9; 3.9]	0.67 [0.43; 1.06]	0.091	0.412
Mild	101	58 (57.4)	2.7 [0.9; 5.9]	96	59 (61.5)	2.0 [0.6; 6.0]	0.83 [0.57; 1.20]	0.315	
Moderate/Severe	41	26 (63.4)	0.9 [0.6; 7.4]	33	16 (48.5)	3.6 [0.5; -]	1.14 [0.60; 2.17]	0.685	
Stratification Factor: Liver Metastases									
Present	38	24 (63.2)	0.9 [0.5; 1.7]	34	18 (52.9)	2.0 [0.6; 8.0]	1.31 [0.71; 2.42]	0.394	0.128
Absent	172	101 (58.7)	2.7 [1.1; 5.9]	155	95 (61.3)	2.0 [0.9; 3.8]	0.77 [0.58; 1.02]	0.071	
Stratification Factor: PD-L1 Expression									
High	122	75 (61.5)	2.0 [0.9; 4.5]	112	73 (65.2)	1.3 [0.8; 3.1]	0.82 [0.59; 1.14]	0.237	0.734
Low	88	50 (56.8)	2.4 [0.8; 8.0]	77	40 (51.9)	3.8 [0.5; 6.7]	0.89 [0.58; 1.35]	0.583	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-53: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Appetite Loss	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	94	56 (59.6)	1.7 [0.6; 3.9]	84	59 (70.2)	0.6 [0.4; 0.9]	0.60 [0.41; 0.87]	0.007	0.080
≥ 65	116	85 (73.3)	0.8 [0.6; 1.3]	105	71 (67.6)	0.8 [0.4; 1.5]	0.93 [0.68; 1.28]	0.665	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Appetite Loss	N ^b	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	174	115 (66.1)	0.9 [0.6; 1.8]	147	101 (68.7)	0.6 [0.4; 0.9]	0.76 [0.58; 1.00]	0.047	0.642
Female	36	26 (72.2)	1.0 [0.4; 5.9]	42	29 (69.0)	0.6 [0.2; 2.7]	0.70 [0.40; 1.22]	0.210	
Geographic Region									
North America	49	29 (59.2)	1.7 [0.5; 3.2]	42	28 (66.7)	0.9 [0.4; 3.8]	0.77 [0.45; 1.33]	0.347	0.194
Europe	80	53 (66.3)	0.9 [0.6; 2.1]	73	50 (68.5)	0.4 [0.2; 0.9]	0.57 [0.38; 0.84]	0.005	
Rest of World	81	59 (72.8)	0.9 [0.4; 1.8]	74	52 (70.3)	0.8 [0.4; 1.3]	0.91 [0.62; 1.33]	0.635	
ECOG at Baseline									
0	117	87 (74.4)	1.0 [0.6; 2.0]	97	73 (75.3)	0.6 [0.2; 1.1]	0.74 [0.54; 1.02]	0.065	0.914
1-2	93	54 (58.1)	0.9 [0.5; 2.0]	91	57 (62.6)	0.7 [0.4; 1.0]	0.78 [0.53; 1.14]	0.200	
Race									
White	140	94 (67.1)	1.1 [0.6; 1.7]	115	80 (69.6)	0.6 [0.4; 0.9]	0.72 [0.53; 0.97]	0.033	0.525
Non-white	70	47 (67.1)	0.9 [0.6; 2.2]	74	50 (67.6)	0.9 [0.4; 1.3]	0.83 [0.56; 1.25]	0.377	
Metastatic Disease Site									
Visceral metastases	148	97 (65.5)	0.9 [0.6; 2.0]	130	88 (67.7)	0.6 [0.4; 0.9]	0.72 [0.53; 0.96]	0.025	0.647
Lymph node only	55	39 (70.9)	0.9 [0.5; 1.9]	49	36 (73.5)	0.8 [0.4; 1.2]	0.82 [0.52; 1.30]	0.399	
Primary Disease Site of Origin									
Upper Tract	54	36 (66.7)	0.6 [0.4; 2.5]	37	24 (64.9)	1.0 [0.3; 1.8]	0.93 [0.53; 1.62]	0.792	0.367
Lower Tract	154	104 (67.5)	1.1 [0.7; 2.0]	152	106 (69.7)	0.6 [0.4; 0.9]	0.72 [0.55; 0.95]	0.021	
Renal Function									
Normal	68	44 (64.7)	1.1 [0.7; 2.1]	60	43 (71.7)	0.6 [0.4; 1.1]	0.64 [0.42; 0.99]	0.043	0.139
Mild	101	69 (68.3)	1.0 [0.6; 2.0]	96	69 (71.9)	0.6 [0.4; 0.9]	0.73 [0.52; 1.03]	0.073	
Moderate/Severe	41	28 (68.3)	0.7 [0.4; 2.5]	33	18 (54.5)	1.3 [0.4; -]	1.21 [0.66; 2.24]	0.535	
Stratification Factor: Liver Metastases									
Present	38	26 (68.4)	0.6 [0.4; 1.3]	34	22 (64.7)	0.4 [0.2; 1.3]	0.87 [0.49; 1.55]	0.645	0.723
Absent	172	115 (66.9)	1.1 [0.7; 2.0]	155	108 (69.7)	0.7 [0.4; 0.9]	0.75 [0.58; 0.98]	0.037	
Stratification Factor: PD-L1 Expression									
High	122	85 (69.7)	0.9 [0.6; 1.8]	112	86 (76.8)	0.4 [0.4; 0.9]	0.67 [0.49; 0.90]	0.008	0.101
Low	88	56 (63.6)	1.0 [0.6; 2.1]	77	44 (57.1)	0.9 [0.4; 2.1]	1.00 [0.67; 1.49]	0.991	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									

Study: KEYNOTE-A39 ^a	EV+Pembro		Plat+Gem		EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Appetite Loss	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
c: From product-limit (Kaplan-Meier) method for censored data							
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization							
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)							
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors							
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome							

Tabelle 4G-54: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro		Plat+Gem		EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f		
Constipation	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	94	54 (57.4)	3.8 [1.3; 10.1]	84	59 (70.2)	0.6 [0.4; 1.5]	0.53 [0.36; 0.78]	0.001	0.474
≥ 65	116	71 (61.2)	1.8 [1.1; 3.9]	105	74 (70.5)	0.8 [0.4; 1.6]	0.62 [0.45; 0.87]	0.005	
Sex									
Male	174	99 (56.9)	2.7 [1.5; 5.9]	147	104 (70.7)	0.9 [0.5; 1.6]	0.55 [0.42; 0.73]	< 0.001	0.436
Female	36	26 (72.2)	0.9 [0.4; 5.2]	42	29 (69.0)	0.3 [0.2; 1.3]	0.64 [0.37; 1.12]	0.121	
ECOG at Baseline									
0	117	74 (63.2)	2.0 [1.3; 5.9]	97	77 (79.4)	0.6 [0.3; 1.1]	0.50 [0.36; 0.70]	< 0.001	0.265
1-2	93	51 (54.8)	2.3 [1.1; 10.1]	91	55 (60.4)	1.1 [0.5; 2.3]	0.68 [0.46; 0.99]	0.047	
Race									
White	140	82 (58.6)	2.0 [1.3; 6.6]	115	82 (71.3)	0.9 [0.4; 1.5]	0.57 [0.42; 0.78]	< 0.001	0.908
Non-white	70	43 (61.4)	3.8 [1.1; 6.7]	74	51 (68.9)	0.6 [0.2; 1.6]	0.60 [0.39; 0.91]	0.018	
Metastatic Disease Site									
Visceral metastases	148	85 (57.4)	1.7 [1.3; 4.5]	130	86 (66.2)	0.9 [0.4; 1.6]	0.64 [0.47; 0.87]	0.004	0.231
Lymph node only	55	35 (63.6)	3.8 [1.1; 6.7]	49	39 (79.6)	0.6 [0.2; 0.9]	0.47 [0.29; 0.76]	0.002	
Primary Disease Site of Origin									
Upper Tract	54	33 (61.1)	2.0 [1.3; 4.5]	37	28 (75.7)	0.6 [0.3; 1.8]	0.64 [0.38; 1.07]	0.091	0.727
Lower Tract	154	91 (59.1)	2.8 [1.5; 6.6]	152	105 (69.1)	0.9 [0.4; 1.3]	0.55 [0.41; 0.73]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Constipation	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	68	37 (54.4)	3.8 [1.1; -]	60	40 (66.7)	0.6 [0.2; 1.8]	0.49 [0.31; 0.78]	0.002	0.317
Mild	101	59 (58.4)	2.2 [1.3; 5.2]	96	69 (71.9)	0.7 [0.4; 1.6]	0.58 [0.40; 0.82]	0.002	
Moderate/Severe	41	29 (70.7)	1.5 [0.6; 5.2]	33	24 (72.7)	0.8 [0.4; 2.1]	0.67 [0.37; 1.21]	0.182	
Stratification Factor: Liver Metastases									
Present	38	22 (57.9)	1.5 [0.6; -]	34	24 (70.6)	1.1 [0.2; 1.6]	0.64 [0.36; 1.14]	0.132	0.979
Absent	172	103 (59.9)	2.5 [1.5; 5.2]	155	109 (70.3)	0.6 [0.4; 1.3]	0.56 [0.43; 0.74]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	122	76 (62.3)	1.8 [1.1; 4.5]	112	77 (68.8)	0.7 [0.4; 1.6]	0.62 [0.45; 0.85]	0.003	0.491
Low	88	49 (55.7)	3.8 [1.3; 8.7]	77	56 (72.7)	0.7 [0.2; 1.8]	0.52 [0.35; 0.77]	0.001	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-55: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Diarrhö des EORTC QLQ-C30 der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Diarrhoea	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	94	54 (57.4)	2.0 [1.1; 17.0]	84	45 (53.6)	3.1 [1.1; -]	0.97 [0.64; 1.45]	0.866	0.140
≥ 65	116	78 (67.2)	1.5 [0.9; 3.8]	105	51 (48.6)	2.8 [1.7; -]	1.39 [0.97; 1.98]	0.071	
Sex									
Male	174	112 (64.4)	1.7 [1.3; 3.2]	147	77 (52.4)	2.8 [1.6; 8.7]	1.13 [0.85; 1.52]	0.402	0.851
Female	36	20 (55.6)	8.7 [0.7; -]	42	19 (45.2)	Not reached [1.6; -]	1.18 [0.62; 2.25]	0.612	
Geographic Region									
North America	49	32 (65.3)	2.0 [1.1; 9.4]	42	21 (50.0)	5.2 [1.6; -]	1.33 [0.76; 2.33]	0.325	0.237

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Diarrhoea									
Europe	80	45 (56.3)	2.0 [0.9; -]	73	39 (53.4)	2.0 [0.9; 8.7]	0.90 [0.58; 1.39]	0.633	
Rest of World	81	55 (67.9)	1.7 [1.1; 3.8]	74	36 (48.6)	3.3 [1.3; -]	1.36 [0.88; 2.08]	0.162	
ECOG at Baseline									
0	117	71 (60.7)	2.0 [1.1; 8.7]	97	53 (54.6)	2.8 [1.7; 10.1]	0.99 [0.69; 1.42]	0.964	0.245
1-2	93	61 (65.6)	1.6 [1.1; 4.5]	91	42 (46.2)	4.5 [1.5; -]	1.39 [0.93; 2.07]	0.105	
Race									
White	140	87 (62.1)	1.6 [1.1; 3.8]	115	61 (53.0)	2.7 [1.5; 8.7]	1.03 [0.74; 1.44]	0.860	0.430
Non-white	70	45 (64.3)	2.0 [1.3; 8.7]	74	35 (47.3)	4.5 [1.6; -]	1.27 [0.81; 1.99]	0.297	
Metastatic Disease Site									
Visceral metastases	148	98 (66.2)	1.6 [1.1; 3.2]	130	65 (50.0)	3.1 [1.3; -]	1.23 [0.89; 1.68]	0.208	0.186
Lymph node only	55	29 (52.7)	3.8 [1.3; -]	49	28 (57.1)	2.7 [1.8; -]	0.82 [0.48; 1.41]	0.471	
Renal Function									
Normal	68	35 (51.5)	2.7 [0.9; -]	60	29 (48.3)	2.2 [1.2; -]	0.96 [0.59; 1.58]	0.879	0.119
Mild	101	64 (63.4)	2.0 [1.3; 9.4]	96	51 (53.1)	3.1 [1.6; -]	1.02 [0.70; 1.49]	0.902	
Moderate/Severe	41	33 (80.5)	1.2 [0.4; 2.0]	33	16 (48.5)	3.8 [1.1; -]	2.11 [1.12; 3.95]	0.020	
Stratification Factor: Liver Metastases									
Present	38	28 (73.7)	1.1 [0.6; 1.7]	34	16 (47.1)	3.8 [0.6; -]	1.59 [0.85; 2.96]	0.148	0.286
Absent	172	104 (60.5)	2.2 [1.3; 8.7]	155	80 (51.6)	3.1 [2.0; 10.1]	1.07 [0.80; 1.44]	0.642	
Stratification Factor: PD-L1 Expression									
High	122	76 (62.3)	2.0 [1.1; 9.4]	112	56 (50.0)	3.3 [1.8; -]	1.20 [0.84; 1.70]	0.311	0.819
Low	88	56 (63.6)	1.6 [1.1; 6.6]	77	40 (51.9)	2.7 [1.3; -]	1.10 [0.73; 1.65]	0.660	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Tabelle 4G-56: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain at its Worst in Last 24 Hours	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	94	53 (56.4)	4.6 [2.7; 16.3]	84	49 (58.3)	1.8 [1.1; 7.3]	0.82 [0.55; 1.22]	0.320	0.490
≥ 65	116	77 (66.4)	1.3 [0.7; 2.0]	105	64 (61.0)	1.4 [0.9; 3.2]	1.03 [0.73; 1.45]	0.863	
Sex									
Male	174	106 (60.9)	2.0 [1.3; 4.5]	147	87 (59.2)	1.5 [1.1; 3.2]	0.97 [0.72; 1.29]	0.814	0.739
Female	36	24 (66.7)	3.3 [1.1; 8.7]	42	26 (61.9)	2.2 [0.8; 5.9]	0.79 [0.45; 1.39]	0.414	
Geographic Region									
North America	49	31 (63.3)	2.7 [1.1; 12.8]	42	23 (54.8)	3.2 [1.1; -]	0.99 [0.56; 1.75]	0.961	0.595
Europe	80	47 (58.8)	3.2 [1.3; 8.0]	73	43 (58.9)	1.3 [0.6; 5.2]	0.75 [0.49; 1.14]	0.177	
Rest of World	81	52 (64.2)	1.5 [0.6; 4.5]	74	47 (63.5)	1.4 [0.9; 3.2]	1.08 [0.73; 1.61]	0.702	
Race									
White	140	87 (62.1)	1.8 [1.1; 4.6]	115	72 (62.6)	1.2 [0.8; 2.2]	0.82 [0.60; 1.13]	0.231	0.325
Non-white	70	43 (61.4)	3.2 [0.6; 6.6]	74	41 (55.4)	3.1 [1.3; 11.5]	1.10 [0.72; 1.70]	0.660	
Metastatic Disease Site									
Visceral metastases	148	86 (58.1)	2.0 [1.3; 5.3]	130	72 (55.4)	2.2 [1.3; 5.9]	0.97 [0.71; 1.34]	0.869	0.916
Lymph node only	55	38 (69.1)	2.0 [0.6; 6.6]	49	33 (67.3)	1.1 [0.6; 3.8]	0.91 [0.56; 1.47]	0.695	
Primary Disease Site of Origin									
Upper Tract	54	31 (57.4)	6.6 [1.1; 10.8]	37	20 (54.1)	3.1 [1.1; -]	0.99 [0.55; 1.79]	0.970	0.726
Lower Tract	154	98 (63.6)	1.8 [1.3; 3.3]	152	93 (61.2)	1.3 [1.1; 2.2]	0.91 [0.68; 1.22]	0.528	
Renal Function									
Normal	68	37 (54.4)	3.9 [1.3; 17.0]	60	31 (51.7)	1.8 [1.1; -]	0.91 [0.56; 1.49]	0.717	0.886
Mild	101	65 (64.4)	2.0 [1.1; 4.6]	96	63 (65.6)	1.3 [0.7; 3.2]	0.85 [0.59; 1.22]	0.375	
Moderate/Severe	41	28 (68.3)	1.3 [0.6; 5.3]	33	19 (57.6)	1.3 [0.5; -]	1.00 [0.55; 1.83]	0.993	
Stratification Factor: Liver Metastases									
Present	38	22 (57.9)	1.3 [0.6; 8.0]	34	18 (52.9)	3.5 [1.1; -]	1.25 [0.66; 2.36]	0.487	0.359
Absent	172	108 (62.8)	2.7 [1.3; 5.3]	155	95 (61.3)	1.5 [1.1; 3.1]	0.88 [0.67; 1.17]	0.379	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Pain at its Worst in Last 24 Hours									
Stratification Factor: PD-L1 Expression									
High	122 78 (63.9)	2.0 [1.3; 4.5]	112	68 (60.7)	1.8 [1.1; 4.5]	1.01 [0.73; 1.40]	0.941	0.413	
Low	88 52 (59.1)	3.2 [0.7; 8.0]	77	45 (58.4)	1.5 [0.8; 3.2]	0.82 [0.55; 1.24]	0.350		
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-57: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Pain Interference									
Age									
< 65	94 53 (56.4)	7.3 [2.3; 10.1]	84	40 (47.6)	7.3 [1.8; -]	1.03 [0.68; 1.56]	0.899	0.690	
≥ 65	116 69 (59.5)	2.7 [1.6; 6.6]	105	57 (54.3)	3.2 [1.3; 5.2]	0.99 [0.69; 1.40]	0.939		
Sex									
Male	174 94 (54.0)	5.2 [2.7; 9.4]	147	70 (47.6)	5.2 [2.7; 11.5]	0.99 [0.73; 1.36]	0.971	0.483	
Female	36 28 (77.8)	1.1 [0.4; 5.9]	42	27 (64.3)	2.0 [0.9; 5.3]	1.29 [0.75; 2.20]	0.360		
Geographic Region									
North America	49 26 (53.1)	3.9 [1.1; -]	42	20 (47.6)	7.3 [1.3; -]	1.05 [0.58; 1.91]	0.862	0.381	
Europe	80 49 (61.3)	5.9 [1.5; 8.0]	73	43 (58.9)	1.7 [0.9; 4.5]	0.80 [0.53; 1.21]	0.288		
Rest of World	81 47 (58.0)	3.2 [1.3; 9.3]	74	34 (45.9)	5.9 [2.7; -]	1.26 [0.81; 1.96]	0.314		
ECOG at Baseline									
0	117 75 (64.1)	3.2 [2.0; 8.0]	97	51 (52.6)	5.2 [1.8; 8.6]	1.08 [0.75; 1.54]	0.690	0.565	
1-2	93 47 (50.5)	5.2 [1.6; 19.7]	91	45 (49.5)	4.5 [1.3; 11.5]	0.94 [0.62; 1.42]	0.772		
Race									
White	140 82 (58.6)	3.9 [1.7; 8.0]	115	61 (53.0)	3.2 [1.1; 5.2]	0.90 [0.65; 1.26]	0.549	0.424	
Non-white	70 40	5.9	74	36	8.1	1.13	0.598		

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain Interference	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
		(57.1)	[1.6; 10.1]		(48.6)	[2.0; -]	[0.72; 1.79]		
Metastatic Disease Site									
Visceral metastases	148	83 (56.1)	3.2 [1.7; 8.0]	130	61 (46.9)	5.2 [2.7; 10.1]	1.15 [0.82; 1.60]	0.423	0.286
Lymph node only	55	33 (60.0)	6.6 [1.5; 11.5]	49	29 (59.2)	2.0 [0.6; -]	0.83 [0.50; 1.39]	0.485	
Primary Disease Site of Origin									
Upper Tract	54	34 (63.0)	1.7 [0.9; 5.9]	37	16 (43.2)	7.3 [0.9; -]	1.56 [0.84; 2.88]	0.156	0.095
Lower Tract	154	87 (56.5)	6.6 [2.7; 9.4]	152	81 (53.3)	3.8 [1.6; 5.9]	0.88 [0.64; 1.19]	0.400	
Renal Function									
Normal	68	38 (55.9)	8.0 [2.8; 10.1]	60	28 (46.7)	10.1 [1.1; -]	0.92 [0.56; 1.51]	0.736	0.875
Mild	101	59 (58.4)	3.2 [1.5; 8.0]	96	54 (56.3)	4.5 [1.8; 5.9]	1.01 [0.69; 1.46]	0.972	
Moderate/Severe	41	25 (61.0)	2.0 [0.5; -]	33	15 (45.5)	3.2 [0.6; -]	1.22 [0.64; 2.35]	0.548	
Stratification Factor: Liver Metastases									
Present	38	20 (52.6)	3.9 [0.7; -]	34	14 (41.2)	Not reached [1.4; -]	1.37 [0.69; 2.72]	0.373	0.418
Absent	172	102 (59.3)	3.9 [2.0; 8.7]	155	83 (53.5)	3.8 [1.5; 5.3]	0.95 [0.71; 1.27]	0.741	
Stratification Factor: PD-L1 Expression									
High	122	78 (63.9)	2.7 [1.5; 6.6]	112	64 (57.1)	3.8 [1.4; 5.9]	1.03 [0.74; 1.43]	0.877	0.784
Low	88	44 (50.0)	8.7 [2.0; -]	77	33 (42.9)	5.2 [1.5; -]	0.97 [0.61; 1.54]	0.899	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-58: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die EQ-5D VAS der Studie KEYNOTE A39 (Cisplatin geeignet)

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	94	57 (60.6)	5.9 [1.8; 10.1]	84	47 (56.0)	2.2 [1.3; -]	0.86 [0.58; 1.27]	0.450	0.357

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
≥ 65	116	81 (69.8)	1.5 [0.7; 2.8]	105	63 (60.0)	2.3 [1.3; 4.5]	1.13 [0.81; 1.59]	0.476	
Sex									
Male	174	117 (67.2)	2.2 [1.3; 3.9]	147	85 (57.8)	2.2 [1.5; 4.5]	1.08 [0.81; 1.43]	0.592	0.159
Female	36	21 (58.3)	9.3 [1.1; 21.1]	42	25 (59.5)	2.5 [0.6; -]	0.63 [0.34; 1.18]	0.153	
Geographic Region									
North America	49	31 (63.3)	2.2 [0.6; 10.8]	42	25 (59.5)	2.2 [1.1; 7.4]	0.97 [0.56; 1.67]	0.914	0.210
Europe	80	52 (65.0)	3.2 [1.3; 8.0]	73	47 (64.4)	1.7 [1.1; 2.7]	0.77 [0.51; 1.15]	0.196	
Rest of World	81	55 (67.9)	2.0 [0.6; 5.3]	74	38 (51.4)	3.8 [1.4; -]	1.27 [0.84; 1.94]	0.256	
ECOG at Baseline									
0	117	76 (65.0)	3.2 [1.8; 8.0]	97	59 (60.8)	1.8 [1.2; 3.2]	0.83 [0.58; 1.17]	0.283	0.120
1-2	93	62 (66.7)	1.6 [0.5; 5.2]	91	50 (54.9)	2.7 [1.7; 7.4]	1.18 [0.80; 1.73]	0.400	
Race									
White	140	91 (65.0)	2.4 [1.1; 6.6]	115	65 (56.5)	2.2 [1.3; 5.2]	0.99 [0.72; 1.37]	0.948	0.864
Non-white	70	47 (67.1)	2.6 [1.1; 6.6]	74	45 (60.8)	2.3 [1.3; 5.9]	0.97 [0.64; 1.48]	0.903	
Metastatic Disease Site									
Visceral metastases	148	92 (62.2)	2.3 [1.1; 8.0]	130	73 (56.2)	2.7 [1.7; 5.9]	1.02 [0.74; 1.39]	0.913	0.869
Lymph node only	55	40 (72.7)	2.6 [0.9; 6.6]	49	31 (63.3)	1.7 [1.1; 5.2]	0.85 [0.52; 1.37]	0.495	
Primary Disease Site of Origin									
Upper Tract	54	38 (70.4)	1.3 [0.6; 3.9]	37	20 (54.1)	3.1 [1.1; -]	1.37 [0.76; 2.45]	0.296	0.259
Lower Tract	154	98 (63.6)	3.2 [1.8; 6.6]	152	90 (59.2)	2.2 [1.6; 3.2]	0.88 [0.66; 1.18]	0.409	
Renal Function									
Normal	68	41 (60.3)	6.6 [1.8; 10.8]	60	33 (55.0)	2.3 [1.1; 8.0]	0.87 [0.54; 1.39]	0.552	0.399
Mild	101	68 (67.3)	2.4 [1.1; 4.6]	96	61 (63.5)	2.1 [1.4; 3.2]	0.96 [0.67; 1.36]	0.803	
Moderate/Severe	41	29 (70.7)	0.6 [0.4; 5.9]	33	16 (48.5)	4.5 [0.4; -]	1.23 [0.65; 2.35]	0.522	
Stratification Factor: PD-L1 Expression									
High	122	80 (65.6)	4.6 [2.3; 8.0]	112	68 (60.7)	1.8 [1.2; 3.1]	0.83 [0.60; 1.16]	0.276	0.176
Low	88	58 (65.9)	1.3 [0.5; 2.5]	77	42 (54.5)	3.2 [1.6; 7.4]	1.28 [0.86; 1.91]	0.230	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome; VAS: Visual Analogue Scale									

Cisplatin ungeeignet

Zeit bis zur ersten Folgetherapie (oder Tod)

Tabelle 4G-59: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis zur ersten Folgetherapie oder Tod aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Time to Subsequent Therapy or Death	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	39	18 (46.2)	20.7 [14.3; -]	29	23 (79.3)	7.7 [4.8; 11.9]	0.24 [0.11; 0.51]	< 0.001	0.247
≥ 65	163	73 (44.8)	18.4 [13.9; -]	173	129 (74.6)	7.1 [6.2; 8.1]	0.42 [0.32; 0.57]	< 0.001	
Race									
White	142	73 (51.4)	15.3 [12.0; 21.2]	141	110 (78.0)	7.4 [6.2; 8.4]	0.44 [0.33; 0.60]	< 0.001	0.073
Non-white	60	18 (30.0)	Not reached [18.2; -]	61	42 (68.9)	6.8 [4.8; 12.2]	0.27 [0.15; 0.48]	< 0.001	
Geographic Region									
North America	46	23 (50.0)	18.4 [6.9; -]	34	27 (79.4)	6.4 [3.3; 9.3]	0.41 [0.22; 0.76]	0.005	0.745
Europe	74	37 (50.0)	20.7 [11.5; -]	95	72 (75.8)	7.7 [6.2; 9.3]	0.39 [0.26; 0.60]	< 0.001	
Rest of World	82	31 (37.8)	20.4 [15.3; -]	73	53 (72.6)	6.9 [5.1; 8.9]	0.33 [0.21; 0.53]	< 0.001	
Sex									
Male	146	64 (43.8)	21.2 [14.5; -]	151	112 (74.2)	7.2 [6.3; 8.3]	0.39 [0.29; 0.54]	< 0.001	0.875
Female	56	27 (48.2)	15.8 [11.7; -]	51	40 (78.4)	7.0 [4.3; 9.2]	0.35 [0.21; 0.59]	< 0.001	
ECOG at Baseline									
0	87	33 (37.9)	21.2 [15.7; -]	87	64 (73.6)	8.1 [6.6; 10.8]	0.34 [0.22; 0.52]	< 0.001	0.498
1-2	115	58 (50.4)	15.3 [11.8; -]	114	87 (76.3)	7.0 [5.1; 7.6]	0.44 [0.31; 0.62]	< 0.001	

Study: KEYNOTE-A39 ^a		EV+Pembro		Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Time to Subsequent Therapy or Death	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	74	31 (41.9)	21.2 [14.3; -]	55	41 (74.5)	6.9 [4.4; 10.3]	0.33 [0.20; 0.55]	< 0.001	0.488
Lower Tract	128	60 (46.9)	18.4 [13.5; -]	146	110 (75.3)	7.2 [6.2; 8.6]	0.41 [0.30; 0.57]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	30 (60.0)	10.9 [6.9; 21.2]	50	43 (86.0)	6.1 [4.7; 7.2]	0.45 [0.27; 0.73]	0.001	0.552
Absent	152	61 (40.1)	22.9 [15.7; -]	152	109 (71.7)	8.0 [6.6; 10.5]	0.37 [0.27; 0.51]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	51 (43.6)	22.9 [15.1; -]	115	87 (75.7)	7.5 [6.2; 9.3]	0.37 [0.26; 0.52]	< 0.001	0.654
Low	85	40 (47.1)	18.2 [11.7; -]	87	65 (74.7)	6.9 [5.4; 8.1]	0.42 [0.28; 0.63]	< 0.001	
Metastatic Disease Site									
Visceral metastases	148	74 (50.0)	15.7 [11.8; 21.2]	157	125 (79.6)	6.7 [5.6; 7.4]	0.39 [0.29; 0.53]	< 0.001	0.901
Lymph node only	43	14 (32.6)	Not reached [15.3; -]	37	22 (59.5)	13.0 [7.3; 19.9]	0.41 [0.21; 0.82]	0.012	
Renal Function									
Normal	6	2 (33.3)	Not reached [0.7; -]	13	9 (69.2)	9.3 [3.7; -]	0.23 [0.03; 1.99]	0.182	0.437
Mild	49	19 (38.8)	21.2 [18.4; -]	40	31 (77.5)	8.0 [6.0; 10.5]	0.27 [0.15; 0.50]	< 0.001	
Moderate/Severe	147	70 (47.6)	15.3 [12.3; -]	149	112 (75.2)	7.0 [5.8; 7.8]	0.44 [0.33; 0.60]	< 0.001	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: intention-to-treat population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization using Wald confidence interval. Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1</p>									

Krankheitssymptomatik und GesundheitszustandTabelle 4G-60: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Erschöpfung des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Fatigue	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	5 (83.3)	1.1 [0.5; -]	10	6 (60.0)	0.4 [0.1; -]	0.20 [0.02; 1.75]	0.145	0.455
Mild	39	31 (79.5)	0.8 [0.4; 2.2]	34	29 (85.3)	0.4 [0.2; 0.4]	0.54 [0.30; 0.95]	0.034	
Moderate/Severe	121	94 (77.7)	0.4 [0.4; 0.7]	122	96 (78.7)	0.4 [0.4; 0.6]	0.91 [0.68; 1.22]	0.526	
Stratification Factor: Liver Metastases									
Present	41	31 (75.6)	0.4 [0.2; 0.9]	41	28 (68.3)	0.6 [0.2; 1.8]	1.14 [0.68; 1.90]	0.621	0.194
Absent	125	99 (79.2)	0.6 [0.4; 1.1]	125	103 (82.4)	0.4 [0.4; 0.6]	0.76 [0.58; 1.01]	0.058	
Stratification Factor: PD-L1 Expression									
High	97	76 (78.4)	0.6 [0.4; 1.1]	98	77 (78.6)	0.4 [0.4; 0.6]	0.79 [0.57; 1.09]	0.153	0.721
Low	69	54 (78.3)	0.4 [0.2; 0.7]	68	54 (79.4)	0.4 [0.2; 0.7]	0.90 [0.62; 1.32]	0.595	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-61: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Nausea and Vomiting	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	33	22 (66.7)	1.1 [0.4; 9.4]	22	15 (68.2)	1.4 [0.4; 3.2]	1.00 [0.50; 1.99]	0.997	0.203
≥ 65	133	81 (60.9)	1.8 [1.3; 2.9]	144	102 (70.8)	0.9 [0.4; 1.3]	0.67 [0.49; 0.90]	0.007	
Sex									
Male	123	77 (62.6)	1.8 [1.1; 3.1]	126	87 (69.0)	1.1 [0.4; 2.2]	0.76 [0.56; 1.03]	0.079	0.354
Female	43	26 (60.5)	1.8 [0.6; 10.7]	40	30 (75.0)	0.6 [0.4; 1.3]	0.55 [0.31; 0.98]	0.042	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Nausea and Vomiting	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Geographic Region									
North America	35	20 (57.1)	2.0 [0.4; 2.9]	28	14 (50.0)	2.2 [1.1; -]	1.30 [0.64; 2.63]	0.468	0.109
Europe	57	35 (61.4)	2.0 [0.9; 5.3]	76	57 (75.0)	0.6 [0.4; 1.5]	0.65 [0.42; 1.00]	0.051	
Rest of World	74	48 (64.9)	1.7 [0.7; 5.5]	62	46 (74.2)	0.7 [0.4; 1.5]	0.63 [0.41; 0.96]	0.033	
ECOG at Baseline									
0	74	50 (67.6)	1.8 [1.1; 3.2]	72	51 (70.8)	0.6 [0.4; 1.5]	0.69 [0.46; 1.03]	0.069	0.988
1-2	92	53 (57.6)	1.8 [0.7; 3.8]	94	66 (70.2)	1.1 [0.4; 2.0]	0.72 [0.50; 1.05]	0.087	
Race									
White	110	65 (59.1)	2.0 [1.1; 2.7]	114	81 (71.1)	1.1 [0.4; 1.7]	0.71 [0.51; 0.99]	0.045	0.959
Non-white	56	38 (67.9)	1.7 [0.6; 5.9]	52	36 (69.2)	0.8 [0.4; 3.2]	0.73 [0.45; 1.17]	0.190	
Metastatic Disease Site									
Visceral metastases	121	76 (62.8)	1.3 [0.8; 2.9]	128	86 (67.2)	0.9 [0.4; 1.7]	0.76 [0.56; 1.05]	0.095	0.162
Lymph node only	36	23 (63.9)	2.2 [1.1; 11.4]	30	26 (86.7)	0.6 [0.4; 1.3]	0.48 [0.27; 0.86]	0.013	
Primary Disease Site of Origin									
Upper Tract	62	36 (58.1)	2.9 [0.8; 11.4]	44	29 (65.9)	1.5 [0.6; 4.6]	0.77 [0.47; 1.28]	0.313	0.880
Lower Tract	104	67 (64.4)	1.5 [0.9; 2.2]	121	87 (71.9)	0.7 [0.4; 1.3]	0.72 [0.52; 1.00]	0.051	
Renal Function									
Normal	6	4 (66.7)	0.4 [0.2; -]	10	8 (80.0)	0.4 [0.2; 2.0]	0.79 [0.19; 3.32]	0.751	0.914
Mild	39	24 (61.5)	2.0 [1.0; 3.2]	34	21 (61.8)	1.1 [0.4; -]	0.82 [0.46; 1.48]	0.515	
Moderate/Severe	121	75 (62.0)	1.8 [0.9; 4.5]	122	88 (72.1)	1.1 [0.4; 1.5]	0.69 [0.50; 0.95]	0.021	
Stratification Factor: Liver Metastases									
Present	41	24 (58.5)	1.8 [0.7; 4.5]	41	21 (51.2)	1.8 [0.7; -]	1.17 [0.65; 2.11]	0.593	0.071
Absent	125	79 (63.2)	1.8 [1.0; 3.1]	125	96 (76.8)	0.6 [0.4; 1.3]	0.62 [0.46; 0.83]	0.002	
Stratification Factor: PD-L1 Expression									
High	97	64 (66.0)	1.3 [0.7; 3.2]	98	69 (70.4)	1.1 [0.4; 2.2]	0.81 [0.57; 1.14]	0.218	0.218
Low	69	39 (56.5)	2.0 [1.0; 9.4]	68	48 (70.6)	0.9 [0.4; 1.3]	0.57 [0.37; 0.88]	0.011	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Nausea and Vomiting	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-62: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerz des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33	20 (60.6)	1.3 [0.4; 8.7]	22	15 (68.2)	2.7 [0.4; 4.6]	1.00 [0.49; 2.01]	0.990	0.531
≥ 65	133	86 (64.7)	1.1 [0.7; 1.8]	144	102 (70.8)	0.8 [0.4; 1.1]	0.76 [0.57; 1.02]	0.066	
Sex									
Male	123	78 (63.4)	1.1 [0.7; 2.4]	126	86 (68.3)	1.1 [0.5; 1.5]	0.81 [0.59; 1.10]	0.176	0.918
Female	43	28 (65.1)	0.9 [0.4; 2.2]	40	31 (77.5)	0.6 [0.2; 1.8]	0.79 [0.46; 1.38]	0.415	
Geographic Region									
North America	35	23 (65.7)	0.9 [0.4; 3.8]	28	17 (60.7)	1.1 [0.7; 2.7]	0.80 [0.41; 1.58]	0.526	0.749
Europe	57	36 (63.2)	0.9 [0.5; 2.2]	76	56 (73.7)	0.8 [0.4; 1.5]	0.81 [0.53; 1.25]	0.350	
Rest of World	74	47 (63.5)	1.3 [0.4; 3.1]	62	44 (71.0)	0.4 [0.4; 1.8]	0.75 [0.50; 1.15]	0.192	
ECOG at Baseline									
0	74	50 (67.6)	1.4 [0.7; 2.7]	72	57 (79.2)	0.6 [0.4; 1.1]	0.64 [0.43; 0.94]	0.022	0.123
1-2	92	56 (60.9)	0.8 [0.4; 2.0]	94	60 (63.8)	1.3 [0.6; 2.2]	0.95 [0.66; 1.37]	0.782	
Race									
White	110	69 (62.7)	1.0 [0.6; 2.2]	114	79 (69.3)	0.9 [0.5; 1.1]	0.83 [0.60; 1.16]	0.277	0.551
Non-white	56	37 (66.1)	1.3 [0.5; 4.5]	52	38 (73.1)	1.3 [0.4; 2.2]	0.70 [0.44; 1.12]	0.138	
Metastatic Disease Site									
Visceral metastases	121	82 (67.8)	0.8 [0.4; 1.6]	128	88 (68.8)	1.1 [0.5; 1.5]	0.95 [0.70; 1.28]	0.728	0.066
Lymph node only	36	20 (55.6)	2.0 [1.1; -]	30	22 (73.3)	0.7 [0.4; 2.7]	0.52 [0.28; 0.96]	0.035	
Primary Disease Site of Origin									
Upper Tract	62	44 (71.0)	0.8 [0.4; 1.8]	44	31 (70.5)	1.3 [0.4; 2.2]	1.10 [0.69; 1.75]	0.685	0.076
Lower Tract	104	62 (59.6)	1.3 [0.7; 2.4]	121	86 (71.1)	0.6 [0.4; 1.1]	0.66 [0.47; 0.92]	0.015	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Renal Function									
Normal	6	5 (83.3)	0.5 [0.1; -]	10	5 (50.0)	0.4 [0.2; -]	0.86 [0.19; 3.79]	0.841	0.069
Mild	39	22 (56.4)	2.0 [0.8; -]	34	28 (82.4)	0.6 [0.4; 1.1]	0.42 [0.24; 0.75]	0.003	
Moderate/Severe	121	79 (65.3)	0.9 [0.4; 1.8]	122	84 (68.9)	1.1 [0.6; 1.7]	0.91 [0.67; 1.24]	0.540	
Stratification Factor: Liver Metastases									
Present	41	25 (61.0)	1.6 [0.4; 3.8]	41	20 (48.8)	1.8 [0.5; -]	1.16 [0.64; 2.10]	0.622	0.146
Absent	125	81 (64.8)	0.9 [0.6; 1.8]	125	97 (77.6)	0.6 [0.4; 1.1]	0.71 [0.52; 0.95]	0.023	
Stratification Factor: PD-L1 Expression									
High	97	66 (68.0)	0.8 [0.5; 1.8]	98	68 (69.4)	0.6 [0.4; 1.1]	0.87 [0.62; 1.22]	0.414	0.348
Low	69	40 (58.0)	1.6 [0.9; 5.2]	68	49 (72.1)	1.1 [0.5; 1.5]	0.67 [0.44; 1.02]	0.061	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-63: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Dyspnoe des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Dyspnoea	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33	26 (78.8)	2.0 [0.6; 5.2]	22	13 (59.1)	4.5 [1.1; 10.1]	1.43 [0.70; 2.92]	0.321	0.071
≥ 65	133	75 (56.4)	2.0 [1.5; 4.6]	144	90 (62.5)	1.3 [0.9; 1.8]	0.79 [0.58; 1.08]	0.139	
Sex									
Male	123	80 (65.0)	1.8 [1.3; 2.5]	126	78 (61.9)	1.8 [1.1; 2.7]	0.97 [0.71; 1.34]	0.874	0.140
Female	43	21 (48.8)	2.0 [0.9; -]	40	25 (62.5)	0.9 [0.4; 2.7]	0.64 [0.34; 1.20]	0.164	
Geographic Region									
North America	35	17 (48.6)	1.8 [0.7; -]	28	20 (71.4)	1.1 [0.4; 2.7]	0.61 [0.30; 1.23]	0.168	0.356
Europe	57	33 (57.9)	2.0 [1.1; 6.0]	76	43 (56.6)	1.5 [0.9; 3.1]	0.94 [0.59; 1.50]	0.789	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Dyspnoea	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	74	51 (68.9)	2.0 [1.1; 5.2]	62	40 (64.5)	1.8 [0.9; 3.8]	0.89 [0.57; 1.37]	0.589	
Race									
White	110	61 (55.5)	2.2 [1.5; 6.0]	114	72 (63.2)	1.3 [1.1; 2.2]	0.76 [0.53; 1.08]	0.122	0.213
Non-white	56	40 (71.4)	1.5 [0.6; 3.1]	52	31 (59.6)	1.8 [0.9; 8.7]	1.21 [0.74; 1.98]	0.449	
Metastatic Disease Site									
Visceral metastases	121	77 (63.6)	1.3 [0.9; 2.4]	128	76 (59.4)	1.7 [1.1; 3.1]	1.04 [0.75; 1.44]	0.816	0.083
Lymph node only	36	19 (52.8)	6.0 [2.0; -]	30	20 (66.7)	1.5 [0.6; 2.8]	0.54 [0.28; 1.02]	0.057	
Primary Disease Site of Origin									
Upper Tract	62	42 (67.7)	2.0 [1.1; 5.2]	44	32 (72.7)	1.0 [0.4; 2.0]	0.72 [0.45; 1.17]	0.183	0.490
Lower Tract	104	59 (56.7)	1.8 [1.3; 6.0]	121	71 (58.7)	1.8 [1.1; 2.7]	0.93 [0.65; 1.32]	0.674	
Renal Function									
Normal	6	3 (50.0)	1.6 [0.6; -]	10	6 (60.0)	1.1 [0.2; -]	0.21 [0.02; 1.82]	0.157	0.137
Mild	39	25 (64.1)	2.5 [1.1; 8.7]	34	28 (82.4)	1.0 [0.6; 1.5]	0.47 [0.26; 0.83]	0.010	
Moderate/Severe	121	73 (60.3)	2.0 [1.1; 2.7]	122	69 (56.6)	2.0 [1.1; 3.8]	1.04 [0.74; 1.46]	0.813	
Stratification Factor: PD-L1 Expression									
High	97	61 (62.9)	1.8 [1.1; 2.7]	98	63 (64.3)	1.7 [1.1; 2.7]	0.89 [0.62; 1.28]	0.537	0.905
Low	69	40 (58.0)	2.0 [1.1; 5.2]	68	40 (58.8)	1.3 [0.8; 3.2]	0.84 [0.54; 1.31]	0.444	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Tabelle 4G-64: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schlaflosigkeit des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Insomnia	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	33	17 (51.5)	2.7 [1.3; -]	22	12 (54.5)	2.3 [0.9; 6.6]	0.67 [0.30; 1.51]	0.334	0.765
≥ 65	133	84 (63.2)	1.3 [0.9; 1.8]	144	80 (55.6)	1.1 [0.7; 2.2]	1.00 [0.73; 1.36]	0.998	
Geographic Region									
North America	35	20 (57.1)	1.1 [0.5; 7.3]	28	13 (46.4)	1.8 [0.4; -]	1.04 [0.49; 2.21]	0.927	0.214
Europe	57	35 (61.4)	1.6 [0.7; 2.7]	76	38 (50.0)	2.3 [1.1; 6.6]	1.28 [0.79; 2.06]	0.311	
Rest of World	74	46 (62.2)	1.8 [1.1; 2.7]	62	41 (66.1)	0.6 [0.4; 2.2]	0.72 [0.46; 1.11]	0.138	
ECOG at Baseline									
0	74	49 (66.2)	1.8 [0.9; 2.7]	72	50 (69.4)	0.8 [0.4; 1.4]	0.78 [0.52; 1.16]	0.225	0.081
1-2	92	52 (56.5)	1.5 [0.9; 2.7]	94	42 (44.7)	3.2 [1.1; 9.4]	1.24 [0.82; 1.88]	0.306	
Race									
White	110	68 (61.8)	1.3 [0.9; 1.8]	114	61 (53.5)	1.8 [1.1; 4.5]	1.15 [0.81; 1.64]	0.441	0.055
Non-white	56	33 (58.9)	1.8 [1.3; 6.6]	52	31 (59.6)	0.6 [0.2; 1.1]	0.65 [0.39; 1.09]	0.101	
Metastatic Disease Site									
Visceral metastases	121	70 (57.9)	1.7 [1.1; 2.7]	128	66 (51.6)	1.6 [0.9; 4.5]	0.94 [0.67; 1.32]	0.722	0.621
Lymph node only	36	26 (72.2)	1.1 [0.7; 1.8]	30	19 (63.3)	1.1 [0.4; 2.7]	1.09 [0.59; 2.00]	0.784	
Primary Disease Site of Origin									
Upper Tract	62	38 (61.3)	2.2 [0.6; 5.9]	44	27 (61.4)	1.8 [0.6; 3.8]	0.90 [0.54; 1.50]	0.688	0.810
Lower Tract	104	63 (60.6)	1.3 [0.9; 1.8]	121	65 (53.7)	1.1 [0.6; 2.7]	0.99 [0.70; 1.41]	0.956	
Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Insomnia	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	4 (66.7)	0.9 [0.1; -]	10	5 (50.0)	1.1 [0.2; -]	0.85 [0.16; 4.49]	0.846	0.984
Mild	39	24 (61.5)	1.5 [0.7; 3.1]	34	19 (55.9)	1.3 [0.4; -]	1.04 [0.56; 1.93]	0.898	
Moderate/Severe	121	73 (60.3)	1.6 [1.1; 2.2]	122	68 (55.7)	1.3 [0.7; 2.7]	0.95 [0.68; 1.33]	0.781	
Stratification Factor: Liver Metastases									
Present	41	25 (61.0)	1.5 [0.4; 6.6]	41	16 (39.0)	1.3 [0.6; -]	1.22 [0.65; 2.32]	0.534	0.263
Absent	125	76	1.6	125	76	1.3	0.90	0.541	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Insomnia	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
		(60.8)	[1.1; 2.5]		(60.8)	[0.7; 2.2]	[0.66; 1.25]		
Stratification Factor: PD-L1 Expression									
High	97	57 (58.8)	1.3 [0.9; 2.7]	98	59 (60.2)	1.1 [0.6; 2.2]	0.92 [0.64; 1.33]	0.649	0.478
Low	69	44 (63.8)	1.7 [1.1; 2.7]	68	33 (48.5)	1.6 [0.7; 6.1]	1.03 [0.66; 1.63]	0.883	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Tabelle 4G-65: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Appetitverlust des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Appetite Loss	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	33	23 (69.7)	0.9 [0.4; 2.5]	22	16 (72.7)	1.8 [0.4; 5.2]	1.54 [0.73; 3.22]	0.254	0.526
≥ 65	133	93 (69.9)	0.9 [0.6; 1.3]	144	94 (65.3)	0.8 [0.4; 1.3]	0.91 [0.68; 1.22]	0.542	
Geographic Region									
North America	35	21 (60.0)	1.3 [0.5; 3.8]	28	10 (35.7)	4.6 [1.3; -]	1.86 [0.86; 4.05]	0.117	0.098
Europe	57	42 (73.7)	0.9 [0.6; 1.3]	76	54 (71.1)	1.1 [0.4; 1.6]	0.97 [0.63; 1.48]	0.871	
Rest of World	74	53 (71.6)	0.9 [0.5; 1.7]	62	46 (74.2)	0.6 [0.4; 1.3]	0.80 [0.53; 1.21]	0.296	
ECOG at Baseline									
0	74	58 (78.4)	0.9 [0.5; 1.3]	72	50 (69.4)	1.3 [0.5; 1.7]	1.04 [0.71; 1.53]	0.832	0.403
1-2	92	58 (63.0)	1.1 [0.6; 1.7]	94	60 (63.8)	0.8 [0.4; 1.5]	0.87 [0.61; 1.26]	0.474	
Metastatic Disease Site									
Visceral metastases	121	84 (69.4)	0.9 [0.7; 1.5]	128	80 (62.5)	1.3 [0.5; 1.7]	1.04 [0.77; 1.42]	0.780	0.069
Lymph node only	36	25 (69.4)	1.1 [0.6; 2.4]	30	23 (76.7)	0.6 [0.2; 1.3]	0.63 [0.35; 1.14]	0.125	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Appetite Loss									
Primary Disease Site of Origin									
Upper Tract	62	45 (72.6)	0.9 [0.4; 1.8]	44	27 (61.4)	1.3 [0.4; 5.9]	1.17 [0.72; 1.89]	0.534	0.470
Lower Tract	104	71 (68.3)	0.9 [0.6; 1.5]	121	83 (68.6)	0.8 [0.4; 1.5]	0.87 [0.63; 1.20]	0.390	
Renal Function									
Normal	6	4 (66.7)	1.5 [0.4; -]	10	5 (50.0)	1.5 [0.1; -]	1.06 [0.19; 5.95]	0.944	0.134
Mild	39	33 (84.6)	0.9 [0.6; 1.1]	34	24 (70.6)	1.6 [0.4; 3.2]	1.70 [0.96; 3.01]	0.071	
Moderate/Severe	121	79 (65.3)	1.1 [0.6; 2.0]	122	81 (66.4)	0.8 [0.4; 1.3]	0.80 [0.58; 1.10]	0.165	
Stratification Factor: Liver Metastases									
Present	41	29 (70.7)	0.9 [0.4; 1.8]	41	20 (48.8)	1.6 [0.4; 3.9]	1.40 [0.79; 2.49]	0.254	0.159
Absent	125	87 (69.6)	0.9 [0.6; 1.3]	125	90 (72.0)	1.1 [0.4; 1.3]	0.85 [0.63; 1.14]	0.273	
Stratification Factor: PD-L1 Expression									
High	97	73 (75.3)	0.9 [0.6; 1.3]	98	67 (68.4)	0.7 [0.4; 1.3]	0.92 [0.66; 1.29]	0.626	0.650
Low	69	43 (62.3)	0.9 [0.6; 2.0]	68	43 (63.2)	1.6 [0.4; 2.5]	0.98 [0.64; 1.51]	0.935	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-66: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Constipation									
Age									
< 65	33	18 (54.5)	2.3 [0.6; -]	22	15 (68.2)	0.8 [0.4; 2.2]	0.67 [0.33; 1.35]	0.259	0.509
≥ 65	133	75 (56.4)	2.0 [1.1; 4.5]	144	97 (67.4)	0.4 [0.4; 0.9]	0.50 [0.37; 0.68]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Constipation									
Sex									
Male	123	67 (54.5)	2.3 [1.5; 4.5]	126	84 (66.7)	0.4 [0.4; 1.1]	0.51 [0.37; 0.70]	< 0.001	0.910
Female	43	26 (60.5)	1.5 [0.4; 8.0]	40	28 (70.0)	0.4 [0.2; 1.3]	0.54 [0.30; 0.99]	0.045	
Geographic Region									
North America	35	20 (57.1)	0.9 [0.4; 2.5]	28	20 (71.4)	0.6 [0.4; 1.1]	0.53 [0.26; 1.05]	0.069	0.700
Europe	57	30 (52.6)	2.3 [1.4; 4.5]	76	47 (61.8)	0.4 [0.2; 1.3]	0.54 [0.33; 0.87]	0.012	
Rest of World	74	43 (58.1)	3.1 [1.1; 8.0]	62	45 (72.6)	0.4 [0.4; 1.1]	0.43 [0.28; 0.67]	< 0.001	
ECOG at Baseline									
0	74	42 (56.8)	2.4 [1.5; 8.0]	72	47 (65.3)	0.6 [0.4; 1.8]	0.53 [0.34; 0.81]	0.003	0.859
1-2	92	51 (55.4)	1.7 [0.8; 3.2]	94	65 (69.1)	0.4 [0.4; 0.9]	0.51 [0.35; 0.74]	< 0.001	
Race									
White	110	63 (57.3)	1.7 [0.9; 2.4]	114	75 (65.8)	0.4 [0.4; 0.9]	0.54 [0.38; 0.76]	< 0.001	0.602
Non-white	56	30 (53.6)	3.2 [1.1; -]	52	37 (71.2)	0.5 [0.4; 1.8]	0.49 [0.30; 0.81]	0.005	
Primary Disease Site of Origin									
Upper Tract	62	38 (61.3)	2.4 [0.9; 5.2]	44	35 (79.5)	0.4 [0.2; 0.6]	0.39 [0.24; 0.64]	< 0.001	0.416
Lower Tract	104	55 (52.9)	2.0 [1.1; 4.8]	121	76 (62.8)	0.4 [0.4; 1.3]	0.57 [0.40; 0.81]	0.002	
Renal Function									
Normal	6	2 (33.3)	0.6 [0.1; -]	10	5 (50.0)	1.8 [0.1; -]	0.80 [0.14; 4.51]	0.803	0.884
Mild	39	21 (53.8)	2.4 [1.1; -]	34	25 (73.5)	0.4 [0.2; 1.3]	0.39 [0.21; 0.73]	0.003	
Moderate/Severe	121	70 (57.9)	2.0 [0.9; 3.2]	122	82 (67.2)	0.4 [0.4; 0.9]	0.52 [0.38; 0.73]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	97	57 (58.8)	2.3 [1.4; 4.5]	98	71 (72.4)	0.4 [0.4; 1.1]	0.49 [0.34; 0.71]	< 0.001	0.986
Low	69	36 (52.2)	1.8 [0.8; 8.0]	68	41 (60.3)	0.4 [0.4; 1.3]	0.54 [0.34; 0.85]	0.008	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Tabelle 4G-67: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Verstopfung des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Diarrhoea									
Age									
< 65	33	26 (78.8)	2.0 [0.6; 3.1]	22	10 (45.5)	10.8 [1.8; -]	2.91 [1.29; 6.57]	0.010	0.119
≥ 65	133	75 (56.4)	2.4 [1.1; 4.5]	144	67 (46.5)	4.5 [1.3; -]	1.23 [0.88; 1.72]	0.219	
Sex									
Male	123	77 (62.6)	2.3 [1.3; 3.8]	126	60 (47.6)	4.5 [1.8; 11.0]	1.42 [1.01; 2.01]	0.044	0.900
Female	43	24 (55.8)	2.0 [0.7; -]	40	17 (42.5)	Not reached [0.9; -]	1.44 [0.76; 2.73]	0.269	
Geographic Region									
North America	35	23 (65.7)	1.4 [0.5; 3.9]	28	13 (46.4)	3.2 [0.7; -]	1.47 [0.73; 2.99]	0.284	0.701
Europe	57	33 (57.9)	2.0 [0.6; 4.5]	76	35 (46.1)	4.5 [1.3; -]	1.41 [0.86; 2.33]	0.172	
Rest of World	74	45 (60.8)	3.1 [1.1; 8.0]	62	29 (46.8)	5.2 [1.3; -]	1.15 [0.71; 1.87]	0.556	
ECOG at Baseline									
0	74	50 (67.6)	2.0 [1.0; 3.8]	72	32 (44.4)	5.2 [2.0; -]	1.49 [0.96; 2.33]	0.078	0.524
1-2	92	51 (55.4)	2.4 [1.1; 5.2]	94	45 (47.9)	3.2 [1.3; -]	1.25 [0.84; 1.88]	0.274	
Primary Disease Site of Origin									
Upper Tract	62	36 (58.1)	2.7 [1.1; 9.4]	44	19 (43.2)	10.8 [2.5; -]	1.42 [0.81; 2.50]	0.224	0.854
Lower Tract	104	65 (62.5)	1.8 [1.0; 3.1]	121	58 (47.9)	2.7 [1.3; -]	1.39 [0.97; 1.99]	0.071	
Renal Function									
Normal	6	4 (66.7)	10.7 [0.4; -]	10	4 (40.0)	2.0 [0.4; -]	0.27 [0.03; 2.57]	0.257	0.679
Mild	39	27 (69.2)	1.3 [0.6; 2.7]	34	18 (52.9)	3.9 [1.3; -]	1.65 [0.89; 3.05]	0.109	
Moderate/Severe	121	70 (57.9)	2.5 [1.3; 4.5]	122	55 (45.1)	5.2 [1.7; -]	1.31 [0.92; 1.87]	0.138	
Stratification Factor: Liver Metastases									
Present	41	28 (68.3)	1.8 [0.6; 4.5]	41	18 (43.9)	4.5 [1.1; -]	1.72 [0.95; 3.12]	0.073	0.362
Absent	125	73 (58.4)	2.4 [1.1; 5.2]	125	59 (47.2)	4.6 [1.8; -]	1.27 [0.90; 1.80]	0.173	
Stratification Factor: PD-L1 Expression									
High	97	57 (58.8)	2.5 [1.3; 4.5]	98	47 (48.0)	3.2 [1.3; -]	1.22 [0.83; 1.80]	0.318	0.355
Low	69	44 (63.8)	1.3 [0.7; 3.1]	68	30 (44.1)	5.2 [1.8; -]	1.63 [1.02; 2.59]	0.041	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Diarrhoea	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-68: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Stärkster Schmerz in den vergangenen 24 Stunden des BPI-SF der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain at its Worst in Last 24 Hours	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33	15 (45.5)	10.7 [2.7; -]	22	10 (45.5)	5.5 [0.8; -]	1.05 [0.46; 2.40]	0.912	0.369
≥ 65	133	70 (52.6)	2.5 [1.1; 8.7]	144	94 (65.3)	1.1 [0.6; 1.8]	0.65 [0.47; 0.88]	0.006	
Sex									
Male	123	64 (52.0)	3.1 [1.5; 10.7]	126	80 (63.5)	1.3 [0.8; 2.4]	0.70 [0.50; 0.97]	0.034	0.619
Female	43	21 (48.8)	8.7 [0.9; -]	40	24 (60.0)	1.3 [0.2; 6.6]	0.58 [0.31; 1.11]	0.103	
Geographic Region									
North America	35	18 (51.4)	2.5 [0.5; -]	28	13 (46.4)	1.8 [0.9; -]	0.94 [0.45; 1.99]	0.877	0.385
Europe	57	27 (47.4)	3.1 [1.1; -]	76	51 (67.1)	0.8 [0.4; 2.0]	0.53 [0.33; 0.87]	0.011	
Rest of World	74	40 (54.1)	3.8 [1.5; -]	62	40 (64.5)	1.8 [0.4; 4.6]	0.69 [0.44; 1.08]	0.105	
Race									
White	110	59 (53.6)	1.6 [0.9; 3.9]	114	74 (64.9)	1.1 [0.6; 1.8]	0.73 [0.51; 1.03]	0.071	0.495
Non-white	56	26 (46.4)	13.5 [3.2; -]	52	30 (57.7)	2.5 [0.7; 10.0]	0.60 [0.35; 1.02]	0.058	
Primary Disease Site of Origin									
Upper Tract	62	31 (50.0)	3.2 [1.1; -]	44	25 (56.8)	1.6 [0.6; -]	0.79 [0.46; 1.34]	0.379	0.636
Lower Tract	104	54 (51.9)	2.7 [1.2; 10.7]	121	79 (65.3)	1.1 [0.6; 2.4]	0.63 [0.45; 0.90]	0.011	
Renal Function									
Normal	6	4 (66.7)	0.9 [0.1; -]	10	3 (30.0)	10.1 [0.2; -]	1.26 [0.19; 8.18]	0.807	0.109
Mild	39	24 (61.5)	2.1 [0.7; -]	34	19 (55.9)	2.0 [0.8; -]	1.05 [0.57; 1.95]	0.873	
Moderate/Severe	121	57 (47.1)	4.5 [1.6; -]	122	82 (67.2)	1.1 [0.6; 2.0]	0.56 [0.40; 0.79]	0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain at its Worst in Last 24 Hours	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Stratification Factor: Liver Metastases									
Present	41 (48.8)	20 (48.8)	5.9 [0.4; -]	41 (56.1)	23 (56.1)	2.0 [0.4; 6.6]	0.74 [0.40; 1.37]	0.336	0.610
Absent	125 (52.0)	65 (52.0)	3.2 [1.5; -]	125 (64.8)	81 (64.8)	1.1 [0.6; 2.2]	0.65 [0.47; 0.90]	0.009	
Stratification Factor: PD-L1 Expression									
High	97 (54.6)	53 (54.6)	2.7 [1.1; 5.9]	98 (62.2)	61 (62.2)	1.3 [0.6; 2.4]	0.77 [0.53; 1.12]	0.171	0.301
Low	69 (46.4)	32 (46.4)	8.7 [1.6; -]	68 (63.2)	43 (63.2)	1.3 [0.4; 5.5]	0.53 [0.33; 0.84]	0.007	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-69: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerzbeeinträchtigung des BPI-SF der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain Interference	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33 (36.4)	12 (36.4)	Not reached [2.7; -]	22 (54.5)	12 (54.5)	4.6 [2.0; -]	0.66 [0.29; 1.51]	0.326	0.825
≥ 65	133 (49.6)	66 (49.6)	5.9 [1.3; 15.6]	144 (58.3)	84 (58.3)	1.5 [1.1; 2.5]	0.70 [0.50; 0.97]	0.034	
Sex									
Male	123 (48.8)	60 (48.8)	5.9 [1.5; -]	126 (58.7)	74 (58.7)	1.8 [1.1; 2.7]	0.69 [0.49; 0.98]	0.039	0.884
Female	43 (41.9)	18 (41.9)	12.1 [0.9; -]	40 (55.0)	22 (55.0)	1.8 [0.9; 6.6]	0.76 [0.40; 1.47]	0.421	
Geographic Region									
North America	35 (37.1)	13 (37.1)	18.3 [1.5; -]	28 (39.3)	11 (39.3)	Not reached [1.1; -]	0.81 [0.35; 1.88]	0.631	0.613
Europe	57 (54.4)	31 (54.4)	2.0 [0.7; 11.4]	76 (64.5)	49 (64.5)	1.8 [0.7; 3.2]	0.83 [0.52; 1.33]	0.435	
Rest of World	74 (45.9)	34 (45.9)	12.1 [1.5; -]	62 (58.1)	36 (58.1)	1.8 [0.4; 4.6]	0.58 [0.36; 0.95]	0.030	
Race									
White	110 (51.8)	57 (51.8)	2.7 [1.1; 12.1]	114 (57.0)	65 (57.0)	1.6 [1.1; 3.2]	0.79 [0.55; 1.15]	0.222	0.068
Non-white	56 (37.5)	21 (37.5)	Not reached [5.9; -]	52 (59.6)	31 (59.6)	2.4 [1.1; 4.6]	0.45 [0.25; 0.80]	0.007	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Pain Interference	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	121	57 (47.1)	5.9 [1.3; -]	128	70 (54.7)	2.0 [1.1; 3.9]	0.77 [0.54; 1.10]	0.153	0.162
Lymph node only	36	16 (44.4)	Not reached [2.0; -]	30	20 (66.7)	1.7 [0.9; 12.8]	0.41 [0.20; 0.82]	0.012	
Primary Disease Site of Origin									
Upper Tract	62	27 (43.5)	12.1 [1.1; -]	44	22 (50.0)	3.9 [1.3; -]	0.91 [0.51; 1.61]	0.741	0.267
Lower Tract	104	51 (49.0)	9.4 [1.5; 18.3]	121	74 (61.2)	1.5 [1.1; 2.7]	0.60 [0.41; 0.86]	0.006	
Renal Function									
Normal	6	5 (83.3)	0.9 [0.1; -]	10	5 (50.0)	2.0 [0.2; -]	1.64 [0.38; 7.02]	0.502	0.193
Mild	39	20 (51.3)	2.7 [0.9; -]	34	18 (52.9)	4.6 [1.3; -]	1.02 [0.54; 1.94]	0.948	
Moderate/Severe	121	53 (43.8)	11.4 [2.7; -]	122	73 (59.8)	1.5 [0.9; 2.5]	0.55 [0.38; 0.80]	0.002	
Stratification Factor: Liver Metastases									
Present	41	18 (43.9)	5.9 [1.1; -]	41	22 (53.7)	2.0 [0.6; 6.6]	0.77 [0.41; 1.45]	0.416	0.669
Absent	125	60 (48.0)	10.7 [1.7; -]	125	74 (59.2)	1.6 [1.1; 3.9]	0.64 [0.45; 0.91]	0.012	
Stratification Factor: PD-L1 Expression									
High	97	52 (53.6)	2.7 [1.1; 12.1]	98	55 (56.1)	1.8 [1.1; 3.9]	0.82 [0.56; 1.22]	0.335	0.089
Low	69	26 (37.7)	Not reached [2.7; -]	68	41 (60.3)	2.0 [1.1; 4.6]	0.48 [0.29; 0.79]	0.004	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-70: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die EQ-5D VAS der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	33	20 (60.6)	3.2 [0.6; 18.4]	22	15 (68.2)	2.1 [0.4; -]	0.80 [0.40; 1.61]	0.535	0.803
≥ 65	133	85 (63.9)	1.3 [0.9; 2.7]	144	95 (66.0)	1.3 [0.9; 1.8]	0.88 [0.66; 1.19]	0.418	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	123	80 (65.0)	1.5 [1.0; 3.2]	126	81 (64.3)	1.5 [0.9; 2.3]	0.91 [0.66; 1.25]	0.560	0.361
Female	43	25 (58.1)	1.3 [0.4; -]	40	29 (72.5)	1.3 [0.4; 2.3]	0.77 [0.43; 1.37]	0.375	
Geographic Region									
North America	35	17 (48.6)	3.8 [0.9; -]	28	13 (46.4)	2.3 [0.9; -]	0.75 [0.35; 1.59]	0.454	0.894
Europe	57	37 (64.9)	1.5 [0.6; 2.7]	76	53 (69.7)	1.1 [0.6; 2.4]	0.92 [0.59; 1.42]	0.697	
Rest of World	74	51 (68.9)	1.1 [0.6; 5.2]	62	44 (71.0)	1.2 [0.6; 2.0]	0.76 [0.50; 1.15]	0.196	
ECOG at Baseline									
0	74	49 (66.2)	2.7 [1.0; 5.2]	72	51 (70.8)	1.1 [0.4; 1.8]	0.67 [0.45; 1.01]	0.057	0.185
1-2	92	56 (60.9)	1.3 [0.6; 5.9]	94	59 (62.8)	1.6 [0.9; 3.2]	1.03 [0.71; 1.49]	0.888	
Race									
White	110	70 (63.6)	1.5 [1.0; 3.2]	114	73 (64.0)	1.3 [0.8; 2.3]	0.93 [0.67; 1.30]	0.680	0.299
Non-white	56	35 (62.5)	1.5 [0.5; 14.9]	52	37 (71.2)	1.5 [0.4; 2.3]	0.68 [0.42; 1.11]	0.122	
Metastatic Disease Site									
Visceral metastases	121	76 (62.8)	1.5 [0.9; 5.2]	128	81 (63.3)	1.5 [1.1; 2.3]	0.90 [0.65; 1.24]	0.521	0.159
Lymph node only	36	23 (63.9)	1.7 [0.7; 14.9]	30	24 (80.0)	0.9 [0.4; 2.0]	0.56 [0.31; 1.02]	0.057	
Primary Disease Site of Origin									
Upper Tract	62	41 (66.1)	1.1 [0.5; 5.2]	44	28 (63.6)	1.8 [0.6; 9.3]	1.07 [0.66; 1.74]	0.790	0.278
Lower Tract	104	64 (61.5)	1.6 [1.1; 5.2]	121	82 (67.8)	1.1 [0.8; 1.8]	0.75 [0.54; 1.06]	0.100	
Renal Function									
Normal	6	3 (50.0)	0.6 [0.2; -]	10	5 (50.0)	1.5 [0.2; -]	0.55 [0.10; 2.98]	0.486	0.406
Mild	39	30 (76.9)	1.3 [0.9; 3.2]	34	23 (67.6)	1.9 [0.6; 7.3]	1.19 [0.67; 2.09]	0.556	
Moderate/Severe	121	72 (59.5)	1.6 [0.7; 5.9]	122	82 (67.2)	1.3 [0.8; 2.0]	0.78 [0.56; 1.07]	0.123	
Stratification Factor: Liver Metastases									
Present	41	25 (61.0)	1.5 [0.5; 6.6]	41	21 (51.2)	2.2 [1.5; -]	1.32 [0.74; 2.37]	0.352	0.081
Absent	125	80 (64.0)	1.5 [1.0; 3.2]	125	89 (71.2)	1.1 [0.6; 1.6]	0.74 [0.54; 1.01]	0.054	
Stratification Factor: PD-L1 Expression									
High	97	63 (64.9)	1.5 [0.6; 3.8]	98	65 (66.3)	1.1 [0.7; 2.3]	0.87 [0.61; 1.24]	0.449	0.675
Low	69	42 (60.9)	1.5 [0.9; 6.6]	68	45 (66.2)	1.6 [0.9; 2.7]	0.79 [0.52; 1.21]	0.279	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
VAS Score	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome; VAS: Visual Analogue Scale									

Gesundheitsbezogene Lebensqualität

Cisplatin geeignet

Globaler Gesundheitsstatus des EORTC QLQ-C30

Tabelle 4G-71: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Globalen Gesundheitsstatus des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
EORTC QLQ-C30 Global Health Status/QoL	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	94 64 (68.1)	1.3 [0.6; 4.6]	84 56 (66.7)	1.1 [0.6; 1.4]	0.90 [0.62; 1.30]	0.562	0.667		
≥ 65	116 94 (81.0)	0.6 [0.6; 0.9]	105 76 (72.4)	0.7 [0.4; 1.1]	0.95 [0.70; 1.29]	0.762			
Sex									
Male	174 124 (71.3)	0.9 [0.6; 2.0]	147 101 (68.7)	1.1 [0.7; 1.3]	0.92 [0.71; 1.20]	0.545	0.903		
Female	36 34 (94.4)	0.6 [0.4; 1.3]	42 31 (73.8)	0.4 [0.2; 0.7]	0.93 [0.57; 1.53]	0.778			
Geographic Region									
North America	49 36 (73.5)	0.9 [0.6; 2.2]	42 32 (76.2)	0.7 [0.4; 1.1]	0.83 [0.52; 1.35]	0.461	0.263		
Europe	80 58 (72.5)	0.9 [0.5; 2.2]	73 48 (65.8)	0.6 [0.4; 0.9]	0.81 [0.55; 1.19]	0.276			
Rest of World	81 64 (79.0)	0.6 [0.5; 1.7]	74 52 (70.3)	1.3 [0.7; 2.2]	1.10 [0.76; 1.61]	0.602			
ECOG at Baseline									
0	117 93 (79.5)	0.7 [0.6; 1.3]	97 75 (77.3)	0.7 [0.4; 1.1]	0.84 [0.62; 1.15]	0.285	0.262		
1-2	93 65 (69.9)	0.9 [0.5; 2.7]	91 56 (61.5)	1.1 [0.6; 2.5]	1.07 [0.74; 1.53]	0.728			
Race									
White	140 101 (72.1)	0.9 [0.6; 2.0]	115 79 (68.7)	0.8 [0.4; 1.1]	0.80 [0.59; 1.08]	0.141	0.137		
Non-white	70 57 (81.4)	0.6 [0.5; 1.5]	74 53 (71.6)	1.1 [0.6; 1.8]	1.15 [0.78; 1.69]	0.477			

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
EORTC QLQ-C30 Global Health Status/QoL	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Metastatic Disease Site									
Visceral metastases	148	103 (69.6)	0.9 [0.6; 2.2]	130	85 (65.4)	0.9 [0.6; 1.3]	0.89 [0.67; 1.20]	0.456	0.465
Lymph node only	55	49 (89.1)	0.6 [0.4; 0.9]	49	40 (81.6)	0.7 [0.4; 1.3]	1.07 [0.69; 1.64]	0.772	
Primary Disease Site of Origin									
Upper Tract	54	40 (74.1)	0.8 [0.4; 1.5]	37	26 (70.3)	1.1 [0.4; 3.8]	1.00 [0.60; 1.65]	0.991	0.619
Lower Tract	154	117 (76.0)	0.7 [0.6; 1.7]	152	106 (69.7)	0.7 [0.5; 1.1]	0.91 [0.69; 1.18]	0.468	
Renal Function									
Normal	68	48 (70.6)	0.9 [0.5; 4.5]	60	42 (70.0)	0.7 [0.4; 1.1]	0.78 [0.51; 1.19]	0.255	0.088
Mild	101	76 (75.2)	1.1 [0.6; 2.2]	96	68 (70.8)	0.9 [0.4; 1.5]	0.85 [0.61; 1.19]	0.333	
Moderate/Severe	41	34 (82.9)	0.5 [0.2; 0.7]	33	22 (66.7)	1.0 [0.7; 2.0]	1.68 [0.95; 2.97]	0.076	
Stratification Factor: Liver Metastases									
Present	38	29 (76.3)	0.6 [0.4; 1.5]	34	19 (55.9)	1.0 [0.4; -]	1.31 [0.73; 2.35]	0.357	0.162
Absent	172	129 (75.0)	0.8 [0.6; 2.0]	155	113 (72.9)	0.9 [0.6; 1.1]	0.86 [0.67; 1.12]	0.262	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome; QoL: Quality of Life									

Funktionsskalen des EORTC QLQ-C30

Tabelle 4G-72: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperliche Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Sex									
Male	174	134 (77.0)	1.3 [0.9; 1.8]	147	102 (69.4)	0.9 [0.6; 1.3]	0.90 [0.70; 1.17]	0.442	0.524
Female	36	31 (86.1)	0.4 [0.2; 0.6]	42	34 (81.0)	0.9 [0.2; 1.8]	0.90 [0.54; 1.50]	0.692	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	49	39 (79.6)	0.6 [0.4; 1.3]	42	30 (71.4)	0.7 [0.4; 2.0]	1.09 [0.67; 1.79]	0.726	0.744
Europe	80	61 (76.3)	1.1 [0.6; 1.8]	73	51 (69.9)	1.1 [0.4; 1.7]	0.86 [0.59; 1.26]	0.451	
Rest of World	81	65 (80.2)	1.3 [0.6; 2.2]	74	55 (74.3)	0.9 [0.6; 1.8]	0.87 [0.60; 1.25]	0.448	
ECOG at Baseline									
0	117	94 (80.3)	1.1 [0.6; 1.8]	97	70 (72.2)	0.9 [0.4; 1.3]	0.88 [0.64; 1.21]	0.436	0.739
1-2	93	71 (76.3)	0.9 [0.5; 1.7]	91	65 (71.4)	0.9 [0.4; 1.8]	0.94 [0.67; 1.32]	0.721	
Race									
White	140	105 (75.0)	1.1 [0.6; 1.7]	115	84 (73.0)	0.7 [0.4; 1.1]	0.80 [0.60; 1.06]	0.122	0.138
Non-white	70	60 (85.7)	0.9 [0.6; 2.0]	74	52 (70.3)	1.3 [0.6; 2.2]	1.11 [0.76; 1.63]	0.585	
Metastatic Disease Site									
Visceral metastases	148	113 (76.4)	0.9 [0.6; 1.3]	130	92 (70.8)	0.9 [0.4; 1.5]	0.90 [0.68; 1.18]	0.432	0.926
Lymph node only	55	45 (81.8)	1.6 [0.6; 2.0]	49	36 (73.5)	0.7 [0.4; 1.7]	0.82 [0.52; 1.29]	0.395	
Primary Disease Site of Origin									
Upper Tract	54	44 (81.5)	1.1 [0.6; 1.8]	37	28 (75.7)	1.3 [0.6; 3.1]	0.92 [0.55; 1.54]	0.757	0.783
Lower Tract	154	120 (77.9)	1.0 [0.6; 1.7]	152	108 (71.1)	0.8 [0.4; 1.1]	0.90 [0.69; 1.17]	0.436	
Renal Function									
Normal	68	50 (73.5)	1.3 [0.7; 4.5]	60	38 (63.3)	1.8 [0.9; 2.7]	1.02 [0.66; 1.57]	0.921	0.610
Mild	101	80 (79.2)	1.1 [0.6; 1.7]	96	74 (77.1)	0.6 [0.4; 1.1]	0.80 [0.58; 1.10]	0.171	
Moderate/Severe	41	35 (85.4)	0.4 [0.2; 2.0]	33	24 (72.7)	0.6 [0.4; 1.2]	1.10 [0.64; 1.89]	0.736	
Stratification Factor: Liver Metastases									
Present	38	27 (71.1)	0.7 [0.4; 1.8]	34	24 (70.6)	1.3 [0.2; 3.8]	0.94 [0.54; 1.64]	0.841	0.938
Absent	172	138 (80.2)	1.1 [0.6; 1.8]	155	112 (72.3)	0.9 [0.6; 1.1]	0.90 [0.70; 1.16]	0.412	
Stratification Factor: PD-L1 Expression									
High	122	101 (82.8)	1.1 [0.6; 1.8]	112	84 (75.0)	0.9 [0.4; 1.3]	0.90 [0.67; 1.20]	0.467	0.939
Low	88	64 (72.7)	0.9 [0.6; 1.6]	77	52 (67.5)	0.9 [0.4; 1.8]	0.92 [0.64; 1.33]	0.674	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome

Tabelle 4G-73: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Social Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Sex									
Male	174	132 (75.9)	0.7 [0.6; 1.1]	147	98 (66.7)	0.9 [0.6; 1.2]	1.15 [0.88; 1.50]	0.294	0.472
Female	36	29 (80.6)	0.6 [0.4; 3.9]	42	31 (73.8)	0.6 [0.2; 1.1]	0.90 [0.53; 1.53]	0.688	
Geographic Region									
North America	49	42 (85.7)	0.5 [0.4; 0.7]	42	29 (69.0)	0.5 [0.4; 1.1]	1.38 [0.83; 2.27]	0.211	0.108
Europe	80	57 (71.3)	1.1 [0.4; 2.2]	73	49 (67.1)	0.6 [0.3; 1.4]	0.81 [0.55; 1.19]	0.281	
Rest of World	81	62 (76.5)	0.8 [0.6; 1.1]	74	51 (68.9)	1.1 [0.6; 1.8]	1.21 [0.84; 1.76]	0.308	
ECOG at Baseline									
0	117	89 (76.1)	0.8 [0.5; 1.1]	97	67 (69.1)	0.9 [0.6; 1.7]	1.10 [0.80; 1.52]	0.561	0.963
1-2	93	72 (77.4)	0.7 [0.4; 1.1]	91	61 (67.0)	0.7 [0.4; 1.1]	1.09 [0.77; 1.54]	0.636	
Race									
White	140	106 (75.7)	0.7 [0.4; 1.1]	115	79 (68.7)	0.6 [0.4; 0.9]	1.02 [0.76; 1.37]	0.883	0.607
Non-white	70	55 (78.6)	0.9 [0.5; 2.0]	74	50 (67.6)	1.1 [0.6; 1.8]	1.13 [0.76; 1.67]	0.542	
Metastatic Disease Site									
Visceral metastases	148	112 (75.7)	0.7 [0.4; 1.1]	130	79 (60.8)	1.1 [0.5; 1.6]	1.25 [0.93; 1.67]	0.134	0.059
Lymph node only	55	42 (76.4)	0.9 [0.4; 1.3]	49	41 (83.7)	0.6 [0.4; 0.9]	0.72 [0.46; 1.13]	0.153	
Primary Disease Site of Origin									
Upper Tract	54	43 (79.6)	0.6 [0.4; 1.1]	37	23 (62.2)	1.1 [0.5; 1.6]	1.49 [0.88; 2.50]	0.136	0.218
Lower Tract	154	117 (76.0)	0.7 [0.5; 1.1]	152	106 (69.7)	0.8 [0.4; 1.1]	1.00 [0.77; 1.31]	0.990	
Renal Function									
Normal	68	51 (75.0)	1.1 [0.5; 2.5]	60	44 (73.3)	0.8 [0.4; 1.1]	0.68 [0.44; 1.04]	0.075	0.117
Mild	101	79 (78.2)	0.7 [0.4; 1.1]	96	63 (65.6)	0.6 [0.4; 1.3]	1.18 [0.84; 1.65]	0.341	
Moderate/Severe	41	31 (75.6)	0.5 [0.4; 1.1]	33	22 (66.7)	1.1 [0.4; 3.2]	1.45 [0.82; 2.57]	0.200	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Social Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Stratification Factor: Liver Metastases									
Present	38	27 (71.1)	0.7 [0.4; 2.0]	34	22 (64.7)	1.3 [0.4; 5.3]	1.14 [0.64; 2.03]	0.666	0.821
Absent	172	134 (77.9)	0.7 [0.5; 1.1]	155	107 (69.0)	0.9 [0.4; 1.1]	1.07 [0.83; 1.38]	0.615	
Stratification Factor: PD-L1 Expression									
High	122	94 (77.0)	0.9 [0.5; 1.6]	112	83 (74.1)	0.6 [0.4; 1.1]	0.92 [0.68; 1.24]	0.586	0.128
Low	88	67 (76.1)	0.6 [0.4; 0.9]	77	46 (59.7)	1.1 [0.5; 1.8]	1.38 [0.95; 2.01]	0.093	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-74: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Emotionale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Emotional Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	94	50 (53.2)	8.0 [2.7; -]	84	41 (48.8)	3.8 [1.8; -]	0.88 [0.58; 1.34]	0.542	0.301
≥ 65	116	70 (60.3)	2.0 [1.1; 6.6]	105	52 (49.5)	3.8 [1.5; -]	1.18 [0.82; 1.69]	0.380	
Sex									
Male	174	102 (58.6)	2.8 [2.0; 6.6]	147	76 (51.7)	3.3 [1.8; 11.4]	1.04 [0.77; 1.40]	0.820	0.902
Female	36	18 (50.0)	10.1 [1.1; -]	42	17 (40.5)	Not reached [1.1; -]	1.06 [0.54; 2.09]	0.861	
Geographic Region									
North America	49	31 (63.3)	2.0 [1.1; 10.1]	42	17 (40.5)	11.4 [2.0; -]	1.89 [1.04; 3.44]	0.038	0.095
Europe	80	42 (52.5)	6.6 [2.0; -]	73	36 (49.3)	2.3 [1.3; -]	0.83 [0.52; 1.30]	0.410	
Rest of World	81	47 (58.0)	3.8 [2.0; 12.1]	74	40 (54.1)	3.2 [1.3; -]	0.97 [0.63; 1.48]	0.870	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Emotional Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	117	63 (53.8)	3.9 [2.0; -]	97	43 (44.3)	7.3 [3.2; -]	1.16 [0.78; 1.72]	0.467	0.601
1-2	93	57 (61.3)	2.3 [1.5; 6.6]	91	49 (53.8)	2.2 [1.1; 4.5]	0.98 [0.67; 1.45]	0.927	
Race									
White	140	81 (57.9)	2.4 [1.7; 10.1]	115	63 (54.8)	2.3 [1.5; 3.9]	0.90 [0.65; 1.26]	0.549	0.213
Non-white	70	39 (55.7)	5.2 [2.0; 16.3]	74	30 (40.5)	Not reached [3.2; -]	1.27 [0.78; 2.07]	0.334	
Metastatic Disease Site									
Visceral metastases	148	81 (54.7)	6.6 [2.0; 10.7]	130	61 (46.9)	3.8 [2.0; -]	1.05 [0.75; 1.47]	0.777	0.919
Lymph node only	55	34 (61.8)	2.2 [0.9; 16.3]	49	26 (53.1)	3.8 [0.9; -]	1.05 [0.62; 1.77]	0.863	
Primary Disease Site of Origin									
Upper Tract	54	31 (57.4)	3.0 [1.5; -]	37	19 (51.4)	3.3 [1.3; -]	0.98 [0.54; 1.76]	0.943	0.994
Lower Tract	154	87 (56.5)	3.9 [2.0; 10.7]	152	74 (48.7)	3.8 [2.0; -]	1.02 [0.74; 1.39]	0.924	
Renal Function									
Normal	68	38 (55.9)	3.9 [1.6; -]	60	31 (51.7)	2.2 [1.1; -]	0.88 [0.54; 1.43]	0.607	0.623
Mild	101	59 (58.4)	2.8 [1.7; 10.1]	96	46 (47.9)	5.9 [2.0; -]	1.12 [0.76; 1.66]	0.562	
Moderate/Severe	41	23 (56.1)	5.2 [1.1; -]	33	16 (48.5)	3.3 [1.1; -]	0.96 [0.50; 1.87]	0.915	
Stratification Factor: PD-L1 Expression									
High	122	71 (58.2)	2.8 [1.8; 9.4]	112	55 (49.1)	3.8 [2.0; -]	1.12 [0.78; 1.59]	0.545	0.544
Low	88	49 (55.7)	3.8 [2.0; 12.1]	77	38 (49.4)	3.2 [1.5; -]	0.95 [0.62; 1.46]	0.811	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Tabelle 4G-75: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Kognitive Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Cognitive Functioning	Participants with Event	Median Time ^c in Months [95 %-CI]	Participants with Event	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
		N ^b	n (%)	N ^b	n (%)				
Age									
< 65	94	58 (61.7)	2.4 [1.3; 5.9]	84	58 (69.0)	0.7 [0.4; 1.8]	0.67 [0.46; 0.97]	0.033	0.080
≥ 65	116	85 (73.3)	1.1 [0.6; 2.0]	105	72 (68.6)	1.1 [0.7; 2.2]	0.98 [0.72; 1.35]	0.925	
Sex									
Male	174	117 (67.2)	2.0 [1.1; 2.7]	147	100 (68.0)	0.9 [0.6; 1.8]	0.80 [0.61; 1.05]	0.110	0.654
Female	36	26 (72.2)	0.9 [0.4; 7.4]	42	30 (71.4)	1.3 [0.6; 3.1]	0.85 [0.49; 1.48]	0.570	
ECOG at Baseline									
0	117	78 (66.7)	2.0 [1.0; 3.2]	97	65 (67.0)	0.9 [0.6; 2.2]	0.80 [0.57; 1.12]	0.191	0.886
1-2	93	65 (69.9)	1.3 [0.7; 2.1]	91	64 (70.3)	1.0 [0.4; 1.8]	0.81 [0.57; 1.15]	0.245	
Race									
White	140	96 (68.6)	1.8 [1.0; 2.5]	115	82 (71.3)	0.9 [0.6; 1.5]	0.77 [0.57; 1.04]	0.091	0.571
Non-white	70	47 (67.1)	1.8 [0.6; 3.9]	74	48 (64.9)	1.1 [0.4; 3.8]	0.95 [0.63; 1.43]	0.812	
Metastatic Disease Site									
Visceral metastases	148	98 (66.2)	1.9 [1.0; 3.9]	130	85 (65.4)	0.9 [0.6; 1.8]	0.82 [0.61; 1.10]	0.191	0.803
Lymph node only	55	39 (70.9)	1.5 [0.6; 3.2]	49	37 (75.5)	1.1 [0.4; 2.3]	0.77 [0.49; 1.23]	0.279	
Primary Disease Site of Origin									
Upper Tract	54	38 (70.4)	1.3 [0.6; 2.0]	37	23 (62.2)	1.1 [0.6; -]	1.19 [0.70; 2.03]	0.516	0.142
Lower Tract	154	103 (66.9)	1.8 [1.1; 3.9]	152	107 (70.4)	0.9 [0.6; 1.7]	0.73 [0.55; 0.96]	0.022	
Renal Function									
Normal	68	45 (66.2)	3.9 [1.0; 6.6]	60	44 (73.3)	0.8 [0.4; 1.5]	0.56 [0.36; 0.86]	0.009	0.135
Mild	101	70 (69.3)	1.8 [0.7; 2.3]	96	66 (68.8)	1.1 [0.6; 2.5]	0.88 [0.63; 1.24]	0.467	
Moderate/Severe	41	28 (68.3)	0.9 [0.4; 7.3]	33	20 (60.6)	1.3 [0.4; -]	1.12 [0.62; 2.03]	0.697	
Stratification Factor: Liver Metastases									
Present	38	25 (65.8)	1.3 [0.4; 5.3]	34	23 (67.6)	0.7 [0.4; 5.3]	0.82 [0.46; 1.45]	0.494	0.940
Absent	172	118 (68.6)	1.8 [1.1; 2.7]	155	107 (69.0)	1.1 [0.6; 1.8]	0.82 [0.63; 1.06]	0.132	
Stratification Factor: PD-L1 Expression									
High	122	84 (68.9)	1.8 [0.9; 2.8]	112	79 (70.5)	0.9 [0.6; 2.0]	0.81 [0.59; 1.11]	0.185	0.994
Low	88	59 (67.0)	1.8 [0.7; 3.9]	77	51 (66.2)	1.1 [0.4; 2.5]	0.83 [0.57; 1.20]	0.319	

a: Database Cutoff Date: 08AUG2023

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Cognitive Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-76: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Social Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Sex									
Male	174	132 (75.9)	0.7 [0.6; 1.1]	147	98 (66.7)	0.9 [0.6; 1.2]	1.15 [0.88; 1.50]	0.294	0.472
Female	36	29 (80.6)	0.6 [0.4; 3.9]	42	31 (73.8)	0.6 [0.2; 1.1]	0.90 [0.53; 1.53]	0.688	
Geographic Region									
North America	49	42 (85.7)	0.5 [0.4; 0.7]	42	29 (69.0)	0.5 [0.4; 1.1]	1.38 [0.83; 2.27]	0.211	0.108
Europe	80	57 (71.3)	1.1 [0.4; 2.2]	73	49 (67.1)	0.6 [0.3; 1.4]	0.81 [0.55; 1.19]	0.281	
Rest of World	81	62 (76.5)	0.8 [0.6; 1.1]	74	51 (68.9)	1.1 [0.6; 1.8]	1.21 [0.84; 1.76]	0.308	
ECOG at Baseline									
0	117	89 (76.1)	0.8 [0.5; 1.1]	97	67 (69.1)	0.9 [0.6; 1.7]	1.10 [0.80; 1.52]	0.561	0.963
1-2	93	72 (77.4)	0.7 [0.4; 1.1]	91	61 (67.0)	0.7 [0.4; 1.1]	1.09 [0.77; 1.54]	0.636	
Race									
White	140	106 (75.7)	0.7 [0.4; 1.1]	115	79 (68.7)	0.6 [0.4; 0.9]	1.02 [0.76; 1.37]	0.883	0.607
Non-white	70	55 (78.6)	0.9 [0.5; 2.0]	74	50 (67.6)	1.1 [0.6; 1.8]	1.13 [0.76; 1.67]	0.542	
Metastatic Disease Site									
Visceral metastases	148	112 (75.7)	0.7 [0.4; 1.1]	130	79 (60.8)	1.1 [0.5; 1.6]	1.25 [0.93; 1.67]	0.134	0.059
Lymph node only	55	42 (76.4)	0.9 [0.4; 1.3]	49	41 (83.7)	0.6 [0.4; 0.9]	0.72 [0.46; 1.13]	0.153	
Primary Disease Site of Origin									
Upper Tract	54	43 (79.6)	0.6 [0.4; 1.1]	37	23 (62.2)	1.1 [0.5; 1.6]	1.49 [0.88; 2.50]	0.136	0.218
Lower Tract	154	117 (76.0)	0.7 [0.5; 1.1]	152	106 (69.7)	0.8 [0.4; 1.1]	1.00 [0.77; 1.31]	0.990	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Social Functioning	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Renal Function									
Normal	68	51 (75.0)	1.1 [0.5; 2.5]	60	44 (73.3)	0.8 [0.4; 1.1]	0.68 [0.44; 1.04]	0.075	0.117
Mild	101	79 (78.2)	0.7 [0.4; 1.1]	96	63 (65.6)	0.6 [0.4; 1.3]	1.18 [0.84; 1.65]	0.341	
Moderate/Severe	41	31 (75.6)	0.5 [0.4; 1.1]	33	22 (66.7)	1.1 [0.4; 3.2]	1.45 [0.82; 2.57]	0.200	
Stratification Factor: Liver Metastases									
Present	38	27 (71.1)	0.7 [0.4; 2.0]	34	22 (64.7)	1.3 [0.4; 5.3]	1.14 [0.64; 2.03]	0.666	0.821
Absent	172	134 (77.9)	0.7 [0.5; 1.1]	155	107 (69.0)	0.9 [0.4; 1.1]	1.07 [0.83; 1.38]	0.615	
Stratification Factor: PD-L1 Expression									
High	122	94 (77.0)	0.9 [0.5; 1.6]	112	83 (74.1)	0.6 [0.4; 1.1]	0.92 [0.68; 1.24]	0.586	0.128
Low	88	67 (76.1)	0.6 [0.4; 0.9]	77	46 (59.7)	1.1 [0.5; 1.8]	1.38 [0.95; 2.01]	0.093	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Cisplatin ungeeignet

Globaler Gesundheitsstatus des EORTC QLQ-C30

Tabelle 4G-77: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Globalen Gesundheitsstatus des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
EORTC QLQ-C30 Global Health Status/QoL	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33	25 (75.8)	2.3 [1.1; 2.7]	22	16 (72.7)	1.0 [0.2; 2.5]	0.89 [0.45; 1.74]	0.729	0.547
≥ 65	133	92 (69.2)	0.7 [0.5; 1.3]	144	97 (67.4)	0.9 [0.6; 1.1]	1.02 [0.76; 1.36]	0.897	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
EORTC QLQ-C30 Global Health Status/QoL	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Sex									
Male	123	87 (70.7)	1.1 [0.6; 1.5]	126	83 (65.9)	1.1 [0.6; 1.8]	1.00 [0.74; 1.36]	0.980	0.475
Female	43	30 (69.8)	1.3 [0.5; 2.3]	40	30 (75.0)	0.4 [0.4; 1.1]	0.77 [0.44; 1.37]	0.375	
Geographic Region									
North America	35	22 (62.9)	0.6 [0.4; 2.3]	28	18 (64.3)	1.1 [0.4; 1.3]	0.95 [0.49; 1.85]	0.878	0.960
Europe	57	41 (71.9)	0.9 [0.2; 2.0]	76	57 (75.0)	0.8 [0.4; 1.7]	1.00 [0.66; 1.53]	0.990	
Rest of World	74	54 (73.0)	1.3 [0.7; 2.3]	62	38 (61.3)	1.1 [0.4; 2.5]	1.07 [0.70; 1.65]	0.746	
ECOG at Baseline									
0	74	56 (75.7)	1.1 [0.6; 1.3]	72	53 (73.6)	0.8 [0.4; 1.3]	1.01 [0.68; 1.48]	0.977	0.772
1-2	92	61 (66.3)	1.3 [0.6; 2.4]	94	60 (63.8)	0.9 [0.6; 1.7]	1.02 [0.71; 1.47]	0.896	
Race									
White	110	72 (65.5)	1.1 [0.6; 1.8]	114	77 (67.5)	1.1 [0.6; 1.7]	0.96 [0.69; 1.32]	0.789	0.857
Non-white	56	45 (80.4)	1.1 [0.5; 1.8]	52	36 (69.2)	0.6 [0.4; 1.3]	1.00 [0.62; 1.61]	0.990	
Metastatic Disease Site									
Visceral metastases	121	84 (69.4)	1.3 [0.6; 2.0]	128	85 (66.4)	0.9 [0.6; 1.7]	0.97 [0.71; 1.32]	0.845	0.455
Lymph node only	36	28 (77.8)	0.8 [0.5; 1.3]	30	24 (80.0)	0.6 [0.2; 1.3]	0.70 [0.39; 1.25]	0.225	
Renal Function									
Normal	6	5 (83.3)	0.6 [0.2; -]	10	6 (60.0)	0.7 [0.2; -]	1.15 [0.25; 5.39]	0.855	0.943
Mild	39	28 (71.8)	1.3 [0.6; 2.0]	34	26 (76.5)	1.3 [0.4; 3.2]	0.99 [0.57; 1.71]	0.972	
Moderate/Severe	121	84 (69.4)	1.1 [0.6; 1.7]	122	81 (66.4)	0.8 [0.5; 1.1]	0.98 [0.72; 1.34]	0.905	
Stratification Factor: Liver Metastases									
Present	41	30 (73.2)	0.4 [0.2; 1.8]	41	23 (56.1)	0.9 [0.4; 3.9]	1.40 [0.81; 2.42]	0.233	0.142
Absent	125	87 (69.6)	1.3 [0.7; 1.8]	125	90 (72.0)	0.9 [0.6; 1.1]	0.87 [0.64; 1.17]	0.347	
Stratification Factor: PD-L1 Expression									
High	97	75 (77.3)	0.9 [0.6; 1.6]	98	70 (71.4)	0.6 [0.4; 1.1]	0.92 [0.66; 1.28]	0.620	0.721
Low	69	42 (60.9)	1.3 [0.6; 2.4]	68	43 (63.2)	1.8 [0.6; 3.2]	1.05 [0.69; 1.61]	0.816	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
EORTC QLQ-C30 Global Health Status/QoL	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome; QoL: Quality of Life

Funktionsskalen des EORTC QLQ-C30

Tabelle 4G-78: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperliche Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33 (69.7)	3.2 [0.7; 10.7]	22 (86.4)	1.6 [0.8; 2.0]	0.58 [0.30; 1.13]	0.109	0.394		
≥ 65	133 (73.7)	0.9 [0.6; 1.3]	144 (72.9)	0.6 [0.4; 0.7]	0.84 [0.63; 1.11]	0.225			
Sex									
Male	123 (73.2)	1.3 [0.7; 2.0]	126 (71.4)	0.8 [0.4; 1.3]	0.82 [0.60; 1.10]	0.186	0.596		
Female	43 (72.1)	0.9 [0.4; 1.3]	40 (85.0)	0.6 [0.4; 0.7]	0.64 [0.37; 1.11]	0.115			
Geographic Region									
North America	35 (74.3)	0.4 [0.4; 3.9]	28 (64.3)	0.7 [0.4; 1.3]	1.07 [0.57; 2.04]	0.826	0.460		
Europe	57 (71.9)	1.2 [0.6; 2.0]	76 (77.6)	0.6 [0.4; 1.3]	0.73 [0.48; 1.12]	0.151			
Rest of World	74 (73.0)	1.3 [0.9; 2.3]	62 (75.8)	0.6 [0.4; 1.6]	0.72 [0.48; 1.08]	0.111			
ECOG at Baseline									
0	74 (78.4)	1.5 [0.7; 2.3]	72 (79.2)	0.6 [0.4; 0.9]	0.59 [0.40; 0.86]	0.007	0.110		
1-2	92 (68.5)	0.9 [0.4; 1.3]	94 (71.3)	0.7 [0.4; 1.6]	0.95 [0.67; 1.35]	0.778			
Race									
White	110 (69.1)	1.1 [0.6; 2.0]	114 (75.4)	0.6 [0.4; 0.8]	0.74 [0.54; 1.02]	0.066	0.562		
Non-white	56 (80.4)	1.1 [0.6; 2.0]	52 (73.1)	1.1 [0.6; 1.6]	0.89 [0.56; 1.42]	0.627			
Metastatic Disease Site									
Visceral metastases	121 (69.4)	1.3 [0.7; 2.2]	128 (74.2)	0.6 [0.4; 1.1]	0.70 [0.52; 0.95]	0.022	0.479		
Lymph node only	36 (83.3)	1.0 [0.6; 1.3]	30 (73.3)	0.7 [0.4; 1.6]	0.82 [0.45; 1.48]	0.505			
Primary Disease Site of Origin									
Upper Tract	62 (79.0)	0.9 [0.4; 1.8]	44 (81.8)	0.6 [0.4; 1.3]	0.87 [0.56; 1.36]	0.543	0.543		
Lower Tract	104 (69.2)	1.2 [0.7; 2.2]	121 (72.7)	0.7 [0.4; 1.1]	0.74 [0.53; 1.01]	0.060			

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	5 (83.3)	0.6 [0.1; -]	10	5 (50.0)	1.6 [0.2; -]	1.19 [0.25; 5.60]	0.823	0.508
Mild	39	28 (71.8)	2.0 [1.1; 3.9]	34	26 (76.5)	0.8 [0.4; 1.6]	0.64 [0.36; 1.12]	0.117	
Moderate/Severe	121	88 (72.7)	0.9 [0.5; 1.3]	122	93 (76.2)	0.6 [0.4; 0.9]	0.78 [0.58; 1.05]	0.106	
Stratification Factor: Liver Metastases									
Present	41	29 (70.7)	0.9 [0.4; 2.0]	41	29 (70.7)	0.6 [0.4; 1.5]	0.85 [0.50; 1.46]	0.562	0.807
Absent	125	92 (73.6)	1.1 [0.7; 2.0]	125	95 (76.0)	0.7 [0.5; 1.1]	0.76 [0.57; 1.02]	0.071	
Stratification Factor: PD-L1 Expression									
High	97	75 (77.3)	1.1 [0.6; 1.8]	98	74 (75.5)	0.7 [0.4; 1.3]	0.81 [0.58; 1.12]	0.207	0.644
Low	69	46 (66.7)	0.9 [0.4; 2.1]	68	50 (73.5)	0.6 [0.4; 1.3]	0.74 [0.49; 1.12]	0.160	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Tabelle 4G-79: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Rollenfunktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	33	23 (69.7)	3.2 [0.7; 10.7]	22	19 (86.4)	1.6 [0.8; 2.0]	0.58 [0.30; 1.13]	0.109	0.394
≥ 65	133	98 (73.7)	0.9 [0.6; 1.3]	144	105 (72.9)	0.6 [0.4; 0.7]	0.84 [0.63; 1.11]	0.225	
Sex									
Male	123	90 (73.2)	1.3 [0.7; 2.0]	126	90 (71.4)	0.8 [0.4; 1.3]	0.82 [0.60; 1.10]	0.186	0.596
Female	43	31 (72.1)	0.9 [0.4; 1.3]	40	34 (85.0)	0.6 [0.4; 0.7]	0.64 [0.37; 1.11]	0.115	
Geographic Region									
North America	35	26 (74.3)	0.4 [0.4; 3.9]	28	18 (64.3)	0.7 [0.4; 1.3]	1.07 [0.57; 2.04]	0.826	0.460
Europe	57	41 (71.9)	1.2 [0.6; 2.0]	76	59 (77.6)	0.6 [0.4; 1.3]	0.73 [0.48; 1.12]	0.151	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Physical Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	74	54 (73.0)	1.3 [0.9; 2.3]	62	47 (75.8)	0.6 [0.4; 1.6]	0.72 [0.48; 1.08]	0.111	
ECOG at Baseline									
0	74	58 (78.4)	1.5 [0.7; 2.3]	72	57 (79.2)	0.6 [0.4; 0.9]	0.59 [0.40; 0.86]	0.007	0.110
1-2	92	63 (68.5)	0.9 [0.4; 1.3]	94	67 (71.3)	0.7 [0.4; 1.6]	0.95 [0.67; 1.35]	0.778	
Race									
White	110	76 (69.1)	1.1 [0.6; 2.0]	114	86 (75.4)	0.6 [0.4; 0.8]	0.74 [0.54; 1.02]	0.066	0.562
Non-white	56	45 (80.4)	1.1 [0.6; 2.0]	52	38 (73.1)	1.1 [0.6; 1.6]	0.89 [0.56; 1.42]	0.627	
Metastatic Disease Site									
Visceral metastases	121	84 (69.4)	1.3 [0.7; 2.2]	128	95 (74.2)	0.6 [0.4; 1.1]	0.70 [0.52; 0.95]	0.022	0.479
Lymph node only	36	30 (83.3)	1.0 [0.6; 1.3]	30	22 (73.3)	0.7 [0.4; 1.6]	0.82 [0.45; 1.48]	0.505	
Primary Disease Site of Origin									
Upper Tract	62	49 (79.0)	0.9 [0.4; 1.8]	44	36 (81.8)	0.6 [0.4; 1.3]	0.87 [0.56; 1.36]	0.543	0.543
Lower Tract	104	72 (69.2)	1.2 [0.7; 2.2]	121	88 (72.7)	0.7 [0.4; 1.1]	0.74 [0.53; 1.01]	0.060	
Renal Function									
Normal	6	5 (83.3)	0.6 [0.1; -]	10	5 (50.0)	1.6 [0.2; -]	1.19 [0.25; 5.60]	0.823	0.508
Mild	39	28 (71.8)	2.0 [1.1; 3.9]	34	26 (76.5)	0.8 [0.4; 1.6]	0.64 [0.36; 1.12]	0.117	
Moderate/Severe	121	88 (72.7)	0.9 [0.5; 1.3]	122	93 (76.2)	0.6 [0.4; 0.9]	0.78 [0.58; 1.05]	0.106	
Stratification Factor: Liver Metastases									
Present	41	29 (70.7)	0.9 [0.4; 2.0]	41	29 (70.7)	0.6 [0.4; 1.5]	0.85 [0.50; 1.46]	0.562	0.807
Absent	125	92 (73.6)	1.1 [0.7; 2.0]	125	95 (76.0)	0.7 [0.5; 1.1]	0.76 [0.57; 1.02]	0.071	
Stratification Factor: PD-L1 Expression									
High	97	75 (77.3)	1.1 [0.6; 1.8]	98	74 (75.5)	0.7 [0.4; 1.3]	0.81 [0.58; 1.12]	0.207	0.644
Low	69	46 (66.7)	0.9 [0.4; 2.1]	68	50 (73.5)	0.6 [0.4; 1.3]	0.74 [0.49; 1.12]	0.160	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-80: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Social Functioning	Participants with Event	Median Time ^c in Months	Participants with Event	Median Time ^c in Months	Hazard Ratio	p-Value ^{d,e}		
		N ^b	n (%)	[95 %-CI]	N ^b	n (%)	[95 %-CI]		
Age									
< 65	33	19 (57.6)	4.5 [0.4; 12.8]	22	13 (59.1)	1.8 [0.4; -]	0.86 [0.40; 1.83]	0.694	0.699
≥ 65	133	99 (74.4)	0.7 [0.5; 1.3]	144	98 (68.1)	0.6 [0.4; 1.1]	1.02 [0.76; 1.35]	0.910	
Geographic Region									
North America	35	25 (71.4)	1.3 [0.2; 5.2]	28	17 (60.7)	1.1 [0.4; 3.9]	0.97 [0.50; 1.89]	0.938	0.449
Europe	57	41 (71.9)	0.7 [0.5; 1.1]	76	52 (68.4)	0.7 [0.4; 1.8]	1.22 [0.80; 1.88]	0.355	
Rest of World	74	52 (70.3)	1.1 [0.5; 2.7]	62	42 (67.7)	0.5 [0.4; 1.3]	0.87 [0.57; 1.33]	0.521	
ECOG at Baseline									
0	74	56 (75.7)	1.1 [0.6; 2.0]	72	50 (69.4)	1.1 [0.6; 1.8]	0.88 [0.59; 1.31]	0.521	0.499
1-2	92	62 (67.4)	0.6 [0.4; 1.5]	94	61 (64.9)	0.6 [0.4; 1.1]	1.10 [0.77; 1.57]	0.613	
Race									
White	110	78 (70.9)	0.7 [0.5; 1.1]	114	78 (68.4)	0.7 [0.4; 1.1]	1.06 [0.77; 1.46]	0.714	0.522
Non-white	56	40 (71.4)	1.3 [0.5; 5.9]	52	33 (63.5)	1.1 [0.4; 2.5]	0.92 [0.56; 1.50]	0.730	
Metastatic Disease Site									
Visceral metastases	121	89 (73.6)	0.9 [0.5; 1.5]	128	86 (67.2)	0.7 [0.4; 1.1]	0.97 [0.72; 1.32]	0.848	0.970
Lymph node only	36	24 (66.7)	1.0 [0.5; 2.4]	30	19 (63.3)	1.4 [0.4; 4.5]	0.97 [0.53; 1.79]	0.929	
Primary Disease Site of Origin									
Upper Tract	62	47 (75.8)	0.6 [0.4; 1.8]	44	30 (68.2)	1.3 [0.4; 2.5]	1.24 [0.78; 1.99]	0.368	0.275
Lower Tract	104	71 (68.3)	1.1 [0.6; 1.7]	121	81 (66.9)	0.6 [0.4; 1.1]	0.87 [0.63; 1.21]	0.423	
Renal Function									
Normal	6	5 (83.3)	1.7 [0.4; -]	10	5 (50.0)	0.7 [0.2; -]	1.04 [0.20; 5.48]	0.962	0.718
Mild	39	26 (66.7)	1.5 [0.6; 2.7]	34	24 (70.6)	0.6 [0.4; 2.4]	0.80 [0.45; 1.41]	0.437	
Moderate/Severe	121	87 (71.9)	0.6 [0.4; 1.1]	122	82 (67.2)	0.9 [0.4; 1.3]	1.04 [0.77; 1.42]	0.784	
Stratification Factor: Liver Metastases									
Present	41	33 (80.5)	0.5 [0.4; 1.5]	41	26 (63.4)	0.6 [0.4; 2.2]	1.20 [0.71; 2.04]	0.499	0.287
Absent	125	85 (68.0)	1.1 [0.6; 1.8]	125	85 (68.0)	0.9 [0.4; 1.3]	0.92 [0.67; 1.24]	0.569	
Stratification Factor: PD-L1 Expression									
High	97	69 (71.1)	0.9 [0.5; 1.8]	98	66 (67.3)	0.6 [0.4; 1.1]	0.94 [0.66; 1.32]	0.713	0.725
Low	69	49 (71.0)	0.9 [0.4; 1.5]	68	45 (66.2)	1.1 [0.4; 2.4]	1.04 [0.69; 1.58]	0.841	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Social Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-81: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Emotionale Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Emotional Functioning	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33 (60.6)	4.5 [2.0; 14.2]	22 (63.6)	14 (63.6)	1.7 [0.4; -]	0.82 [0.40; 1.69]	0.596	0.913	
≥ 65	133 (52.6)	7.0 [1.8; 10.1]	144 (55.6)	80 (55.6)	2.5 [1.1; 3.8]	0.78 [0.56; 1.08]	0.132		
Geographic Region									
North America	35 (34.3)	12 [2.5; -]	Not reached	28 (46.4)	13 [1.1; -]	2.5 [0.19; 1.11]	0.46 [0.19; 1.11]	0.085	0.403
Europe	57 (56.1)	32 [0.9; 11.4]	6.6	76 (52.6)	40 [1.1; -]	3.1 [0.58; 1.55]	0.94 [0.58; 1.55]	0.817	
Rest of World	74 (62.2)	46 [1.5; 6.6]	2.7	62 (66.1)	41 [0.7; 2.7]	1.1 [0.44; 1.05]	0.68 [0.44; 1.05]	0.079	
ECOG at Baseline									
0	74 (51.4)	38 [1.8; -]	5.9	72 (59.7)	43 [1.1; 3.2]	1.4 [0.41; 1.00]	0.64 [0.41; 1.00]	0.052	0.220
1-2	92 (56.5)	52 [1.5; 9.4]	3.2	94 (54.3)	51 [1.1; 5.9]	2.7 [0.61; 1.35]	0.91 [0.61; 1.35]	0.640	
Race									
White	110 (51.8)	57 [2.1; 10.7]	5.9	114 (55.3)	63 [1.1; 3.8]	2.0 [0.52; 1.09]	0.75 [0.52; 1.09]	0.130	0.986
Non-white	56 (58.9)	33 [1.5; 12.8]	4.5	52 (59.6)	31 [0.7; 10.8]	2.7 [0.47; 1.31]	0.79 [0.47; 1.31]	0.355	
Metastatic Disease Site									
Visceral metastases	121 (51.2)	62 [1.8; 12.8]	3.4	128 (58.6)	75 [1.1; 3.1]	1.8 [0.53; 1.04]	0.74 [0.53; 1.04]	0.087	0.265
Lymph node only	36 (58.3)	21 [1.5; 11.5]	6.6	30 (43.3)	13 [1.1; -]	12.1 [0.52; 2.21]	1.07 [0.52; 2.21]	0.853	
Primary Disease Site of Origin									
Upper Tract	62 (50.0)	31 [2.1; -]	6.6	44 (56.8)	25 [0.5; 10.8]	3.2 [0.40; 1.16]	0.68 [0.40; 1.16]	0.161	0.524
Lower Tract	104 (56.7)	59 [1.5; 9.4]	2.7	121 (57.0)	69 [1.1; 3.2]	1.7 [0.58; 1.18]	0.83 [0.58; 1.18]	0.294	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Emotional Functioning	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Renal Function									
Normal	6 (50.0)	3 1.8 [0.6; -]	10 (30.0)	3 Not reached [0.2; -]	n.a. [n.a.; n.a.]	0.997	0.537		
Mild	39 (53.8)	21 2.8 [1.5; 14.2]	34 (50.0)	17 8.7 [0.8; -]	1.09 [0.56; 2.12]	0.796			
Moderate/Severe	121 (54.5)	66 5.9 [1.8; 10.1]	122 (60.7)	74 1.7 [1.1; 3.1]	0.69 [0.49; 0.98]	0.037			
Stratification Factor: Liver Metastases									
Present	41 (56.1)	23 2.8 [0.6; 12.8]	41 (51.2)	21 2.7 [0.6; -]	0.96 [0.53; 1.74]	0.888	0.449		
Absent	125 (53.6)	67 5.9 [2.5; 10.7]	125 (58.4)	73 1.8 [1.1; 3.2]	0.72 [0.52; 1.01]	0.061			
Stratification Factor: PD-L1 Expression									
High	97 (56.7)	55 4.5 [1.8; 9.4]	98 (59.2)	58 1.7 [1.1; 4.5]	0.76 [0.52; 1.11]	0.161	0.964		
Low	69 (50.7)	35 3.8 [1.7; 14.2]	68 (52.9)	36 2.7 [1.1; -]	0.79 [0.49; 1.27]	0.330			
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: PRO full-analysis-set population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome									

Tabelle 4G-82: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Kognitive Funktion des EORTC QLQ-C30 der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Cognitive Functioning	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Participants with Event n (%)	Median Time ^e in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	33 (63.6)	21 2.4 [0.9; 8.0]	22 (68.2)	15 1.7 [0.4; -]	0.83 [0.42; 1.66]	0.607	0.986		
≥ 65	133 (68.4)	91 1.3 [0.9; 1.7]	144 (68.8)	99 0.9 [0.6; 1.3]	0.86 [0.64; 1.14]	0.287			
Sex									
Male	123 (68.3)	84 1.5 [1.1; 2.6]	126 (65.1)	82 1.1 [0.6; 2.1]	0.93 [0.68; 1.27]	0.650	0.077		
Female	43 (65.1)	28 1.5 [0.7; 2.1]	40 (80.0)	32 0.8 [0.4; 1.3]	0.57 [0.32; 0.99]	0.045			
Geographic Region									
North America	35 (45.7)	16 1.5 [0.6; -]	28 (64.3)	18 0.9 [0.4; 2.5]	0.64 [0.31; 1.32]	0.227	0.051		
Europe	57 (70.2)	40 1.1 [0.6; 2.0]	76 (64.5)	49 1.1 [0.7; 3.1]	1.21 [0.79; 1.85]	0.389			

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Cognitive Functioning	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	74	56 (75.7)	1.6 [1.1; 2.7]	62	47 (75.8)	0.6 [0.4; 1.3]	0.61 [0.41; 0.92]	0.019	
ECOG at Baseline									
0	74	54 (73.0)	1.3 [0.9; 2.7]	72	46 (63.9)	1.1 [0.6; 1.8]	0.98 [0.66; 1.45]	0.906	0.370
1-2	92	58 (63.0)	1.5 [0.9; 2.3]	94	68 (72.3)	0.7 [0.6; 1.5]	0.76 [0.54; 1.09]	0.141	
Race									
White	110	68 (61.8)	1.5 [0.9; 2.3]	114	74 (64.9)	0.9 [0.6; 1.5]	0.87 [0.62; 1.21]	0.399	0.587
Non-white	56	44 (78.6)	1.5 [0.9; 3.8]	52	40 (76.9)	1.1 [0.4; 1.8]	0.75 [0.48; 1.19]	0.220	
Metastatic Disease Site									
Visceral metastases	121	81 (66.9)	1.3 [0.9; 1.8]	128	86 (67.2)	0.9 [0.6; 1.3]	0.88 [0.64; 1.19]	0.397	0.864
Lymph node only	36	26 (72.2)	1.6 [0.9; 2.7]	30	22 (73.3)	1.8 [0.6; 3.1]	0.81 [0.45; 1.44]	0.474	
Primary Disease Site of Origin									
Upper Tract	62	43 (69.4)	1.5 [0.9; 2.1]	44	34 (77.3)	0.7 [0.4; 1.8]	0.78 [0.50; 1.24]	0.298	0.616
Lower Tract	104	69 (66.3)	1.5 [0.9; 2.4]	121	79 (65.3)	1.1 [0.6; 1.8]	0.86 [0.62; 1.19]	0.363	
Stratification Factor: Liver Metastases									
Present	41	24 (58.5)	1.3 [0.6; 12.8]	41	25 (61.0)	0.6 [0.4; 7.3]	0.87 [0.49; 1.52]	0.617	0.944
Absent	125	88 (70.4)	1.5 [1.1; 2.3]	125	89 (71.2)	1.1 [0.6; 1.5]	0.82 [0.61; 1.11]	0.202	
Stratification Factor: PD-L1 Expression									
High	97	70 (72.2)	1.5 [0.9; 2.1]	98	69 (70.4)	1.3 [0.6; 2.0]	0.93 [0.66; 1.30]	0.661	0.270
Low	69	42 (60.9)	1.5 [1.1; 3.8]	68	45 (66.2)	0.7 [0.5; 1.1]	0.70 [0.46; 1.07]	0.101	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: PRO full-analysis-set population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model stratified by PD-L1 expression (high or low), and liver metastases (present or absent) at randomization, with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term). Subgroups liver metastases, and PD-L1 expression are removed from their own respective stratification factors</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1; PRO: Patient Reported Outcome</p>									

Nebenwirkungen**Cisplatin geeignet*****Unerwünschte Ereignisse gesamt****Unerwünschte Ereignisse gesamt*Tabelle 4G-83: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]		Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{de}	
Adverse Events									
Age									
< 65	105	105 (100.0)	1.0 [0.7; 1.1]	102	101 (99.0)	0.6 [0.4; 0.7]	0.72 [0.54; 0.95]	0.021	0.148
≥ 65	134	134 (100.0)	0.9 [0.7; 1.0]	134	133 (99.3)	0.6 [0.4; 0.9]	0.94 [0.74; 1.19]	0.597	
Sex									
Male	197	197 (100.0)	1.0 [0.7; 1.1]	181	179 (98.9)	0.6 [0.6; 0.9]	0.84 [0.69; 1.03]	0.103	0.631
Female	42	42 (100.0)	0.7 [0.3; 0.9]	55	55 (100.0)	0.4 [0.3; 0.9]	0.84 [0.56; 1.26]	0.391	
Geographic Region									
North America	57	57 (100.0)	0.6 [0.3; 0.9]	51	51 (100.0)	0.4 [0.3; 0.4]	0.63 [0.42; 0.93]	0.020	0.160
Europe	97	97 (100.0)	1.0 [0.9; 1.1]	101	100 (99.0)	0.9 [0.6; 1.0]	0.82 [0.62; 1.09]	0.177	
Rest of World	85	85 (100.0)	0.9 [0.7; 1.1]	84	83 (98.8)	0.6 [0.4; 0.9]	0.87 [0.64; 1.19]	0.387	
Race									
White	166	166 (100.0)	0.9 [0.7; 1.0]	147	145 (98.6)	0.7 [0.4; 0.9]	0.89 [0.71; 1.12]	0.332	0.237
Non-white	73	73 (100.0)	1.0 [0.7; 1.1]	89	89 (100.0)	0.6 [0.4; 0.7]	0.67 [0.49; 0.91]	0.012	
Primary Disease Site of Origin									
Upper Tract	61	61 (100.0)	0.9 [0.6; 1.1]	44	44 (100.0)	0.6 [0.4; 0.9]	0.94 [0.63; 1.39]	0.739	0.344
Lower Tract	176	176 (100.0)	1.0 [0.7; 1.0]	192	190 (99.0)	0.6 [0.4; 0.9]	0.78 [0.64; 0.96]	0.020	
Renal Function									
Normal	78	78 (100.0)	0.9 [0.4; 1.1]	81	80 (98.8)	0.6 [0.4; 0.9]	0.76 [0.55; 1.05]	0.093	0.853
Mild	115	115 (100.0)	1.0 [0.7; 1.1]	118	118 (100.0)	0.6 [0.4; 0.9]	0.86 [0.67; 1.12]	0.272	
Moderate/Severe	46	46 (100.0)	0.9 [0.7; 1.1]	37	36 (97.3)	0.6 [0.4; 1.0]	0.80 [0.51; 1.24]	0.312	
Stratification Factor: Liver Metastases									
Present	47	47 (100.0)	0.9 [0.6; 1.1]	47	46 (97.9)	0.9 [0.4; 1.1]	1.04 [0.69; 1.56]	0.854	0.179
Absent	192	192 (100.0)	1.0 [0.7; 1.0]	189	188 (99.5)	0.6 [0.4; 0.7]	0.77 [0.63; 0.94]	0.011	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: PD-L1 Expression	
High	138	138 (100.0)	0.9 [0.6; 1.0]	138	138 (100.0)	0.6 [0.4; 0.7]	0.79 [0.62; 1.01]	0.057	0.661	
Low	101	101 (100.0)	1.0 [0.7; 1.1]	98	96 (98.0)	0.6 [0.6; 1.0]	0.85 [0.64; 1.13]	0.266		
a: Database Cutoff Date: 08AUG2023 b: Number of participants: all-participants-as-treated population, cisplatin eligible c: From product-limit (Kaplan-Meier) method for censored data d: Based on Cox regression model with treatment as a covariate using Wald confidence interval e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) CI: Confidence Interval; PD-L1: Programmed Cell Death - Ligand 1										

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-84: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Age	
< 65	105	35 (33.3)	Not reached [-; -]	102	29 (28.4)	Not reached [-; -]	0.86 [0.51; 1.45]	0.571	0.551	
≥ 65	134	72 (53.7)	35.6 [20.9; -]	134	54 (40.3)	Not reached [18.3; -]	0.97 [0.67; 1.42]	0.893		
Sex										
Male	197	89 (45.2)	74.9 [41.0; -]	181	62 (34.3)	Not reached [-; -]	0.94 [0.66; 1.32]	0.703	0.821	
Female	42	18 (42.9)	Not reached [20.9; -]	55	21 (38.2)	Not reached [16.4; -]	0.92 [0.47; 1.79]	0.805		
Geographic Region										
North America	57	27 (47.4)	69.3 [24.7; -]	51	20 (39.2)	Not reached [12.4; -]	0.87 [0.47; 1.61]	0.652	0.431	
Europe	97	37 (38.1)	Not reached [74.9; -]	101	36 (35.6)	Not reached [-; -]	0.85 [0.53; 1.37]	0.498		
Rest of World	85	43 (50.6)	49.6 [21.1; -]	84	27 (32.1)	Not reached [-; -]	1.09 [0.65; 1.82]	0.745		
ECOG at Baseline										
0	136	55 (40.4)	Not reached [66.9; -]	124	38 (30.6)	Not reached [-; -]	1.05 [0.68; 1.61]	0.837	0.585	
1-2	103	52 (50.5)	43.3 [24.0; -]	111	45 (40.5)	Not reached [18.0; -]	0.84 [0.55; 1.28]	0.409		
Race										
White	166	65 (39.2)	Not reached [74.9; -]	147	52 (35.4)	Not reached [-; -]	0.79 [0.54; 1.16]	0.236	0.058	
Non-white	73	42 (57.5)	35.6 [14.1; 66.9]	89	31 (34.8)	Not reached [20.6; -]	1.27 [0.77; 2.08]	0.343		

Study: KEYNOTE-A39 ^a		EV+Pembro		Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
									Renal Function
Normal	78	25 (32.1)	Not reached [-; -]	81	27 (33.3)	Not reached [-; -]	0.82 [0.47; 1.44]	0.487	0.496
Mild	115	58 (50.4)	41.7 [26.0; -]	118	42 (35.6)	Not reached [-; -]	0.95 [0.62; 1.46]	0.821	
Moderate/Severe	46	24 (52.2)	54.7 [13.6; -]	37	14 (37.8)	Not reached [16.1; -]	1.01 [0.50; 2.01]	0.984	
Stratification Factor: PD-L1 Expression									
High	138	61 (44.2)	Not reached [41.0; -]	138	47 (34.1)	Not reached [-; -]	0.86 [0.57; 1.29]	0.459	0.955
Low	101	46 (45.5)	Not reached [17.4; -]	98	36 (36.7)	Not reached [20.6; -]	1.02 [0.65; 1.59]	0.943	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: all-participants-as-treated population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1									

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

Tabelle 4G-85: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro		Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Events (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
									Age
< 65	105	62 (59.0)	26.7 [18.1; 54.0]	102	69 (67.6)	7.1 [5.6; 10.0]	0.44 [0.30; 0.65]	< 0.001	0.279
≥ 65	134	102 (76.1)	11.6 [7.9; 19.0]	134	106 (79.1)	5.1 [3.0; 7.1]	0.57 [0.42; 0.76]	< 0.001	
Sex									
Male	197	135 (68.5)	19.0 [12.9; 27.0]	181	131 (72.4)	5.9 [4.1; 9.0]	0.51 [0.40; 0.67]	< 0.001	0.817
Female	42	29 (69.0)	16.4 [4.6; 35.3]	55	44 (80.0)	6.3 [3.0; 9.0]	0.52 [0.32; 0.87]	0.012	
Geographic Region									
North America	57	41 (71.9)	15.0 [5.9; 30.1]	51	40 (78.4)	6.9 [3.0; 9.0]	0.49 [0.30; 0.79]	0.003	0.957
Europe	97	63 (64.9)	19.1 [11.9; 33.4]	101	73 (72.3)	6.1 [4.0; 9.0]	0.51 [0.35; 0.73]	< 0.001	
Rest of World	85	60 (70.6)	18.1 [7.6; 32.7]	84	62 (73.8)	5.9 [3.1; 9.9]	0.54 [0.37; 0.80]	0.002	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Severe Adverse Events (CTCAE-Grade 3-5)	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	136	91 (66.9)	18.1 [11.9; 28.7]	124	84 (67.7)	9.0 [6.3; 12.1]	0.65 [0.47; 0.89]	0.008	0.056
1-2	103	73 (70.9)	18.3 [8.0; 30.1]	111	90 (81.1)	3.9 [2.1; 5.9]	0.39 [0.28; 0.55]	< 0.001	
Race									
White	166	112 (67.5)	20.9 [12.9; 28.7]	147	112 (76.2)	5.9 [3.0; 7.1]	0.45 [0.34; 0.60]	< 0.001	0.165
Non-white	73	52 (71.2)	16.3 [6.6; 30.1]	89	63 (70.8)	8.0 [4.1; 12.6]	0.64 [0.43; 0.96]	0.030	
Metastatic Disease Site									
Visceral metastases	169	122 (72.2)	15.0 [9.1; 25.7]	157	118 (75.2)	5.9 [4.0; 8.0]	0.55 [0.42; 0.73]	< 0.001	0.450
Lymph node only	60	37 (61.7)	26.1 [13.6; 49.6]	65	46 (70.8)	7.4 [4.0; 9.9]	0.44 [0.27; 0.71]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	47 (77.0)	16.3 [6.6; 29.1]	44	31 (70.5)	7.4 [3.1; 12.3]	0.65 [0.40; 1.06]	0.083	0.160
Lower Tract	176	117 (66.5)	19.0 [12.9; 28.7]	192	144 (75.0)	6.0 [4.1; 7.7]	0.49 [0.37; 0.63]	< 0.001	
Renal Function									
Normal	78	43 (55.1)	26.1 [7.9; -]	81	54 (66.7)	8.9 [5.3; 13.1]	0.54 [0.35; 0.83]	0.005	0.960
Mild	115	83 (72.2)	16.3 [11.6; 26.7]	118	90 (76.3)	5.6 [3.9; 7.4]	0.51 [0.37; 0.71]	< 0.001	
Moderate/Severe	46	38 (82.6)	15.0 [6.1; 35.6]	37	31 (83.8)	4.0 [2.1; 9.1]	0.43 [0.26; 0.74]	0.002	
Stratification Factor: Liver Metastases									
Present	47	35 (74.5)	7.9 [4.7; 16.7]	47	33 (70.2)	7.1 [2.3; 10.1]	0.78 [0.47; 1.28]	0.318	0.074
Absent	192	129 (67.2)	22.0 [14.1; 30.1]	189	142 (75.1)	6.1 [4.1; 8.3]	0.46 [0.35; 0.60]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	98 (71.0)	19.1 [12.9; 28.3]	138	102 (73.9)	7.1 [5.7; 9.7]	0.51 [0.37; 0.69]	< 0.001	0.709
Low	101	66 (65.3)	16.3 [7.6; 30.7]	98	73 (74.5)	4.1 [2.3; 6.1]	0.52 [0.36; 0.74]	< 0.001	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1</p>									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

*Therapieabbruch wegen unerwünschter Ereignisse*Tabelle 4G-86: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events Leading to Treatment Discontinuation	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	105	31 (29.5)	Not reached [61.7; -]	102	16 (15.7)	Not reached [-; -]	0.96 [0.49; 1.90]	0.917	0.581
≥ 65	134	61 (45.5)	32.1 [25.3; -]	134	42 (31.3)	Not reached [-; -]	0.92 [0.60; 1.41]	0.708	
Sex									
Male	197	79 (40.1)	83.9 [33.1; -]	181	44 (24.3)	Not reached [-; -]	0.96 [0.64; 1.44]	0.841	0.466
Female	42	13 (31.0)	Not reached [49.1; -]	55	14 (25.5)	Not reached [-; -]	0.82 [0.36; 1.89]	0.648	
Geographic Region									
North America	57	23 (40.4)	60.7 [26.9; -]	51	15 (29.4)	Not reached [-; -]	0.68 [0.32; 1.46]	0.325	0.870
Europe	97	46 (47.4)	38.1 [26.1; -]	101	29 (28.7)	Not reached [-; -]	0.94 [0.56; 1.57]	0.813	
Rest of World	85	23 (27.1)	Not reached [83.9; -]	84	14 (16.7)	Not reached [-; -]	1.17 [0.58; 2.36]	0.651	
ECOG at Baseline									
0	136	57 (41.9)	61.7 [32.1; -]	124	31 (25.0)	Not reached [-; -]	1.00 [0.62; 1.61]	> 0.999	0.666
1-2	103	35 (34.0)	Not reached [33.1; -]	111	26 (23.4)	Not reached [-; -]	0.89 [0.51; 1.54]	0.666	
Race									
White	166	68 (41.0)	61.7 [29.1; -]	147	41 (27.9)	Not reached [-; -]	0.82 [0.54; 1.25]	0.361	0.618
Non-white	73	24 (32.9)	83.9 [49.1; -]	89	17 (19.1)	Not reached [-; -]	1.26 [0.65; 2.44]	0.503	
Metastatic Disease Site									
Visceral metastases	169	56 (33.1)	Not reached [61.7; -]	157	37 (23.6)	Not reached [-; -]	0.87 [0.55; 1.37]	0.542	0.284
Lymph node only	60	33 (55.0)	38.1 [22.1; 83.9]	65	17 (26.2)	Not reached [-; -]	1.19 [0.63; 2.26]	0.588	
Primary Disease Site of Origin									
Upper Tract	61	22 (36.1)	Not reached [33.1; -]	44	7 (15.9)	Not reached [-; -]	1.85 [0.77; 4.45]	0.171	0.259
Lower Tract	176	70 (39.8)	63.1 [33.1; -]	192	51 (26.6)	Not reached [-; -]	0.82 [0.55; 1.23]	0.332	
Renal Function									
Normal	78	29 (37.2)	Not reached [31.3; -]	81	13 (16.0)	Not reached [-; -]	1.50 [0.74; 3.03]	0.258	0.182
Mild	115	46 (40.0)	83.9 [33.1; -]	118	33 (28.0)	Not reached [-; -]	0.81 [0.49; 1.33]	0.408	
Moderate/Severe	46	17 (37.0)	Not reached [26.0; -]	37	12 (32.4)	Not reached [17.9; -]	0.68 [0.30; 1.52]	0.345	
Stratification Factor: Liver Metastases									
Present	47	16 (34.0)	61.7 [26.0; -]	47	9 (19.1)	Not reached [-; -]	0.83 [0.32; 2.14]	0.696	0.526

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events Leading to Treatment Discontinuation	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Absent	192 76 (39.6)	83.9 [52.0; -]	189 49 (25.9)	Not reached [-; -]	0.95 [0.64; 1.40]	0.799			
Stratification Factor: PD-L1 Expression									
High	138 55 (39.9)	61.7 [32.1; -]	138 36 (26.1)	Not reached [-; -]	0.87 [0.55; 1.38]	0.547	0.650		
Low	101 37 (36.6)	83.9 [33.1; -]	98 22 (22.4)	Not reached [-; -]	1.06 [0.60; 1.88]	0.846			
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: all-participants-as-treated population, cisplatin eligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1									

Unerwünschte Ereignisse gesamt (SOC und PT)

Unerwünschte Ereignisse gesamt

Tabelle 4G-87: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse (SOC) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event N ^b n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC^c: Blood and lymphatic system disorders									
Age									
< 65	105 22 (21.0)	Not reached [-; -]	102 69 (67.6)	5.71 [4.14; 9.14]	0.15 [0.09; 0.25]	< 0.001	0.138		
≥ 65	134 47 (35.1)	Not reached [55.00; -]	134 101 (75.4)	5.14 [3.14; 8.71]	0.21 [0.14; 0.31]	< 0.001			
Race									
White	166 52 (31.3)	Not reached [67.86; -]	147 114 (77.6)	4.86 [3.00; 5.71]	0.17 [0.12; 0.24]	< 0.001	0.747		
Non-white	73 17 (23.3)	Not reached [-; -]	89 56 (62.9)	9.29 [4.00; 15.14]	0.20 [0.11; 0.37]	< 0.001			
Sex									
Male	197 61 (31.0)	Not reached [-; -]	181 126 (69.6)	5.14 [4.14; 9.00]	0.22 [0.16; 0.31]	< 0.001	0.051		
Female	42 8 (19.0)	Not reached [-; -]	55 44 (80.0)	5.14 [2.14; 9.00]	0.07 [0.03; 0.18]	< 0.001			
ECOG at Baseline									
0	136 39 (28.7)	Not reached [-; -]	124 88 (71.0)	6.00 [4.14; 9.29]	0.18 [0.11; 0.27]	< 0.001	0.938		
1-2	103 30 (29.1)	Not reached [-; -]	111 81 (73.0)	5.14 [3.00; 6.14]	0.20 [0.13; 0.31]	< 0.001			

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events									
Primary Disease Site of Origin									
Upper Tract	61	15 (24.6)	Not reached [55.00; -]	44	31 (70.5)	5.50 [4.14; 10.00]	0.13 [0.06; 0.28]	< 0.001	0.756
Lower Tract	176	54 (30.7)	Not reached [-; -]	192	139 (72.4)	5.14 [3.14; 7.43]	0.21 [0.15; 0.29]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	16 (34.0)	67.86 [27.14; -]	47	35 (74.5)	5.14 [2.14; 10.00]	0.22 [0.11; 0.41]	< 0.001	0.455
Absent	192	53 (27.6)	Not reached [-; -]	189	135 (71.4)	5.14 [4.14; 7.43]	0.18 [0.13; 0.25]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	40 (29.0)	Not reached [-; -]	138	99 (71.7)	5.14 [4.00; 9.00]	0.19 [0.12; 0.28]	< 0.001	0.964
Low	101	29 (28.7)	Not reached [67.86; -]	98	71 (72.4)	5.14 [3.14; 8.71]	0.18 [0.11; 0.29]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	48 (28.4)	Not reached [-; -]	157	112 (71.3)	5.14 [4.00; 8.29]	0.19 [0.13; 0.28]	< 0.001	0.585
Lymph node only	60	15 (25.0)	Not reached [-; -]	65	47 (72.3)	5.21 [3.14; 9.29]	0.15 [0.08; 0.29]	< 0.001	
Renal Function									
Normal	78	13 (16.7)	Not reached [-; -]	81	54 (66.7)	6.43 [3.14; 11.14]	0.10 [0.05; 0.21]	< 0.001	0.166
Mild	115	40 (34.8)	Not reached [67.86; -]	118	87 (73.7)	5.00 [3.29; 6.86]	0.24 [0.16; 0.36]	< 0.001	
Moderate/Severe	46	16 (34.8)	Not reached [29.86; -]	37	29 (78.4)	5.14 [2.14; 9.14]	0.16 [0.08; 0.33]	< 0.001	
SOC ^g : Ear and labyrinth disorders									
Race									
White	166	13 (7.8)	Not reached [-; -]	147	21 (14.3)	Not reached [-; -]	0.20 [0.08; 0.51]	< 0.001	0.663
Non-white	73	4 (5.5)	Not reached [-; -]	89	12 (13.5)	Not reached [-; -]	0.10 [0.01; 0.75]	0.025	
Geographic Region									
North America	57	11 (19.3)	Not reached [56.29; -]	51	16 (31.4)	Not reached [-; -]	0.22 [0.08; 0.62]	0.004	0.332
Europe	97	2 (2.1)	Not reached [-; -]	101	11 (10.9)	Not reached [-; -]	0.03 [0.00; 0.43]	0.010	
Rest of World	85	4 (4.7)	Not reached [-; -]	84	6 (7.1)	Not reached [-; -]	0.16 [0.02; 1.32]	0.089	
Sex									
Male	197	13 (6.6)	Not reached [-; -]	181	24 (13.3)	Not reached [-; -]	0.18 [0.07; 0.46]	< 0.001	0.802
Female	42	4 (9.5)	Not reached [-; -]	55	9 (16.4)	Not reached [-; -]	0.16 [0.03; 0.99]	0.049	
ECOG at Baseline									
0	136	9 (6.6)	Not reached [-; -]	124	20 (16.1)	Not reached [-; -]	0.13 [0.04; 0.42]	< 0.001	0.336
1-2	103	8 (7.8)	Not reached [-; -]	111	13 (11.7)	Not reached [-; -]	0.23 [0.07; 0.80]	0.021	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	0.11 [0.01; 0.95]	0.045	0.356
Lower Tract	176	14 (8.0)	Not reached [-; -]	192	27 (14.1)	Not reached [-; -]	0.19 [0.08; 0.48]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	5 (10.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994	0.968
Absent	192	15 (7.8)	Not reached [-; -]	189	28 (14.8)	Not reached [-; -]	0.20 [0.08; 0.47]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	14 (10.1)	Not reached [-; -]	138	19 (13.8)	Not reached [-; -]	0.25 [0.09; 0.65]	0.005	0.066
Low	101	3 (3.0)	Not reached [-; -]	98	14 (14.3)	Not reached [-; -]	0.06 [0.01; 0.48]	0.008	
Metastatic Disease Site									
Visceral metastases	169	10 (5.9)	Not reached [-; -]	157	25 (15.9)	Not reached [-; -]	0.14 [0.05; 0.39]	< 0.001	0.390
Lymph node only	60	5 (8.3)	Not reached [-; -]	65	7 (10.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.993	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	10 (12.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.992	0.559
Mild	115	10 (8.7)	Not reached [-; -]	118	19 (16.1)	Not reached [-; -]	0.25 [0.09; 0.65]	0.005	
Moderate/Severe	46	4 (8.7)	Not reached [79.14; -]	37	4 (10.8)	Not reached [-; -]	0.22 [0.03; 1.58]	0.133	
SOC^g: Endocrine disorders									
Geographic Region									
North America	57	8 (14.0)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	4.87 [0.59; 40.51]	0.143	0.335
Europe	97	13 (13.4)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	
Rest of World	85	13 (15.3)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	8.89 [1.13; 70.14]	0.038	
Sex									
Male	197	24 (12.2)	Not reached [-; -]	181	2 (1.1)	Not reached [-; -]	7.54 [1.74; 32.61]	0.007	0.158
Female	42	10 (23.8)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
ECOG at Baseline									
0	136	20 (14.7)	Not reached [-; -]	124	1 (0.8)	Not reached [-; -]	13.75 [1.82; 104.03]	0.011	0.886
1-2	103	14 (13.6)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	11.01 [1.42; 85.57]	0.022	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.031	0.377
Lower Tract	176	26 (14.8)	Not reached [-; -]	192	2 (1.0)	Not reached [-; -]	10.04 [2.34; 43.09]	0.002	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	47	7 (14.9)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	5.34 [0.62; 45.68]	0.126	0.439
Absent	192	27 (14.1)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	19.27 [2.59; 143.43]	0.004	
Stratification Factor: PD-L1 Expression									
High	138	25 (18.1)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	18.81 [2.52; 140.46]	0.004	0.471
Low	101	9 (8.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	5.97 [0.73; 49.09]	0.097	
Metastatic Disease Site									
Visceral metastases	169	23 (13.6)	Not reached [-; -]	157	1 (0.6)	Not reached [-; -]	14.82 [1.97; 111.43]	0.009	0.463
Lymph node only	60	7 (11.7)	Not reached [-; -]	65	1 (1.5)	Not reached [-; -]	5.35 [0.63; 45.82]	0.126	
Renal Function									
Normal	78	10 (12.8)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	0.315
Mild	115	18 (15.7)	Not reached [-; -]	118	1 (0.8)	Not reached [-; -]	11.83 [1.54; 90.80]	0.017	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	4.51 [0.54; 37.41]	0.163	
SOC ^g : Eye disorders									
Age									
< 65	105	37 (35.2)	Not reached [36.57; -]	102	6 (5.9)	Not reached [-; -]	4.88 [2.02; 11.77]	< 0.001	0.848
≥ 65	134	51 (38.1)	77.57 [40.57; -]	134	8 (6.0)	Not reached [-; -]	5.63 [2.64; 12.01]	< 0.001	
Geographic Region									
North America	57	34 (59.6)	16.86 [12.00; 23.29]	51	9 (17.6)	Not reached [-; -]	3.90 [1.86; 8.18]	< 0.001	0.054
Europe	97	39 (40.2)	71.00 [29.14; -]	101	2 (2.0)	Not reached [-; -]	15.98 [3.81; 67.07]	< 0.001	
Rest of World	85	15 (17.6)	Not reached [-; -]	84	3 (3.6)	Not reached [-; -]	2.98 [0.81; 10.97]	0.101	
Sex									
Male	197	74 (37.6)	85.57 [53.14; -]	181	11 (6.1)	Not reached [-; -]	5.10 [2.67; 9.73]	< 0.001	0.994
Female	42	14 (33.3)	Not reached [21.14; -]	55	3 (5.5)	Not reached [-; -]	5.93 [1.69; 20.80]	0.005	
ECOG at Baseline									
0	136	52 (38.2)	85.57 [36.57; -]	124	9 (7.3)	Not reached [-; -]	4.28 [2.07; 8.84]	< 0.001	0.470
1-2	103	36 (35.0)	Not reached [29.14; -]	111	5 (4.5)	Not reached [-; -]	7.07 [2.75; 18.20]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	24 (39.3)	71.00 [26.43; -]	44	1 (2.3)	Not reached [-; -]	14.25 [1.90; 106.71]	0.010	0.177
Lower Tract	176	63 (35.8)	Not reached [53.14; -]	192	13 (6.8)	Not reached [-; -]	4.53 [2.46; 8.34]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	47	23 (48.9)	22.29 [17.14; -]	47	2 (4.3)	Not reached [-; -]	12.07 [2.81; 51.77]	< 0.001	0.148
Absent	192	65 (33.9)	Not reached [77.57; -]	189	12 (6.3)	Not reached [-; -]	4.36 [2.32; 8.19]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	47 (34.1)	Not reached [71.00; -]	138	9 (6.5)	Not reached [-; -]	4.35 [2.10; 9.01]	< 0.001	0.380
Low	101	41 (40.6)	85.57 [26.43; -]	98	5 (5.1)	Not reached [-; -]	6.95 [2.71; 17.83]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	63 (37.3)	Not reached [35.57; -]	157	9 (5.7)	Not reached [-; -]	5.71 [2.81; 11.59]	< 0.001	0.517
Lymph node only	60	21 (35.0)	77.57 [36.57; -]	65	5 (7.7)	Not reached [-; -]	3.45 [1.26; 9.50]	0.016	
Renal Function									
Normal	78	33 (42.3)	36.57 [23.14; -]	81	8 (9.9)	Not reached [-; -]	3.57 [1.61; 7.91]	0.002	0.149
Mild	115	42 (36.5)	Not reached [71.00; -]	118	6 (5.1)	Not reached [-; -]	6.52 [2.74; 15.53]	< 0.001	
Moderate/Severe	46	13 (28.3)	Not reached [53.14; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	
SOC ^g : Gastrointestinal disorders									
Age									
< 65	105	72 (68.6)	9.14 [3.14; 28.14]	102	79 (77.5)	1.14 [0.57; 3.29]	0.54 [0.39; 0.76]	< 0.001	0.106
≥ 65	134	107 (79.9)	3.71 [2.71; 5.86]	134	105 (78.4)	2.57 [1.14; 4.14]	0.74 [0.56; 0.98]	0.038	
Race									
White	166	124 (74.7)	4.21 [3.00; 9.14]	147	110 (74.8)	2.86 [1.14; 4.86]	0.73 [0.56; 0.95]	0.021	0.157
Non-white	73	55 (75.3)	5.86 [2.57; 13.29]	89	74 (83.1)	1.14 [0.71; 3.29]	0.51 [0.35; 0.74]	< 0.001	
Geographic Region									
North America	57	49 (86.0)	1.86 [0.71; 3.43]	51	43 (84.3)	0.71 [0.57; 1.14]	0.84 [0.55; 1.27]	0.409	0.287
Europe	97	68 (70.1)	5.00 [3.29; 16.00]	101	83 (82.2)	2.71 [1.14; 3.57]	0.55 [0.40; 0.77]	< 0.001	
Rest of World	85	62 (72.9)	9.86 [3.57; 27.71]	84	58 (69.0)	4.29 [1.00; 10.29]	0.62 [0.43; 0.91]	0.015	
Sex									
Male	197	148 (75.1)	4.71 [3.00; 8.14]	181	137 (75.7)	2.71 [1.14; 4.14]	0.69 [0.54; 0.88]	0.003	0.275
Female	42	31 (73.8)	5.00 [2.43; 21.14]	55	47 (85.5)	1.00 [0.57; 3.00]	0.51 [0.32; 0.82]	0.006	
Primary Disease Site of Origin									
Upper Tract	61	46 (75.4)	4.43 [2.43; 16.00]	44	38 (86.4)	1.71 [0.71; 3.29]	0.55 [0.35; 0.86]	0.008	0.409
Lower Tract	176	132 (75.0)	4.86 [3.14; 8.86]	192	146 (76.0)	2.29 [1.00; 4.14]	0.67 [0.52; 0.85]	0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: PD-L1 Expression									
High	138	106 (76.8)	5.71 [3.00; 10.57]	138	115 (83.3)	1.14 [0.71; 2.71]	0.55 [0.41; 0.72]	< 0.001	0.086
Low	101	73 (72.3)	4.00 [3.00; 9.86]	98	69 (70.4)	3.57 [2.14; 9.14]	0.82 [0.58; 1.15]	0.244	
Metastatic Disease Site									
Visceral metastases	169	128 (75.7)	4.86 [3.00; 8.86]	157	118 (75.2)	2.71 [1.14; 4.14]	0.70 [0.54; 0.91]	0.007	0.079
Lymph node only	60	42 (70.0)	5.00 [2.57; 11.71]	65	56 (86.2)	1.29 [0.57; 3.29]	0.51 [0.34; 0.77]	0.001	
Renal Function									
Normal	78	61 (78.2)	3.43 [1.71; 8.14]	81	64 (79.0)	1.57 [0.57; 5.14]	0.73 [0.51; 1.05]	0.095	0.726
Mild	115	84 (73.0)	4.86 [3.00; 14.29]	118	93 (78.8)	2.57 [1.00; 4.14]	0.60 [0.44; 0.82]	0.001	
Moderate/Severe	46	34 (73.9)	8.21 [2.43; 16.57]	37	27 (73.0)	2.14 [0.86; 6.14]	0.62 [0.37; 1.05]	0.076	
SOC ^g : General disorders and administration site conditions									
Age									
< 65	105	62 (59.0)	24.71 [8.71; 60.00]	102	67 (65.7)	8.14 [3.86; 13.86]	0.60 [0.41; 0.87]	0.006	0.417
≥ 65	134	97 (72.4)	5.14 [3.14; 12.00]	134	100 (74.6)	3.79 [2.14; 5.00]	0.74 [0.56; 1.00]	0.047	
Race									
White	166	116 (69.9)	11.00 [5.14; 20.71]	147	108 (73.5)	4.14 [3.00; 6.86]	0.66 [0.50; 0.87]	0.003	0.700
Non-white	73	43 (58.9)	16.29 [3.29; -]	89	59 (66.3)	5.14 [3.29; 10.00]	0.70 [0.47; 1.06]	0.090	
Geographic Region									
North America	57	46 (80.7)	3.43 [1.00; 6.71]	51	40 (78.4)	3.14 [1.00; 4.14]	0.81 [0.52; 1.26]	0.353	0.514
Europe	97	68 (70.1)	6.00 [3.43; 12.57]	101	84 (83.2)	3.29 [1.86; 6.00]	0.61 [0.44; 0.85]	0.004	
Rest of World	85	45 (52.9)	46.43 [19.14; 83.86]	84	43 (51.2)	15.29 [4.86; -]	0.66 [0.42; 1.05]	0.079	
Sex									
Male	197	134 (68.0)	10.86 [5.14; 20.71]	181	125 (69.1)	5.14 [3.86; 9.14]	0.74 [0.57; 0.95]	0.019	0.099
Female	42	25 (59.5)	12.57 [3.14; -]	55	42 (76.4)	2.00 [1.14; 6.00]	0.50 [0.30; 0.85]	0.011	
Primary Disease Site of Origin									
Upper Tract	61	40 (65.6)	12.00 [4.00; 36.86]	44	33 (75.0)	4.14 [1.14; 6.00]	0.54 [0.33; 0.88]	0.014	0.566
Lower Tract	176	118 (67.0)	8.43 [4.71; 20.71]	192	134 (69.8)	4.57 [3.29; 8.86]	0.73 [0.56; 0.94]	0.017	
Stratification Factor: Liver Metastases									
Present	47	37 (78.7)	4.14 [2.14; 12.57]	47	33 (70.2)	5.14 [2.14; 15.29]	0.95 [0.58; 1.55]	0.838	0.063
Absent	192	122 (63.5)	13.14 [6.00; 31.14]	189	134 (70.9)	4.14 [3.29; 6.43]	0.62 [0.48; 0.81]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: PD-L1 Expression									
High	138	94 (68.1)	5.57 [4.14; 19.14]	138	100 (72.5)	4.57 [3.71; 8.71]	0.77 [0.57; 1.03]	0.082	0.446
Low	101	65 (64.4)	18.14 [6.43; 36.86]	98	67 (68.4)	3.71 [2.29; 8.86]	0.57 [0.40; 0.82]	0.003	
Metastatic Disease Site									
Visceral metastases	169	113 (66.9)	12.00 [3.43; 24.86]	157	108 (68.8)	5.00 [3.29; 8.14]	0.72 [0.55; 0.96]	0.023	0.230
Lymph node only	60	39 (65.0)	11.29 [5.00; 39.14]	65	49 (75.4)	4.00 [2.00; 8.00]	0.58 [0.37; 0.90]	0.015	
Renal Function									
Normal	78	46 (59.0)	13.57 [4.57; 69.00]	81	62 (76.5)	6.00 [3.00; 9.14]	0.57 [0.38; 0.84]	0.005	0.299
Mild	115	80 (69.6)	9.14 [4.00; 24.14]	118	81 (68.6)	4.50 [2.86; 7.86]	0.76 [0.55; 1.05]	0.095	
Moderate/Severe	46	33 (71.7)	12.00 [3.14; 39.14]	37	24 (64.9)	3.71 [1.86; 8.86]	0.74 [0.42; 1.28]	0.279	
SOC ^g : Hepatobiliary disorders									
Age									
< 65	105	10 (9.5)	Not reached [-; -]	102	1 (1.0)	Not reached [-; -]	8.99 [1.14; 70.99]	0.037	0.277
≥ 65	134	22 (16.4)	Not reached [-; -]	134	7 (5.2)	Not reached [-; -]	2.68 [1.12; 6.39]	0.026	
Race									
White	166	21 (12.7)	Not reached [-; -]	147	7 (4.8)	Not reached [-; -]	2.21 [0.92; 5.29]	0.076	0.089
Non-white	73	11 (15.1)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	12.93 [1.66; 101.05]	0.015	
Geographic Region									
North America	57	6 (10.5)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.017	0.232
Europe	97	18 (18.6)	Not reached [-; -]	101	5 (5.0)	Not reached [-; -]	3.14 [1.14; 8.65]	0.027	
Rest of World	85	8 (9.4)	Not reached [-; -]	84	3 (3.6)	Not reached [-; -]	2.27 [0.59; 8.76]	0.236	
Sex									
Male	197	24 (12.2)	Not reached [-; -]	181	6 (3.3)	Not reached [-; -]	3.01 [1.21; 7.51]	0.018	0.653
Female	42	8 (19.0)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	5.45 [1.16; 25.67]	0.032	
ECOG at Baseline									
0	136	25 (18.4)	Not reached [-; -]	124	5 (4.0)	Not reached [-; -]	4.04 [1.52; 10.71]	0.005	0.428
1-2	103	7 (6.8)	Not reached [-; -]	111	3 (2.7)	Not reached [-; -]	2.23 [0.57; 8.71]	0.248	
Stratification Factor: Liver Metastases									
Present	47	5 (10.6)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	2.53 [0.49; 13.05]	0.267	0.570
Absent	192	27 (14.1)	Not reached [-; -]	189	6 (3.2)	Not reached [-; -]	3.75 [1.53; 9.24]	0.004	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: PD-L1 Expression									
High	138	21 (15.2)	Not reached [-; -]	138	3 (2.2)	Not reached [-; -]	6.42 [1.90; 21.73]	0.003	0.127
Low	101	11 (10.9)	Not reached [-; -]	98	5 (5.1)	Not reached [-; -]	1.71 [0.57; 5.12]	0.334	
Metastatic Disease Site									
Visceral metastases	169	24 (14.2)	Not reached [-; -]	157	5 (3.2)	Not reached [-; -]	4.00 [1.51; 10.61]	0.005	0.940
Lymph node only	60	8 (13.3)	Not reached [-; -]	65	2 (3.1)	Not reached [-; -]	3.49 [0.72; 16.96]	0.122	
Renal Function									
Normal	78	14 (17.9)	Not reached [-; -]	81	4 (4.9)	Not reached [-; -]	3.18 [1.02; 9.85]	0.045	0.927
Mild	115	14 (12.2)	Not reached [-; -]	118	3 (2.5)	Not reached [-; -]	3.96 [1.11; 14.10]	0.034	
Moderate/Severe	46	4 (8.7)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	3.15 [0.35; 28.21]	0.304	
SOC^g: Infections and infestations									
Age									
< 65	105	64 (61.0)	26.71 [16.57; 36.71]	102	33 (32.4)	Not reached [-; -]	1.31 [0.84; 2.05]	0.234	0.667
≥ 65	134	81 (60.4)	17.86 [12.86; 24.43]	134	52 (38.8)	Not reached [19.29; -]	1.41 [0.99; 2.02]	0.058	
Race									
White	166	106 (63.9)	21.00 [14.14; 27.29]	147	54 (36.7)	Not reached [-; -]	1.32 [0.94; 1.86]	0.109	0.970
Non-white	73	39 (53.4)	22.57 [12.43; -]	89	31 (34.8)	Not reached [-; -]	1.41 [0.86; 2.30]	0.168	
Geographic Region									
North America	57	43 (75.4)	15.71 [8.57; 22.86]	51	17 (33.3)	Not reached [18.29; -]	1.77 [0.98; 3.16]	0.056	0.214
Europe	97	57 (58.8)	21.29 [13.14; 33.71]	101	44 (43.6)	Not reached [14.86; -]	1.10 [0.73; 1.65]	0.659	
Rest of World	85	45 (52.9)	33.14 [17.86; -]	84	24 (28.6)	Not reached [-; -]	1.52 [0.90; 2.55]	0.116	
Sex									
Male	197	117 (59.4)	21.29 [15.86; 28.43]	181	64 (35.4)	Not reached [-; -]	1.36 [0.99; 1.87]	0.056	0.634
Female	42	28 (66.7)	23.43 [8.43; 40.00]	55	21 (38.2)	Not reached [16.00; -]	1.40 [0.76; 2.59]	0.286	
ECOG at Baseline									
0	136	85 (62.5)	19.57 [13.86; 27.00]	124	43 (34.7)	Not reached [-; -]	1.60 [1.09; 2.34]	0.015	0.205
1-2	103	60 (58.3)	23.86 [15.71; 40.14]	111	42 (37.8)	Not reached [18.57; -]	1.13 [0.74; 1.71]	0.576	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	61	35 (57.4)	26.71 [12.43; 48.71]	44	10 (22.7)	Not reached [-; -]	2.22 [1.08; 4.57]	0.030	0.122
Lower Tract	176	110 (62.5)	21.29 [14.57; 27.00]	192	75 (39.1)	Not reached [-; -]	1.27 [0.93; 1.73]	0.129	
Stratification Factor: Liver Metastases									
Present	47	33 (70.2)	19.86 [9.14; 26.71]	47	16 (34.0)	Not reached [19.00; -]	1.58 [0.84; 2.97]	0.153	0.246
Absent	192	112 (58.3)	21.71 [15.71; 36.14]	189	69 (36.5)	Not reached [-; -]	1.32 [0.97; 1.80]	0.082	
Stratification Factor: PD-L1 Expression									
High	138	81 (58.7)	23.86 [17.43; 36.71]	138	49 (35.5)	Not reached [-; -]	1.29 [0.89; 1.87]	0.186	0.764
Low	101	64 (63.4)	16.57 [12.43; 24.43]	98	36 (36.7)	Not reached [19.29; -]	1.46 [0.96; 2.23]	0.075	
Metastatic Disease Site									
Visceral metastases	169	103 (60.9)	21.57 [15.71; 28.43]	157	53 (33.8)	Not reached [-; -]	1.47 [1.04; 2.07]	0.029	0.221
Lymph node only	60	37 (61.7)	21.57 [9.00; 54.43]	65	29 (44.6)	Not reached [14.29; -]	1.02 [0.61; 1.71]	0.929	
Renal Function									
Normal	78	47 (60.3)	23.43 [13.14; 34.00]	81	34 (42.0)	Not reached [14.86; -]	1.05 [0.66; 1.68]	0.835	0.400
Mild	115	71 (61.7)	18.86 [12.43; 29.86]	118	37 (31.4)	Not reached [-; -]	1.74 [1.16; 2.63]	0.008	
Moderate/Severe	46	27 (58.7)	22.57 [14.57; 36.14]	37	14 (37.8)	Not reached [16.00; -]	1.17 [0.59; 2.29]	0.657	
SOC ^g : Nervous system disorders									
Age									
< 65	105	80 (76.2)	13.43 [9.14; 17.00]	102	39 (38.2)	Not reached [22.00; -]	1.75 [1.18; 2.61]	0.006	0.627
≥ 65	134	106 (79.1)	9.57 [6.86; 15.00]	134	57 (42.5)	Not reached [13.86; -]	1.89 [1.36; 2.63]	< 0.001	
Race									
White	166	132 (79.5)	11.86 [9.14; 15.00]	147	55 (37.4)	Not reached [-; -]	1.95 [1.41; 2.69]	< 0.001	0.332
Non-white	73	54 (74.0)	11.00 [6.43; 17.00]	89	41 (46.1)	22.00 [13.00; -]	1.66 [1.10; 2.53]	0.017	
Geographic Region									
North America	57	49 (86.0)	6.57 [3.14; 12.86]	51	33 (64.7)	5.71 [3.14; 13.29]	1.05 [0.66; 1.66]	0.841	0.093
Europe	97	76 (78.4)	10.57 [7.86; 13.57]	101	39 (38.6)	Not reached [17.00; -]	2.20 [1.48; 3.27]	< 0.001	
Rest of World	85	61	17.29	84	24	Not reached	2.27	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
		(71.8)	[11.00; 20.86]		(28.6)	[22.00; -]	[1.39; 3.68]		
Sex									
Male	197	152 (77.2)	11.00 [9.00; 13.86]	181	72 (39.8)	Not reached [17.71; -]	1.91 [1.43; 2.55]	< 0.001	0.503
Female	42	34 (81.0)	13.29 [6.29; 20.57]	55	24 (43.6)	Not reached [6.43; -]	1.55 [0.90; 2.66]	0.113	
ECOG at Baseline									
0	136	112 (82.4)	9.29 [7.00; 13.86]	124	52 (41.9)	Not reached [17.14; -]	2.03 [1.45; 2.85]	< 0.001	0.359
1-2	103	74 (71.8)	13.29 [9.14; 20.57]	111	43 (38.7)	Not reached [15.14; -]	1.62 [1.10; 2.39]	0.015	
Primary Disease Site of Origin									
Upper Tract	61	48 (78.7)	9.00 [6.29; 15.00]	44	19 (43.2)	22.00 [12.29; -]	2.05 [1.20; 3.53]	0.009	0.603
Lower Tract	176	137 (77.8)	13.14 [9.14; 15.00]	192	77 (40.1)	Not reached [17.71; -]	1.74 [1.31; 2.33]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	29 (61.7)	14.43 [8.71; 23.57]	47	21 (44.7)	Not reached [9.29; -]	1.50 [0.84; 2.66]	0.167	0.411
Absent	192	157 (81.8)	10.57 [8.71; 13.86]	189	75 (39.7)	Not reached [22.00; -]	1.90 [1.43; 2.52]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	113 (81.9)	11.86 [9.14; 15.00]	138	60 (43.5)	Not reached [13.43; -]	1.75 [1.27; 2.42]	< 0.001	0.769
Low	101	73 (72.3)	10.14 [6.57; 18.29]	98	36 (36.7)	Not reached [17.00; -]	1.95 [1.30; 2.94]	0.001	
Metastatic Disease Site									
Visceral metastases	169	129 (76.3)	11.86 [8.86; 15.00]	157	67 (42.7)	Not reached [13.86; -]	1.69 [1.24; 2.28]	< 0.001	0.688
Lymph node only	60	48 (80.0)	11.00 [6.14; 15.29]	65	25 (38.5)	Not reached [17.14; -]	1.99 [1.20; 3.30]	0.008	
Renal Function									
Normal	78	61 (78.2)	11.00 [6.57; 14.57]	81	38 (46.9)	22.00 [8.71; -]	1.61 [1.06; 2.43]	0.025	0.588
Mild	115	91 (79.1)	11.00 [7.71; 16.57]	118	46 (39.0)	Not reached [17.00; -]	1.78 [1.23; 2.58]	0.002	
Moderate/Severe	46	34 (73.9)	13.29 [7.00; 17.00]	37	12 (32.4)	Not reached [13.43; -]	2.74 [1.41; 5.32]	0.003	
SOC ^g : Renal and urinary disorders									
Age									
< 65	105	27 (25.7)	Not reached [-; -]	102	26 (25.5)	Not reached [-; -]	0.82 [0.46; 1.44]	0.489	0.814
≥ 65	134	47 (35.1)	96.29 [47.71; -]	134	50 (37.3)	Not reached [-; -]	0.63 [0.41; 0.97]	0.037	
Race									
White	166	56 (33.7)	Not reached [96.29; -]	147	55 (37.4)	Not reached [-; -]	0.70 [0.47; 1.04]	0.076	0.707
Non-white	73	18 (24.7)	Not reached [-; -]	89	21 (23.6)	Not reached [-; -]	0.56 [0.26; 1.18]	0.128	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	57	20 (35.1)	96.29 [96.29; -]	51	18 (35.3)	Not reached [15.57; -]	0.83 [0.43; 1.61]	0.588	0.981
Europe	97	33 (34.0)	Not reached [46.00; -]	101	39 (38.6)	Not reached [19.00; -]	0.72 [0.44; 1.18]	0.191	
Rest of World	85	21 (24.7)	Not reached [-; -]	84	19 (22.6)	Not reached [-; -]	0.54 [0.26; 1.12]	0.099	
Sex									
Male	197	62 (31.5)	Not reached [-; -]	181	60 (33.1)	Not reached [-; -]	0.71 [0.49; 1.04]	0.078	0.949
Female	42	12 (28.6)	96.29 [47.71; -]	55	16 (29.1)	Not reached [-; -]	0.57 [0.24; 1.36]	0.207	
ECOG at Baseline									
0	136	39 (28.7)	Not reached [96.29; -]	124	37 (29.8)	Not reached [-; -]	0.60 [0.36; 0.99]	0.046	0.881
1-2	103	35 (34.0)	Not reached [47.71; -]	111	39 (35.1)	Not reached [-; -]	0.81 [0.50; 1.30]	0.387	
Primary Disease Site of Origin									
Upper Tract	61	17 (27.9)	Not reached [55.43; -]	44	11 (25.0)	Not reached [-; -]	0.57 [0.24; 1.38]	0.213	0.659
Lower Tract	176	57 (32.4)	Not reached [-; -]	192	65 (33.9)	Not reached [-; -]	0.75 [0.52; 1.09]	0.137	
Stratification Factor: Liver Metastases									
Present	47	14 (29.8)	Not reached [50.14; -]	47	15 (31.9)	Not reached [-; -]	0.77 [0.36; 1.68]	0.514	0.851
Absent	192	60 (31.3)	Not reached [96.29; -]	189	61 (32.3)	Not reached [-; -]	0.68 [0.46; 1.00]	0.047	
Metastatic Disease Site									
Visceral metastases	169	48 (28.4)	Not reached [96.29; -]	157	50 (31.8)	Not reached [-; -]	0.62 [0.40; 0.96]	0.032	0.770
Lymph node only	60	21 (35.0)	Not reached [30.14; -]	65	23 (35.4)	Not reached [14.00; -]	0.74 [0.39; 1.38]	0.342	
SOC ^g : Skin and subcutaneous tissue disorders									
Age									
< 65	105	89 (84.8)	2.29 [2.00; 3.29]	102	22 (21.6)	Not reached [-; -]	7.21 [4.48; 11.61]	< 0.001	0.386
≥ 65	134	115 (85.8)	2.00 [1.71; 2.71]	134	39 (29.1)	Not reached [-; -]	5.15 [3.56; 7.46]	< 0.001	
Race									
White	166	137 (82.5)	3.07 [2.14; 4.57]	147	37 (25.2)	Not reached [-; -]	5.22 [3.61; 7.55]	< 0.001	0.069
Non-white	73	67 (91.8)	1.57 [1.29; 1.86]	89	24 (27.0)	Not reached [-; -]	8.36 [5.12; 13.64]	< 0.001	
Geographic Region									
North America	57	49 (86.0)	2.14 [1.86; 3.14]	51	19 (37.3)	Not reached [15.00; -]	4.47 [2.59; 7.74]	< 0.001	0.177
Europe	97	75 (77.3)	3.14 [2.00; 9.00]	101	21 (20.8)	Not reached [-; -]	5.44 [3.32; 8.90]	< 0.001	
Rest of World	85	80 (94.1)	1.71 [1.29; 2.29]	84	21 (25.0)	Not reached [-; -]	8.35 [5.10; 13.68]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	197	170 (86.3)	2.29 [2.00; 3.14]	181	43 (23.8)	Not reached [-; -]	6.57 [4.67; 9.24]	< 0.001	0.437
Female	42	34 (81.0)	1.64 [1.14; 2.29]	55	18 (32.7)	Not reached [-; -]	4.35 [2.42; 7.83]	< 0.001	
ECOG at Baseline									
0	136	122 (89.7)	1.71 [1.57; 2.14]	124	31 (25.0)	Not reached [-; -]	7.26 [4.84; 10.88]	< 0.001	0.052
1-2	103	82 (79.6)	3.14 [2.14; 5.14]	111	30 (27.0)	Not reached [-; -]	4.45 [2.91; 6.80]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	56 (91.8)	2.00 [1.57; 2.43]	44	17 (38.6)	Not reached [7.43; -]	4.30 [2.47; 7.49]	< 0.001	0.253
Lower Tract	176	147 (83.5)	2.29 [1.86; 3.14]	192	44 (22.9)	Not reached [-; -]	6.44 [4.57; 9.07]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	37 (78.7)	2.71 [1.86; 8.71]	47	9 (19.1)	Not reached [-; -]	7.09 [3.39; 14.84]	< 0.001	0.602
Absent	192	167 (87.0)	2.14 [1.71; 2.71]	189	52 (27.5)	Not reached [-; -]	5.70 [4.14; 7.83]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	141 (83.4)	2.29 [2.00; 3.14]	157	45 (28.7)	Not reached [-; -]	5.14 [3.65; 7.24]	< 0.001	0.238
Lymph node only	60	53 (88.3)	1.64 [1.14; 2.86]	65	15 (23.1)	Not reached [-; -]	6.68 [3.72; 12.00]	< 0.001	
Renal Function									
Normal	78	64 (82.1)	2.14 [1.57; 3.14]	81	16 (19.8)	Not reached [-; -]	7.65 [4.38; 13.36]	< 0.001	0.231
Mild	115	102 (88.7)	2.43 [1.86; 3.14]	118	37 (31.4)	Not reached [-; -]	4.81 [3.27; 7.07]	< 0.001	
Moderate/Severe	46	38 (82.6)	2.07 [1.14; 3.29]	37	8 (21.6)	Not reached [-; -]	6.80 [3.15; 14.71]	< 0.001	
SOC^g: Vascular disorders									
Age									
< 65	105	14 (13.3)	Not reached [-; -]	102	17 (16.7)	Not reached [-; -]	0.50 [0.23; 1.12]	0.092	0.854
≥ 65	134	24 (17.9)	Not reached [-; -]	134	29 (21.6)	Not reached [-; -]	0.55 [0.30; 1.00]	0.048	
Race									
White	166	26 (15.7)	Not reached [-; -]	147	27 (18.4)	Not reached [-; -]	0.56 [0.31; 1.02]	0.057	0.905
Non-white	73	12 (16.4)	Not reached [-; -]	89	19 (21.3)	Not reached [-; -]	0.49 [0.21; 1.12]	0.091	
Geographic Region									
North America	57	11 (19.3)	Not reached [61.14; -]	51	19 (37.3)	Not reached [13.14; -]	0.24 [0.09; 0.60]	0.002	0.176
Europe	97	14 (14.4)	Not reached [-; -]	101	16 (15.8)	Not reached [-; -]	0.63 [0.29; 1.40]	0.258	
Rest of World	85	13 (15.3)	Not reached [-; -]	84	11 (13.1)	Not reached [-; -]	0.89 [0.38; 2.11]	0.798	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	197	35 (17.8)	Not reached [-; -]	181	36 (19.9)	Not reached [-; -]	0.55 [0.33; 0.93]	0.026	0.208
Female	42	3 (7.1)	Not reached [-; -]	55	10 (18.2)	Not reached [-; -]	0.39 [0.11; 1.40]	0.149	
ECOG at Baseline									
0	136	22 (16.2)	Not reached [-; -]	124	28 (22.6)	Not reached [-; -]	0.49 [0.27; 0.91]	0.024	0.460
1-2	103	16 (15.5)	Not reached [-; -]	111	18 (16.2)	Not reached [-; -]	0.58 [0.27; 1.25]	0.167	
Primary Disease Site of Origin									
Upper Tract	61	10 (16.4)	Not reached [-; -]	44	9 (20.5)	Not reached [-; -]	0.48 [0.17; 1.33]	0.156	0.934
Lower Tract	176	28 (15.9)	Not reached [-; -]	192	37 (19.3)	Not reached [-; -]	0.56 [0.32; 0.96]	0.034	
Stratification Factor: Liver Metastases									
Present	47	8 (17.0)	Not reached [-; -]	47	7 (14.9)	Not reached [-; -]	0.88 [0.30; 2.60]	0.819	0.314
Absent	192	30 (15.6)	Not reached [-; -]	189	39 (20.6)	Not reached [-; -]	0.47 [0.27; 0.80]	0.006	
Stratification Factor: PD-L1 Expression									
High	138	23 (16.7)	Not reached [-; -]	138	26 (18.8)	Not reached [-; -]	0.52 [0.27; 0.99]	0.045	0.707
Low	101	15 (14.9)	Not reached [-; -]	98	20 (20.4)	Not reached [-; -]	0.55 [0.27; 1.12]	0.099	
Metastatic Disease Site									
Visceral metastases	169	30 (17.8)	Not reached [-; -]	157	30 (19.1)	Not reached [-; -]	0.53 [0.30; 0.96]	0.035	0.146
Lymph node only	60	6 (10.0)	Not reached [-; -]	65	14 (21.5)	Not reached [-; -]	0.44 [0.17; 1.14]	0.090	
Renal Function									
Normal	78	11 (14.1)	Not reached [-; -]	81	21 (25.9)	Not reached [-; -]	0.33 [0.14; 0.77]	0.011	0.244
Mild	115	21 (18.3)	Not reached [-; -]	118	21 (17.8)	Not reached [-; -]	0.65 [0.33; 1.27]	0.207	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	4 (10.8)	Not reached [-; -]	0.99 [0.27; 3.70]	0.993	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A system organ class appears on this report only if its incidence $\geq 10\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class</p>									

Tabelle 4G-88: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Blood and lymphatic system disorders - PT^g: Anaemia									
Age									
< 65	105	13 (12.4)	Not reached [-; -]	102	51 (50.0)	15.29 [10.00; -]	0.17 [0.09; 0.32]	< 0.001	0.414
≥ 65	134	28 (20.9)	Not reached [-; -]	134	81 (60.4)	12.00 [9.14; 13.29]	0.17 [0.11; 0.28]	< 0.001	
Race									
White	166	34 (20.5)	Not reached [-; -]	147	87 (59.2)	11.00 [9.14; 14.14]	0.19 [0.12; 0.29]	< 0.001	0.240
Non-white	73	7 (9.6)	Not reached [-; -]	89	45 (50.6)	17.00 [11.00; -]	0.12 [0.05; 0.28]	< 0.001	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	24 (47.1)	Not reached [9.71; -]	0.06 [0.01; 0.25]	< 0.001	0.126
Europe	97	21 (21.6)	Not reached [67.86; -]	101	60 (59.4)	12.86 [9.14; 17.00]	0.17 [0.10; 0.31]	< 0.001	
Rest of World	85	17 (20.0)	Not reached [-; -]	84	48 (57.1)	11.14 [8.00; -]	0.25 [0.14; 0.43]	< 0.001	
Sex									
Male	197	36 (18.3)	Not reached [-; -]	181	97 (53.6)	13.00 [10.14; 22.29]	0.19 [0.13; 0.30]	< 0.001	0.200
Female	42	5 (11.9)	Not reached [-; -]	55	35 (63.6)	10.00 [7.43; 17.00]	0.10 [0.04; 0.29]	< 0.001	
ECOG at Baseline									
0	136	21 (15.4)	Not reached [-; -]	124	69 (55.6)	13.14 [10.00; -]	0.15 [0.08; 0.25]	< 0.001	0.447
1-2	103	20 (19.4)	Not reached [-; -]	111	62 (55.9)	12.14 [9.14; 18.14]	0.21 [0.12; 0.36]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	25 (56.8)	12.29 [6.00; -]	0.10 [0.04; 0.25]	< 0.001	0.295
Lower Tract	176	33 (18.8)	Not reached [-; -]	192	107 (55.7)	13.00 [10.00; 17.00]	0.20 [0.13; 0.31]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	24 (17.4)	Not reached [-; -]	138	74 (53.6)	13.14 [10.00; -]	0.18 [0.11; 0.30]	< 0.001	0.631
Low	101	17 (16.8)	Not reached [-; -]	98	58 (59.2)	12.00 [6.86; 17.00]	0.17 [0.09; 0.30]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	30 (17.8)	Not reached [-; -]	157	85 (54.1)	12.86 [10.00; 21.43]	0.19 [0.12; 0.31]	< 0.001	0.272
Lymph node only	60	7 (11.7)	Not reached [-; -]	65	37 (56.9)	12.71 [9.14; -]	0.11 [0.05; 0.28]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	6 (7.7)	Not reached [-; -]	81	38 (46.9)	Not reached [12.14; -]	0.10 [0.04; 0.26]	< 0.001	0.356
Mild	115	24 (20.9)	Not reached [-; -]	118	71 (60.2)	11.14 [8.57; 15.00]	0.20 [0.12; 0.33]	< 0.001	
Moderate/Severe	46	11 (23.9)	Not reached [52.00; -]	37	23 (62.2)	9.29 [6.14; 21.43]	0.17 [0.07; 0.39]	< 0.001	
SOC: Blood and lymphatic system disorders - PT^g: Leukopenia									
Age									
< 65	105	4 (3.8)	Not reached [-; -]	102	12 (11.8)	Not reached [-; -]	0.15 [0.03; 0.68]	0.014	0.862
≥ 65	134	5 (3.7)	Not reached [-; -]	134	14 (10.4)	Not reached [-; -]	0.27 [0.09; 0.82]	0.021	
Race									
White	166	7 (4.2)	Not reached [-; -]	147	20 (13.6)	Not reached [-; -]	0.20 [0.08; 0.54]	0.001	0.722
Non-white	73	2 (2.7)	Not reached [-; -]	89	6 (6.7)	Not reached [-; -]	0.20 [0.02; 1.65]	0.134	
Geographic Region									
North America	57	0 (0.0)	Not reached [-; -]	51	4 (7.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.032	0.149
Europe	97	2 (2.1)	Not reached [-; -]	101	10 (9.9)	Not reached [-; -]	0.20 [0.04; 0.91]	0.037	
Rest of World	85	7 (8.2)	Not reached [-; -]	84	12 (14.3)	Not reached [-; -]	0.30 [0.10; 0.94]	0.040	
Sex									
Male	197	7 (3.6)	Not reached [-; -]	181	22 (12.2)	Not reached [-; -]	0.23 [0.09; 0.58]	0.002	0.438
Female	42	2 (4.8)	Not reached [-; -]	55	4 (7.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.995	
ECOG at Baseline									
0	136	5 (3.7)	Not reached [-; -]	124	11 (8.9)	Not reached [-; -]	0.24 [0.07; 0.86]	0.029	0.717
1-2	103	4 (3.9)	Not reached [-; -]	111	14 (12.6)	Not reached [-; -]	0.21 [0.06; 0.74]	0.015	
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	4 (9.1)	Not reached [-; -]	0.17 [0.02; 1.55]	0.116	0.917
Lower Tract	176	7 (4.0)	Not reached [-; -]	192	22 (11.5)	Not reached [-; -]	0.23 [0.09; 0.61]	0.003	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	6 (12.8)	Not reached [-; -]	0.32 [0.06; 1.58]	0.162	0.899
Absent	192	7 (3.6)	Not reached [-; -]	189	20 (10.6)	Not reached [-; -]	0.18 [0.06; 0.54]	0.002	
Stratification Factor: PD-L1 Expression									
High	138	7 (5.1)	Not reached [-; -]	138	16 (11.6)	Not reached [-; -]	0.23 [0.08; 0.70]	0.010	0.380
Low	101	2 (2.0)	Not reached [-; -]	98	10 (10.2)	Not reached [-; -]	0.18 [0.04; 0.84]	0.028	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	10 (12.3)	Not reached [-; -]	0.20 [0.04; 0.90]	0.036	0.587
Mild	115	5 (4.3)	Not reached [-; -]	118	11 (9.3)	Not reached [-; -]	0.36 [0.11; 1.12]	0.079	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	5 (13.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994	
SOC: Blood and lymphatic system disorders - PT^g: Neutropenia									
Race									
White	166	16 (9.6)	Not reached [-; -]	147	66 (44.9)	Not reached [10.14; -]	0.13 [0.07; 0.24]	< 0.001	0.381
Non-white	73	5 (6.8)	Not reached [-; -]	89	20 (22.5)	Not reached [-; -]	0.27 [0.10; 0.73]	0.009	
ECOG at Baseline									
0	136	14 (10.3)	Not reached [-; -]	124	44 (35.5)	Not reached [-; -]	0.19 [0.10; 0.37]	< 0.001	0.308
1-2	103	7 (6.8)	Not reached [-; -]	111	42 (37.8)	Not reached [15.14; -]	0.14 [0.06; 0.31]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	7 (11.5)	Not reached [-; -]	44	15 (34.1)	Not reached [14.00; -]	0.25 [0.10; 0.65]	0.004	0.293
Lower Tract	176	14 (8.0)	Not reached [-; -]	192	71 (37.0)	Not reached [-; -]	0.15 [0.08; 0.27]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	22 (46.8)	Not reached [9.00; -]	0.14 [0.05; 0.41]	< 0.001	0.569
Absent	192	17 (8.9)	Not reached [-; -]	189	64 (33.9)	Not reached [-; -]	0.18 [0.10; 0.31]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	12 (8.7)	Not reached [-; -]	138	54 (39.1)	Not reached [-; -]	0.16 [0.08; 0.31]	< 0.001	0.637
Low	101	9 (8.9)	Not reached [-; -]	98	32 (32.7)	Not reached [-; -]	0.18 [0.08; 0.40]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	16 (9.5)	Not reached [-; -]	157	58 (36.9)	Not reached [-; -]	0.17 [0.10; 0.31]	< 0.001	0.673
Lymph node only	60	4 (6.7)	Not reached [-; -]	65	21 (32.3)	Not reached [-; -]	0.16 [0.06; 0.48]	< 0.001	
Renal Function									
Normal	78	4 (5.1)	Not reached [-; -]	81	31 (38.3)	Not reached [13.29; -]	0.11 [0.04; 0.30]	< 0.001	0.233
Mild	115	15 (13.0)	Not reached [-; -]	118	46 (39.0)	Not reached [15.14; -]	0.22 [0.11; 0.41]	< 0.001	
Moderate/Severe	46	2 (4.3)	Not reached [-; -]	37	9 (24.3)	Not reached [-; -]	0.15 [0.03; 0.72]	0.017	
SOC: Blood and lymphatic system disorders - PT^g: Thrombocytopenia									
Race									
White	166	6 (3.6)	Not reached [-; -]	147	42 (28.6)	Not reached [-; -]	0.06 [0.02; 0.18]	< 0.001	0.368
Non-white	73	3 (4.1)	Not reached [-; -]	89	15 (16.9)	Not reached [-; -]	0.11 [0.02; 0.52]	0.005	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	9 (17.6)	Not reached [-; -]	0.08 [0.01; 0.66]	0.019	0.803
Europe	97	5 (5.2)	Not reached [-; -]	101	27 (26.7)	Not reached [-; -]	0.09 [0.03; 0.30]	< 0.001	
Rest of World	85	3 (3.5)	Not reached [-; -]	84	21 (25.0)	Not reached [-; -]	0.07 [0.02; 0.29]	< 0.001	
Sex									
Male	197	7 (3.6)	Not reached [-; -]	181	42 (23.2)	Not reached [-; -]	0.09 [0.03; 0.22]	< 0.001	0.866
Female	42	2 (4.8)	Not reached [-; -]	55	15 (27.3)	Not reached [-; -]	0.06 [0.01; 0.45]	0.007	
ECOG at Baseline									
0	136	4 (2.9)	Not reached [-; -]	124	23 (18.5)	Not reached [-; -]	0.09 [0.03; 0.31]	< 0.001	0.991
1-2	103	5 (4.9)	Not reached [-; -]	111	33 (29.7)	Not reached [-; -]	0.07 [0.02; 0.24]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	4 (6.6)	Not reached [-; -]	44	9 (20.5)	Not reached [-; -]	0.11 [0.02; 0.55]	0.007	0.157
Lower Tract	176	5 (2.8)	Not reached [-; -]	192	48 (25.0)	Not reached [-; -]	0.07 [0.02; 0.20]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	12 (25.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.991	0.789
Absent	192	7 (3.6)	Not reached [-; -]	189	45 (23.8)	Not reached [-; -]	0.09 [0.04; 0.23]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	Not reached [-; -]	138	37 (26.8)	Not reached [-; -]	0.05 [0.01; 0.19]	< 0.001	0.194
Low	101	5 (5.0)	Not reached [-; -]	98	20 (20.4)	Not reached [-; -]	0.13 [0.04; 0.40]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	40 (25.5)	Not reached [-; -]	0.02 [0.00; 0.13]	< 0.001	0.131
Lymph node only	60	4 (6.7)	Not reached [-; -]	65	14 (21.5)	Not reached [-; -]	0.23 [0.07; 0.72]	0.012	
Renal Function									
Normal	78	2 (2.6)	Not reached [-; -]	81	17 (21.0)	Not reached [-; -]	0.04 [0.01; 0.34]	0.003	0.875
Mild	115	5 (4.3)	Not reached [-; -]	118	28 (23.7)	Not reached [-; -]	0.09 [0.03; 0.31]	< 0.001	
Moderate/Severe	46	2 (4.3)	Not reached [-; -]	37	12 (32.4)	Not reached [5.14; -]	0.09 [0.02; 0.43]	0.002	
SOC: Ear and labyrinth disorders - PT ^g : Tinnitus									
Age									
< 65	105	1 (1.0)	Not reached [-; -]	102	17 (16.7)	Not reached [-; -]	0.05 [0.01; 0.39]	0.004	0.056
≥ 65	134	4 (3.0)	Not reached [-; -]	134	10 (7.5)	Not reached [-; -]	0.21 [0.05; 0.85]	0.028	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	166	4 (2.4)	Not reached [-; -]	147	16 (10.9)	Not reached [-; -]	0.12 [0.03; 0.43]	0.001	0.569
Non-white	73	1 (1.4)	Not reached [-; -]	89	11 (12.4)	Not reached [-; -]	0.11 [0.01; 0.83]	0.032	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	15 (29.4)	Not reached [-; -]	0.09 [0.02; 0.41]	0.002	0.992
Europe	97	1 (1.0)	Not reached [-; -]	101	6 (5.9)	Not reached [-; -]	0.04 [0.00; 0.86]	0.039	
Rest of World	85	1 (1.2)	Not reached [-; -]	84	6 (7.1)	Not reached [-; -]	0.16 [0.02; 1.32]	0.089	
Sex									
Male	197	3 (1.5)	Not reached [-; -]	181	21 (11.6)	Not reached [-; -]	0.09 [0.02; 0.34]	< 0.001	0.263
Female	42	2 (4.8)	Not reached [-; -]	55	6 (10.9)	Not reached [-; -]	0.24 [0.04; 1.63]	0.144	
ECOG at Baseline									
0	136	3 (2.2)	Not reached [-; -]	124	17 (13.7)	Not reached [-; -]	0.11 [0.03; 0.42]	0.001	0.750
1-2	103	2 (1.9)	Not reached [-; -]	111	10 (9.0)	Not reached [-; -]	0.11 [0.02; 0.73]	0.022	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	0.11 [0.01; 0.95]	0.045	0.665
Lower Tract	176	4 (2.3)	Not reached [-; -]	192	21 (10.9)	Not reached [-; -]	0.11 [0.03; 0.40]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	Not reached [-; -]	47	5 (10.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022	0.195
Absent	192	5 (2.6)	Not reached [-; -]	189	22 (11.6)	Not reached [-; -]	0.14 [0.04; 0.41]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	22 (14.0)	Not reached [-; -]	0.09 [0.02; 0.32]	< 0.001	0.249
Lymph node only	60	0 (0.0)	Not reached [-; -]	65	5 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.029	
Renal Function									
Normal	78	0 (0.0)	Not reached [-; -]	81	10 (12.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.067
Mild	115	3 (2.6)	Not reached [-; -]	118	15 (12.7)	Not reached [-; -]	0.13 [0.03; 0.53]	0.005	
Moderate/Severe	46	2 (4.3)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	0.44 [0.05; 4.16]	0.470	
SOC: Endocrine disorders - PT ^g : Hypothyroidism									
Age									
< 65	105	7 (6.7)	Not reached [-; -]	102	1 (1.0)	Not reached [-; -]	4.74 [0.56; 40.41]	0.155	0.122
≥ 65	134	16 (11.9)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	166	17 (10.2)	Not reached [-; -]	147	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.147
Non-white	73	6 (8.2)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	6.20 [0.72; 53.06]	0.096	
Geographic Region									
North America	57	4 (7.0)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.100	0.344
Europe	97	11 (11.3)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	
Rest of World	85	8 (9.4)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	4.78 [0.56; 40.95]	0.153	
Sex									
Male	197	18 (9.1)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	12.00 [1.58; 91.37]	0.016	0.418
Female	42	5 (11.9)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.025	
ECOG at Baseline									
0	136	16 (11.8)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.141
1-2	103	7 (6.8)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	5.00 [0.58; 42.79]	0.142	
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.083	0.545
Lower Tract	176	18 (10.2)	Not reached [-; -]	192	1 (0.5)	Not reached [-; -]	13.93 [1.83; 106.04]	0.011	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.079	0.506
Absent	192	19 (9.9)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	13.53 [1.79; 102.54]	0.012	
Stratification Factor: PD-L1 Expression									
High	138	16 (11.6)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	10.82 [1.40; 83.33]	0.022	0.397
Low	101	7 (6.9)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.016	
Metastatic Disease Site									
Visceral metastases	169	15 (8.9)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.112
Lymph node only	60	5 (8.3)	Not reached [-; -]	65	1 (1.5)	Not reached [-; -]	3.18 [0.33; 30.39]	0.315	
Renal Function									
Normal	78	6 (7.7)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.040	0.150
Mild	115	13 (11.3)	Not reached [-; -]	118	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Moderate/Severe	46	4 (8.7)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	2.95 [0.33; 26.40]	0.333	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]		Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Eye disorders - PT^g: Dry eye									
Age									
< 65	105	16 (15.2)	Not reached [-; -]	102	1 (1.0)	Not reached [-; -]	12.52 [1.64; 95.86]	0.015	0.471
≥ 65	134	13 (9.7)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	4.83 [1.06; 22.03]	0.042	
Geographic Region									
North America	57	13 (22.8)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	11.36 [1.48; 87.41]	0.020	0.781
Europe	97	11 (11.3)	Not reached [-; -]	101	1 (1.0)	Not reached [-; -]	7.72 [0.96; 61.92]	0.054	
Rest of World	85	5 (5.9)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	2.96 [0.31; 28.19]	0.346	
ECOG at Baseline									
0	136	16 (11.8)	Not reached [-; -]	124	2 (1.6)	Not reached [-; -]	6.03 [1.36; 26.74]	0.018	0.596
1-2	103	13 (12.6)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	10.15 [1.30; 79.47]	0.027	
Primary Disease Site of Origin									
Upper Tract	61	11 (18.0)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.018	0.150
Lower Tract	176	18 (10.2)	Not reached [-; -]	192	3 (1.6)	Not reached [-; -]	5.38 [1.56; 18.60]	0.008	
Stratification Factor: Liver Metastases									
Present	47	8 (17.0)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	7.01 [0.86; 57.19]	0.069	0.923
Absent	192	21 (10.9)	Not reached [-; -]	189	2 (1.1)	Not reached [-; -]	7.82 [1.80; 33.98]	0.006	
Stratification Factor: PD-L1 Expression									
High	138	13 (9.4)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	5.34 [1.18; 24.09]	0.029	0.457
Low	101	16 (15.8)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	11.46 [1.49; 88.21]	0.019	
Metastatic Disease Site									
Visceral metastases	169	21 (12.4)	Not reached [-; -]	157	2 (1.3)	Not reached [-; -]	7.66 [1.77; 33.19]	0.007	0.832
Lymph node only	60	7 (11.7)	Not reached [-; -]	65	1 (1.5)	Not reached [-; -]	5.31 [0.62; 45.47]	0.127	
Renal Function									
Normal	78	9 (11.5)	Not reached [-; -]	81	2 (2.5)	Not reached [-; -]	3.74 [0.78; 17.96]	0.100	0.382
Mild	115	13 (11.3)	Not reached [-; -]	118	1 (0.8)	Not reached [-; -]	10.86 [1.40; 84.32]	0.023	
Moderate/Severe	46	7 (15.2)	Not reached [62.29; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.055	
SOC: Eye disorders - PT^g: Lacrimation increased									
Age									
< 65	105	7 (6.7)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.046	0.438
≥ 65	134	18 (13.4)	Not reached [-; -]	134	1 (0.7)	Not reached [-; -]	12.48 [1.63; 95.60]	0.015	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	166	21 (12.7)	Not reached [-; -]	147	1 (0.7)	Not reached [-; -]	11.88 [1.56; 90.45]	0.017	0.505
Non-white	73	4 (5.5)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.056	
Geographic Region									
North America	57	6 (10.5)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	3.59 [0.40; 32.03]	0.252	0.223
Europe	97	16 (16.5)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Rest of World	85	3 (3.5)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.174	
Sex									
Male	197	23 (11.7)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	15.08 [2.00; 113.44]	0.008	0.641
Female	42	2 (4.8)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.728	
ECOG at Baseline									
0	136	17 (12.5)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.158
1-2	103	8 (7.8)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	6.64 [0.81; 54.46]	0.078	
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.086	0.539
Lower Tract	176	19 (10.8)	Not reached [-; -]	192	1 (0.5)	Not reached [-; -]	13.59 [1.77; 104.08]	0.012	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.147	0.532
Absent	192	21 (10.9)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	14.02 [1.85; 106.36]	0.011	
Stratification Factor: PD-L1 Expression									
High	138	13 (9.4)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.232
Low	101	12 (11.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	5.95 [0.72; 49.11]	0.098	
Metastatic Disease Site									
Visceral metastases	169	17 (10.1)	Not reached [-; -]	157	1 (0.6)	Not reached [-; -]	9.41 [1.21; 73.36]	0.032	0.417
Lymph node only	60	6 (10.0)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.019	
Renal Function									
Normal	78	7 (9.0)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.032	0.691
Mild	115	17 (14.8)	Not reached [-; -]	118	1 (0.8)	Not reached [-; -]	12.65 [1.65; 97.24]	0.015	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.855	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
SOC: Gastrointestinal disorders - PT^g: Constipation									
Age									
< 65	105	23 (21.9)	108.00 [108.00; -]	102	30 (29.4)	Not reached [-; -]	0.40 [0.21; 0.75]	0.004	0.335
≥ 65	134	44 (32.8)	Not reached [60.29; -]	134	46 (34.3)	Not reached [-; -]	0.65 [0.42; 1.02]	0.059	
Race									
White	166	47 (28.3)	108.00 [83.86; -]	147	44 (29.9)	Not reached [-; -]	0.60 [0.38; 0.94]	0.024	0.517
Non-white	73	20 (27.4)	Not reached [-; -]	89	32 (36.0)	Not reached [-; -]	0.49 [0.26; 0.91]	0.025	
Geographic Region									
North America	57	22 (38.6)	Not reached [22.14; -]	51	21 (41.2)	Not reached [5.14; -]	0.74 [0.40; 1.38]	0.344	0.738
Europe	97	21 (21.6)	Not reached [108.00; -]	101	30 (29.7)	Not reached [-; -]	0.44 [0.23; 0.82]	0.010	
Rest of World	85	24 (28.2)	Not reached [83.86; -]	84	25 (29.8)	Not reached [-; -]	0.50 [0.26; 0.95]	0.036	
Sex									
Male	197	55 (27.9)	Not reached [108.00; -]	181	57 (31.5)	Not reached [-; -]	0.58 [0.38; 0.86]	0.007	0.852
Female	42	12 (28.6)	Not reached [35.29; -]	55	19 (34.5)	Not reached [17.00; -]	0.48 [0.21; 1.09]	0.078	
ECOG at Baseline									
0	136	39 (28.7)	108.00 [108.00; -]	124	46 (37.1)	Not reached [-; -]	0.47 [0.30; 0.76]	0.002	0.240
1-2	103	28 (27.2)	Not reached [83.86; -]	111	30 (27.0)	Not reached [-; -]	0.67 [0.38; 1.16]	0.154	
Primary Disease Site of Origin									
Upper Tract	61	15 (24.6)	Not reached [-; -]	44	15 (34.1)	Not reached [13.43; -]	0.40 [0.18; 0.90]	0.026	0.499
Lower Tract	176	51 (29.0)	108.00 [108.00; -]	192	61 (31.8)	Not reached [-; -]	0.59 [0.39; 0.88]	0.011	
Stratification Factor: Liver Metastases									
Present	47	10 (21.3)	108.00 [-; -]	47	10 (21.3)	Not reached [-; -]	0.74 [0.29; 1.87]	0.522	0.556
Absent	192	57 (29.7)	Not reached [-; -]	189	66 (34.9)	Not reached [-; -]	0.52 [0.35; 0.77]	0.001	
Stratification Factor: PD-L1 Expression									
High	138	37 (26.8)	Not reached [-; -]	138	47 (34.1)	Not reached [-; -]	0.42 [0.26; 0.69]	< 0.001	0.370
Low	101	30 (29.7)	108.00 [108.00; -]	98	29 (29.6)	Not reached [-; -]	0.78 [0.46; 1.32]	0.350	
Metastatic Disease Site									
Visceral metastases	169	44 (26.0)	108.00 [83.86; -]	157	46 (29.3)	Not reached [-; -]	0.56 [0.35; 0.88]	0.012	0.478
Lymph node only	60	19 (31.7)	Not reached [-; -]	65	27 (41.5)	Not reached [13.43; -]	0.52 [0.28; 0.97]	0.039	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	20 (25.6)	Not reached [83.86; -]	81	23 (28.4)	Not reached [-; -]	0.55 [0.28; 1.07]	0.080	0.518
Mild	115	33 (28.7)	108.00 [108.00; -]	118	43 (36.4)	Not reached [-; -]	0.48 [0.29; 0.79]	0.004	
Moderate/Severe	46	14 (30.4)	Not reached [58.57; -]	37	10 (27.0)	Not reached [16.71; -]	0.80 [0.34; 1.88]	0.606	
SOC: Gastrointestinal disorders - PT^g: Diarrhoea									
Age									
< 65	105	35 (33.3)	Not reached [87.00; -]	102	16 (15.7)	Not reached [-; -]	1.61 [0.86; 3.00]	0.135	0.769
≥ 65	134	54 (40.3)	Not reached [28.29; -]	134	24 (17.9)	Not reached [-; -]	2.11 [1.29; 3.45]	0.003	
Race									
White	166	63 (38.0)	Not reached [69.29; -]	147	28 (19.0)	Not reached [-; -]	1.74 [1.10; 2.75]	0.019	0.554
Non-white	73	26 (35.6)	Not reached [59.43; -]	89	12 (13.5)	Not reached [-; -]	2.23 [1.10; 4.52]	0.027	
Geographic Region									
North America	57	29 (50.9)	30.29 [6.43; -]	51	13 (25.5)	Not reached [-; -]	1.73 [0.87; 3.41]	0.116	0.848
Europe	97	32 (33.0)	Not reached [87.00; -]	101	17 (16.8)	Not reached [-; -]	1.84 [1.01; 3.36]	0.047	
Rest of World	85	28 (32.9)	Not reached [-; -]	84	10 (11.9)	Not reached [-; -]	2.18 [1.03; 4.60]	0.040	
Sex									
Male	197	80 (40.6)	Not reached [59.43; -]	181	31 (17.1)	Not reached [-; -]	2.01 [1.31; 3.09]	0.001	0.220
Female	42	9 (21.4)	Not reached [-; -]	55	9 (16.4)	Not reached [-; -]	1.32 [0.53; 3.34]	0.552	
ECOG at Baseline									
0	136	45 (33.1)	Not reached [71.14; -]	124	20 (16.1)	Not reached [-; -]	1.72 [1.00; 2.96]	0.051	0.584
1-2	103	44 (42.7)	87.00 [26.14; -]	111	20 (18.0)	Not reached [-; -]	2.13 [1.24; 3.68]	0.006	
Primary Disease Site of Origin									
Upper Tract	61	23 (37.7)	Not reached [29.14; -]	44	4 (9.1)	Not reached [-; -]	3.81 [1.30; 11.21]	0.015	0.146
Lower Tract	176	65 (36.9)	Not reached [71.14; -]	192	36 (18.8)	Not reached [-; -]	1.70 [1.12; 2.59]	0.013	
Stratification Factor: PD-L1 Expression									
High	138	45 (32.6)	Not reached [-; -]	138	20 (14.5)	Not reached [-; -]	2.00 [1.16; 3.43]	0.012	0.968
Low	101	44 (43.6)	87.00 [24.29; -]	98	20 (20.4)	Not reached [-; -]	1.82 [1.05; 3.15]	0.033	
Metastatic Disease Site									
Visceral metastases	169	61 (36.1)	Not reached [69.29; -]	157	24 (15.3)	Not reached [-; -]	2.07 [1.28; 3.37]	0.003	0.702
Lymph node only	60	23 (38.3)	87.00 [29.14; -]	65	12 (18.5)	Not reached [-; -]	1.60 [0.77; 3.35]	0.208	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	30 (38.5)	87.00 [30.29; -]	81	15 (18.5)	Not reached [-; -]	1.84 [0.97; 3.50]	0.064	0.891
Mild	115	44 (38.3)	Not reached [59.43; -]	118	19 (16.1)	Not reached [-; -]	2.15 [1.24; 3.74]	0.006	
Moderate/Severe	46	15 (32.6)	Not reached [29.14; -]	37	6 (16.2)	Not reached [-; -]	1.39 [0.52; 3.75]	0.510	
SOC: Gastrointestinal disorders - PT^g: Dry mouth									
Age									
< 65	105	8 (7.6)	Not reached [-; -]	102	2 (2.0)	Not reached [-; -]	3.36 [0.70; 16.19]	0.130	0.938
≥ 65	134	16 (11.9)	Not reached [-; -]	134	4 (3.0)	Not reached [-; -]	2.99 [0.96; 9.27]	0.058	
Race									
White	166	17 (10.2)	Not reached [-; -]	147	4 (2.7)	Not reached [-; -]	2.98 [0.98; 9.07]	0.054	0.856
Non-white	73	7 (9.6)	Not reached [-; -]	89	2 (2.2)	Not reached [-; -]	3.16 [0.61; 16.28]	0.169	
Geographic Region									
North America	57	11 (19.3)	Not reached [-; -]	51	2 (3.9)	Not reached [-; -]	3.51 [0.74; 16.54]	0.113	0.900
Europe	97	9 (9.3)	Not reached [-; -]	101	3 (3.0)	Not reached [-; -]	2.81 [0.74; 10.58]	0.128	
Rest of World	85	4 (4.7)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	2.92 [0.30; 28.07]	0.354	
Sex									
Male	197	19 (9.6)	Not reached [-; -]	181	6 (3.3)	Not reached [-; -]	2.42 [0.95; 6.18]	0.065	0.066
Female	42	5 (11.9)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.050 ^h	
ECOG at Baseline									
0	136	12 (8.8)	Not reached [-; -]	124	1 (0.8)	Not reached [-; -]	9.49 [1.21; 74.12]	0.032	0.159
1-2	103	12 (11.7)	Not reached [-; -]	111	5 (4.5)	Not reached [-; -]	1.88 [0.63; 5.61]	0.257	
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	2.84 [0.32; 25.43]	0.350	0.882
Lower Tract	176	17 (9.7)	Not reached [-; -]	192	5 (2.6)	Not reached [-; -]	3.27 [1.19; 9.00]	0.022	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	0.99 [0.14; 7.03]	0.991	0.161
Absent	192	22 (11.5)	Not reached [-; -]	189	4 (2.1)	Not reached [-; -]	4.15 [1.40; 12.34]	0.010	
Stratification Factor: PD-L1 Expression									
High	138	16 (11.6)	Not reached [-; -]	138	5 (3.6)	Not reached [-; -]	2.63 [0.94; 7.39]	0.066	0.427
Low	101	8 (7.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	5.63 [0.68; 46.78]	0.109	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	8 (10.3)	Not reached [-; -]	81	2 (2.5)	Not reached [-; -]	3.19 [0.64; 15.82]	0.155	0.444
Mild	115	12 (10.4)	Not reached [-; -]	118	4 (3.4)	Not reached [-; -]	2.52 [0.79; 8.03]	0.118	
Moderate/Severe	46	4 (8.7)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.128	
SOC: Gastrointestinal disorders - PT ^g : Nausea									
Race									
White	166	47 (28.3)	Not reached [-; -]	147	72 (49.0)	16.43 [6.57; -]	0.39 [0.26; 0.58]	< 0.001	0.161
Non-white	73	14 (19.2)	Not reached [-; -]	89	48 (53.9)	10.29 [4.29; -]	0.29 [0.16; 0.52]	< 0.001	
Geographic Region									
North America	57	22 (38.6)	Not reached [26.14; -]	51	34 (66.7)	3.71 [0.86; 13.14]	0.35 [0.20; 0.62]	< 0.001	0.943
Europe	97	25 (25.8)	Not reached [96.00; -]	101	55 (54.5)	12.43 [6.00; -]	0.33 [0.20; 0.55]	< 0.001	
Rest of World	85	14 (16.5)	Not reached [-; -]	84	31 (36.9)	Not reached [15.71; -]	0.36 [0.19; 0.68]	0.002	
Sex									
Male	197	47 (23.9)	Not reached [-; -]	181	83 (45.9)	Not reached [10.86; -]	0.38 [0.26; 0.55]	< 0.001	0.568
Female	42	14 (33.3)	Not reached [38.71; -]	55	37 (67.3)	4.00 [1.00; 11.00]	0.31 [0.16; 0.60]	< 0.001	
ECOG at Baseline									
0	136	29 (21.3)	Not reached [96.00; -]	124	67 (54.0)	13.00 [6.29; -]	0.28 [0.18; 0.44]	< 0.001	0.055
1-2	103	32 (31.1)	Not reached [-; -]	111	52 (46.8)	Not reached [8.71; -]	0.47 [0.29; 0.75]	0.001	
Primary Disease Site of Origin									
Upper Tract	61	18 (29.5)	Not reached [-; -]	44	19 (43.2)	Not reached [10.29; -]	0.57 [0.30; 1.11]	0.097	0.115
Lower Tract	176	42 (23.9)	Not reached [-; -]	192	101 (52.6)	10.86 [6.43; -]	0.30 [0.21; 0.44]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	40 (29.0)	Not reached [-; -]	138	80 (58.0)	9.86 [4.29; 16.43]	0.33 [0.22; 0.49]	< 0.001	0.714
Low	101	21 (20.8)	Not reached [96.00; -]	98	40 (40.8)	Not reached [10.29; -]	0.40 [0.23; 0.69]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	43 (25.4)	Not reached [96.00; -]	157	73 (46.5)	Not reached [9.86; -]	0.39 [0.26; 0.58]	< 0.001	0.111
Lymph node only	60	13 (21.7)	Not reached [-; -]	65	40 (61.5)	7.29 [2.86; 15.14]	0.25 [0.13; 0.46]	< 0.001	
Renal Function									
Normal	78	21 (26.9)	Not reached [-; -]	81	48 (59.3)	6.43 [1.29; 18.57]	0.31 [0.18; 0.52]	< 0.001	0.282
Mild	115	27 (23.5)	Not reached [96.00; -]	118	59 (50.0)	14.14 [9.14; -]	0.33 [0.20; 0.54]	< 0.001	
Moderate/Severe	46	13	Not reached	37	13	Not reached	0.61	0.228	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
		(28.3)	[-; -]		(35.1)	[10.14; -]	[0.28; 1.36]		
SOC: Gastrointestinal disorders - PT^g: Vomiting									
Age									
< 65	105	11 (10.5)	Not reached [96.00; -]	102	28 (27.5)	Not reached [-; -]	0.28 [0.13; 0.58]	< 0.001	0.053
≥ 65	134	13 (9.7)	Not reached [-; -]	134	14 (10.4)	Not reached [-; -]	0.78 [0.36; 1.71]	0.532	
Race									
White	166	15 (9.0)	Not reached [-; -]	147	26 (17.7)	Not reached [-; -]	0.37 [0.19; 0.73]	0.004	0.472
Non-white	73	9 (12.3)	Not reached [-; -]	89	16 (18.0)	Not reached [-; -]	0.62 [0.27; 1.42]	0.256	
Geographic Region									
North America	57	10 (17.5)	Not reached [70.14; -]	51	11 (21.6)	Not reached [-; -]	0.59 [0.24; 1.46]	0.253	0.170
Europe	97	6 (6.2)	Not reached [-; -]	101	21 (20.8)	Not reached [-; -]	0.23 [0.09; 0.61]	0.003	
Rest of World	85	8 (9.4)	Not reached [-; -]	84	10 (11.9)	Not reached [-; -]	0.70 [0.27; 1.80]	0.457	
Sex									
Male	197	18 (9.1)	Not reached [-; -]	181	26 (14.4)	Not reached [-; -]	0.47 [0.25; 0.90]	0.023	0.649
Female	42	6 (14.3)	Not reached [-; -]	55	16 (29.1)	Not reached [-; -]	0.45 [0.18; 1.15]	0.096	
ECOG at Baseline									
0	136	10 (7.4)	Not reached [-; -]	124	25 (20.2)	Not reached [-; -]	0.28 [0.13; 0.61]	0.001	0.087
1-2	103	14 (13.6)	Not reached [-; -]	111	17 (15.3)	Not reached [-; -]	0.70 [0.34; 1.48]	0.354	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	0.99 [0.34; 2.86]	0.988	0.206
Lower Tract	176	16 (9.1)	Not reached [-; -]	192	36 (18.8)	Not reached [-; -]	0.34 [0.18; 0.64]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	8 (17.0)	96.00 [70.14; -]	47	7 (14.9)	Not reached [-; -]	0.71 [0.22; 2.22]	0.552	0.072
Absent	192	16 (8.3)	Not reached [-; -]	189	35 (18.5)	Not reached [-; -]	0.40 [0.22; 0.72]	0.002	
Stratification Factor: PD-L1 Expression									
High	138	14 (10.1)	Not reached [-; -]	138	27 (19.6)	Not reached [-; -]	0.39 [0.19; 0.77]	0.007	0.601
Low	101	10 (9.9)	Not reached [96.00; -]	98	15 (15.3)	Not reached [-; -]	0.56 [0.24; 1.27]	0.164	
Metastatic Disease Site									
Visceral metastases	169	16 (9.5)	Not reached [-; -]	157	29 (18.5)	Not reached [-; -]	0.39 [0.20; 0.74]	0.004	0.799
Lymph node only	60	6 (10.0)	Not reached [-; -]	65	11 (16.9)	Not reached [-; -]	0.49 [0.17; 1.37]	0.172	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	9 (11.5)	Not reached [-; -]	81	21 (25.9)	Not reached [-; -]	0.37 [0.16; 0.83]	0.016	0.378
Mild	115	10 (8.7)	Not reached [-; -]	118	18 (15.3)	Not reached [-; -]	0.49 [0.22; 1.08]	0.077	
Moderate/Severe	46	5 (10.9)	Not reached [70.14; -]	37	3 (8.1)	Not reached [-; -]	0.82 [0.17; 3.87]	0.798	
SOC: General disorders and administration site conditions - PT^g: Fatigue									
Age									
< 65	105	31 (29.5)	Not reached [70.86; -]	102	41 (40.2)	Not reached [14.29; -]	0.43 [0.25; 0.72]	0.001	0.496
≥ 65	134	48 (35.8)	Not reached [83.86; -]	134	60 (44.8)	Not reached [10.43; -]	0.60 [0.40; 0.90]	0.013	
Race									
White	166	56 (33.7)	Not reached [68.71; -]	147	57 (38.8)	Not reached [-; -]	0.56 [0.38; 0.84]	0.005	0.257
Non-white	73	23 (31.5)	Not reached [-; -]	89	44 (49.4)	18.14 [8.86; -]	0.48 [0.29; 0.82]	0.006	
Geographic Region									
North America	57	33 (57.9)	22.86 [4.14; 38.43]	51	34 (66.7)	4.14 [1.43; 9.14]	0.60 [0.36; 1.00]	0.049	0.309
Europe	97	25 (25.8)	Not reached [-; -]	101	45 (44.6)	Not reached [13.00; -]	0.43 [0.26; 0.72]	0.001	
Rest of World	85	21 (24.7)	Not reached [83.86; -]	84	22 (26.2)	Not reached [-; -]	0.50 [0.25; 1.00]	0.049	
Sex									
Male	197	66 (33.5)	Not reached [83.86; -]	181	70 (38.7)	Not reached [-; -]	0.61 [0.43; 0.87]	0.007	0.119
Female	42	13 (31.0)	Not reached [38.43; -]	55	31 (56.4)	8.71 [2.86; -]	0.32 [0.15; 0.67]	0.002	
Primary Disease Site of Origin									
Upper Tract	61	19 (31.1)	Not reached [39.29; -]	44	21 (47.7)	Not reached [3.71; -]	0.42 [0.21; 0.82]	0.011	0.480
Lower Tract	176	59 (33.5)	Not reached [70.86; -]	192	80 (41.7)	Not reached [15.29; -]	0.57 [0.40; 0.81]	0.002	
Stratification Factor: Liver Metastases									
Present	47	19 (40.4)	68.71 [24.14; -]	47	18 (38.3)	Not reached [15.29; -]	0.83 [0.42; 1.64]	0.592	0.080
Absent	192	60 (31.3)	Not reached [83.86; -]	189	83 (43.9)	Not reached [13.00; -]	0.47 [0.33; 0.67]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	50 (36.2)	Not reached [68.71; -]	138	62 (44.9)	Not reached [10.43; -]	0.55 [0.37; 0.83]	0.004	0.720
Low	101	29 (28.7)	Not reached [-; -]	98	39 (39.8)	Not reached [15.29; -]	0.48 [0.29; 0.81]	0.006	
Renal Function									
Normal	78	27 (34.6)	Not reached [83.86; -]	81	39 (48.1)	18.14 [9.00; -]	0.50 [0.29; 0.84]	0.009	0.841
Mild	115	38 (33.0)	Not reached [70.86; -]	118	47 (39.8)	Not reached [15.29; -]	0.57 [0.36; 0.90]	0.016	
Moderate/Severe	46	14	Not reached	37	15	Not reached	0.49	0.072	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
		(30.4)	[68.71; -]		(40.5)	[5.43; -]	[0.23; 1.07]		
SOC: Infections and infestations - PT^g: Conjunctivitis									
Age									
< 65	105	6 (5.7)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.047	0.997
≥ 65	134	12 (9.0)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Race									
White	166	13 (7.8)	Not reached [-; -]	147	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	0.997
Non-white	73	5 (6.8)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.189	
Geographic Region									
North America	57	5 (8.8)	Not reached [84.29; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.099	> 0.999
Europe	97	10 (10.3)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.007	
Rest of World	85	3 (3.5)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.244	
Sex									
Male	197	15 (7.6)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	0.997
Female	42	3 (7.1)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.104	
ECOG at Baseline									
0	136	11 (8.1)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.009	0.997
1-2	103	7 (6.8)	Not reached [-; -]	111	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.039	
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.086	0.997
Lower Tract	176	13 (7.4)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.102	0.997
Absent	192	15 (7.8)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	11 (8.0)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	0.997
Low	101	7 (6.9)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.049	
Metastatic Disease Site									
Visceral metastases	169	14 (8.3)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.997
Lymph node only	60	4 (6.7)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.075	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.137	> 0.999
Mild	115	10 (8.7)	Not reached [-; -]	118	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Moderate/Severe	46	5 (10.9)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.218	
SOC: Investigations - PT^g: Alanine aminotransferase increased									
Age									
< 65	105	26 (24.8)	Not reached [-; -]	102	4 (3.9)	Not reached [-; -]	5.63 [1.94; 16.34]	0.001	0.141
≥ 65	134	23 (17.2)	Not reached [-; -]	134	9 (6.7)	Not reached [-; -]	2.25 [1.03; 4.94]	0.043	
Race									
White	166	33 (19.9)	Not reached [-; -]	147	11 (7.5)	Not reached [-; -]	2.17 [1.08; 4.38]	0.030	0.067
Non-white	73	16 (21.9)	Not reached [-; -]	89	2 (2.2)	Not reached [-; -]	9.88 [2.26; 43.23]	0.002	
Geographic Region									
North America	57	4 (7.0)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	3.44 [0.38; 30.84]	0.269	0.277
Europe	97	19 (19.6)	Not reached [86.00; -]	101	8 (7.9)	Not reached [-; -]	1.75 [0.74; 4.17]	0.205	
Rest of World	85	26 (30.6)	Not reached [-; -]	84	4 (4.8)	Not reached [-; -]	6.82 [2.37; 19.64]	< 0.001	
Sex									
Male	197	41 (20.8)	Not reached [-; -]	181	12 (6.6)	Not reached [-; -]	2.63 [1.36; 5.08]	0.004	0.208
Female	42	8 (19.0)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	11.32 [1.42; 90.56]	0.022	
ECOG at Baseline									
0	136	30 (22.1)	Not reached [-; -]	124	7 (5.6)	Not reached [-; -]	3.31 [1.43; 7.65]	0.005	0.859
1-2	103	19 (18.4)	Not reached [-; -]	111	6 (5.4)	Not reached [-; -]	3.18 [1.25; 8.06]	0.015	
Stratification Factor: Liver Metastases									
Present	47	8 (17.0)	Not reached [-; -]	47	3 (6.4)	Not reached [-; -]	2.45 [0.63; 9.49]	0.193	0.658
Absent	192	41 (21.4)	Not reached [-; -]	189	10 (5.3)	Not reached [-; -]	3.52 [1.74; 7.10]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	23 (16.7)	Not reached [-; -]	138	8 (5.8)	Not reached [-; -]	2.29 [1.00; 5.25]	0.051	0.300
Low	101	26 (25.7)	Not reached [-; -]	98	5 (5.1)	Not reached [-; -]	4.92 [1.88; 12.91]	0.001	
Metastatic Disease Site									
Visceral metastases	169	34 (20.1)	Not reached [-; -]	157	9 (5.7)	Not reached [-; -]	2.86 [1.34; 6.07]	0.006	0.559
Lymph node only	60	9 (15.0)	Not reached [-; -]	65	4 (6.2)	Not reached [-; -]	2.39 [0.73; 7.75]	0.148	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	11 (14.1)	Not reached [-; -]	81	4 (4.9)	Not reached [-; -]	2.22 [0.69; 7.20]	0.182	0.623
Mild	115	28 (24.3)	Not reached [-; -]	118	8 (6.8)	Not reached [-; -]	3.13 [1.40; 7.00]	0.005	
Moderate/Severe	46	10 (21.7)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	8.27 [1.06; 64.59]	0.044	
SOC: Investigations - PT^g: Aspartate aminotransferase increased									
Age									
< 65	105	23 (21.9)	Not reached [-; -]	102	4 (3.9)	Not reached [-; -]	5.33 [1.83; 15.55]	0.002	0.604
≥ 65	134	24 (17.9)	Not reached [-; -]	134	6 (4.5)	Not reached [-; -]	3.45 [1.39; 8.58]	0.008	
Race									
White	166	30 (18.1)	Not reached [-; -]	147	8 (5.4)	Not reached [-; -]	2.80 [1.26; 6.20]	0.011	0.121
Non-white	73	17 (23.3)	Not reached [-; -]	89	2 (2.2)	Not reached [-; -]	10.57 [2.43; 46.00]	0.002	
Geographic Region									
North America	57	5 (8.8)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.049	0.118
Europe	97	18 (18.6)	Not reached [-; -]	101	7 (6.9)	Not reached [-; -]	2.13 [0.86; 5.26]	0.100	
Rest of World	85	24 (28.2)	Not reached [-; -]	84	3 (3.6)	Not reached [-; -]	8.11 [2.43; 27.09]	< 0.001	
Sex									
Male	197	41 (20.8)	Not reached [-; -]	181	8 (4.4)	Not reached [-; -]	4.13 [1.91; 8.89]	< 0.001	0.866
Female	42	6 (14.3)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	4.20 [0.85; 20.81]	0.079	
ECOG at Baseline									
0	136	25 (18.4)	Not reached [-; -]	124	6 (4.8)	Not reached [-; -]	3.33 [1.34; 8.25]	0.009	0.483
1-2	103	22 (21.4)	Not reached [-; -]	111	4 (3.6)	Not reached [-; -]	5.63 [1.93; 16.45]	0.002	
Stratification Factor: Liver Metastases									
Present	47	10 (21.3)	Not reached [-; -]	47	3 (6.4)	Not reached [-; -]	3.59 [0.99; 13.06]	0.052	0.630
Absent	192	37 (19.3)	Not reached [-; -]	189	7 (3.7)	Not reached [-; -]	4.48 [1.97; 10.16]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	21 (15.2)	Not reached [-; -]	138	6 (4.3)	Not reached [-; -]	2.82 [1.12; 7.15]	0.029	0.338
Low	101	26 (25.7)	Not reached [-; -]	98	4 (4.1)	Not reached [-; -]	6.38 [2.22; 18.40]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	31 (18.3)	Not reached [-; -]	157	7 (4.5)	Not reached [-; -]	3.66 [1.59; 8.41]	0.002	0.764
Lymph node only	60	10 (16.7)	Not reached [-; -]	65	2 (3.1)	Not reached [-; -]	4.93 [1.06; 22.80]	0.041	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	11 (14.1)	Not reached [-; -]	81	4 (4.9)	Not reached [-; -]	2.74 [0.86; 8.66]	0.087	0.138
Mild	115	26 (22.6)	Not reached [-; -]	118	6 (5.1)	Not reached [-; -]	3.69 [1.49; 9.15]	0.005	
Moderate/Severe	46	10 (21.7)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	
SOC: Investigations - PT^g: Blood creatinine increased									
Age									
< 65	105	4 (3.8)	Not reached [-; -]	102	14 (13.7)	Not reached [-; -]	0.13 [0.03; 0.56]	0.007	0.231
≥ 65	134	8 (6.0)	Not reached [-; -]	134	13 (9.7)	Not reached [-; -]	0.45 [0.17; 1.17]	0.103	
Sex									
Male	197	10 (5.1)	Not reached [-; -]	181	21 (11.6)	Not reached [-; -]	0.29 [0.13; 0.68]	0.004	0.958
Female	42	2 (4.8)	Not reached [-; -]	55	6 (10.9)	Not reached [-; -]	0.21 [0.03; 1.75]	0.149	
ECOG at Baseline									
0	136	6 (4.4)	Not reached [-; -]	124	17 (13.7)	Not reached [-; -]	0.20 [0.07; 0.60]	0.004	0.289
1-2	103	6 (5.8)	Not reached [-; -]	111	10 (9.0)	Not reached [-; -]	0.43 [0.14; 1.31]	0.136	
Primary Disease Site of Origin									
Upper Tract	61	4 (6.6)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	0.71 [0.14; 3.50]	0.671	0.215
Lower Tract	176	8 (4.5)	Not reached [-; -]	192	24 (12.5)	Not reached [-; -]	0.22 [0.09; 0.56]	0.002	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	5 (10.6)	Not reached [-; -]	0.40 [0.08; 2.07]	0.274	0.528
Absent	192	9 (4.7)	Not reached [-; -]	189	22 (11.6)	Not reached [-; -]	0.26 [0.11; 0.62]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	3 (2.2)	Not reached [-; -]	138	14 (10.1)	Not reached [-; -]	0.14 [0.03; 0.60]	0.008	0.114
Low	101	9 (8.9)	Not reached [-; -]	98	13 (13.3)	Not reached [-; -]	0.43 [0.17; 1.11]	0.081	
Metastatic Disease Site									
Visceral metastases	169	10 (5.9)	Not reached [-; -]	157	18 (11.5)	Not reached [-; -]	0.35 [0.15; 0.83]	0.017	0.503
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	7 (10.8)	Not reached [-; -]	0.15 [0.02; 1.18]	0.072	
Renal Function									
Normal	78	1 (1.3)	Not reached [-; -]	81	9 (11.1)	Not reached [-; -]	0.06 [0.01; 0.59]	0.016	0.195
Mild	115	9 (7.8)	Not reached [-; -]	118	14 (11.9)	Not reached [-; -]	0.48 [0.20; 1.20]	0.117	
Moderate/Severe	46	2 (4.3)	Not reached [-; -]	37	4 (10.8)	Not reached [-; -]	0.18 [0.02; 1.62]	0.127	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
SOC: Investigations - PT^g: Lipase increased									
Age									
< 65	105	7 (6.7)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.016	0.997
≥ 65	134	10 (7.5)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.025	
Race									
White	166	16 (9.6)	Not reached [-; -]	147	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	0.997
Non-white	73	1 (1.4)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.259	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.345	> 0.999
Europe	97	12 (12.4)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	
Rest of World	85	4 (4.7)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.702	
Sex									
Male	197	17 (8.6)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.996
Female	42	0 (0.0)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
ECOG at Baseline									
0	136	9 (6.6)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	8 (7.8)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	10 (16.4)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.021	0.997
Lower Tract	176	7 (4.0)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.037	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.150	0.997
Absent	192	14 (7.3)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	8 (5.8)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	9 (8.9)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	13 (7.7)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
Lymph node only	60	3 (5.0)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.145	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	6 (7.7)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	7 (6.1)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	
Moderate/Severe	46	4 (8.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Investigations - PT^g: Neutrophil count decreased									
Age									
< 65	105	2 (1.9)	Not reached [-; -]	102	15 (14.7)	Not reached [-; -]	0.12 [0.03; 0.51]	0.004	0.350
≥ 65	134	5 (3.7)	Not reached [-; -]	134	17 (12.7)	Not reached [-; -]	0.22 [0.07; 0.64]	0.006	
Race									
White	166	4 (2.4)	Not reached [-; -]	147	10 (6.8)	Not reached [-; -]	0.33 [0.10; 1.06]	0.064	0.315
Non-white	73	3 (4.1)	Not reached [-; -]	89	22 (24.7)	Not reached [-; -]	0.09 [0.02; 0.40]	0.001	
Geographic Region									
North America	57	0 (0.0)	Not reached [-; -]	51	9 (17.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.097
Europe	97	3 (3.1)	Not reached [-; -]	101	10 (9.9)	Not reached [-; -]	0.30 [0.08; 1.09]	0.067	
Rest of World	85	4 (4.7)	Not reached [-; -]	84	13 (15.5)	Not reached [-; -]	0.20 [0.06; 0.71]	0.012	
Sex									
Male	197	5 (2.5)	Not reached [-; -]	181	25 (13.8)	Not reached [-; -]	0.17 [0.06; 0.44]	< 0.001	0.470
Female	42	2 (4.8)	Not reached [-; -]	55	7 (12.7)	Not reached [-; -]	0.16 [0.02; 1.32]	0.089	
ECOG at Baseline									
0	136	4 (2.9)	Not reached [-; -]	124	23 (18.5)	Not reached [-; -]	0.11 [0.03; 0.35]	< 0.001	0.321
1-2	103	3 (2.9)	Not reached [-; -]	111	9 (8.1)	Not reached [-; -]	0.34 [0.09; 1.26]	0.107	
Primary Disease Site of Origin									
Upper Tract	61	3 (4.9)	Not reached [-; -]	44	8 (18.2)	Not reached [-; -]	0.17 [0.04; 0.79]	0.024	0.640
Lower Tract	176	4 (2.3)	Not reached [-; -]	192	24 (12.5)	Not reached [-; -]	0.16 [0.06; 0.47]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	Not reached [-; -]	47	6 (12.8)	Not reached [-; -]	0.16 [0.02; 1.34]	0.091	0.839
Absent	192	6 (3.1)	Not reached [-; -]	189	26 (13.8)	Not reached [-; -]	0.17 [0.06; 0.44]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	5 (3.6)	Not reached [-; -]	138	16 (11.6)	Not reached [-; -]	0.23 [0.08; 0.68]	0.008	0.272
Low	101	2 (2.0)	Not reached [-; -]	98	16 (16.3)	Not reached [-; -]	0.11 [0.03; 0.48]	0.003	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	21 (13.4)	Not reached [-; -]	0.12 [0.04; 0.42]	< 0.001	0.842
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	10 (15.4)	Not reached [-; -]	0.19 [0.04; 0.85]	0.030	
Renal Function									
Normal	78	4 (5.1)	Not reached [-; -]	81	10 (12.3)	Not reached [-; -]	0.38 [0.12; 1.22]	0.104	0.280
Mild	115	2 (1.7)	Not reached [-; -]	118	13 (11.0)	Not reached [-; -]	0.15 [0.03; 0.66]	0.012	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	9 (24.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.993	
SOC: Investigations - PT^g: Weight decreased									
Age									
< 65	105	25 (23.8)	Not reached [-; -]	102	5 (4.9)	Not reached [-; -]	4.19 [1.58; 11.11]	0.004	0.301
≥ 65	134	48 (35.8)	98.00 [62.14; -]	134	18 (13.4)	Not reached [-; -]	2.32 [1.33; 4.04]	0.003	
Race									
White	166	46 (27.7)	Not reached [98.00; -]	147	13 (8.8)	Not reached [-; -]	2.68 [1.43; 5.02]	0.002	0.893
Non-white	73	27 (37.0)	Not reached [28.14; -]	89	10 (11.2)	Not reached [-; -]	2.92 [1.39; 6.14]	0.005	
Geographic Region									
North America	57	18 (31.6)	Not reached [-; -]	51	5 (9.8)	Not reached [-; -]	3.17 [1.17; 8.59]	0.024	0.542
Europe	97	28 (28.9)	98.00 [75.86; -]	101	12 (11.9)	Not reached [-; -]	1.85 [0.92; 3.75]	0.086	
Rest of World	85	27 (31.8)	Not reached [-; -]	84	6 (7.1)	Not reached [-; -]	4.05 [1.65; 9.92]	0.002	
Sex									
Male	197	62 (31.5)	Not reached [98.00; -]	181	19 (10.5)	Not reached [-; -]	2.55 [1.51; 4.31]	< 0.001	0.775
Female	42	11 (26.2)	Not reached [-; -]	55	4 (7.3)	Not reached [-; -]	3.29 [1.03; 10.48]	0.044	
ECOG at Baseline									
0	136	37 (27.2)	98.00 [98.00; -]	124	9 (7.3)	Not reached [-; -]	2.87 [1.35; 6.07]	0.006	0.551
1-2	103	36 (35.0)	Not reached [27.14; -]	111	14 (12.6)	Not reached [-; -]	2.68 [1.44; 4.98]	0.002	
Primary Disease Site of Origin									
Upper Tract	61	13 (21.3)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	2.33 [0.64; 8.48]	0.199	0.912
Lower Tract	176	60 (34.1)	Not reached [98.00; -]	192	20 (10.4)	Not reached [-; -]	2.93 [1.75; 4.90]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	17 (36.2)	Not reached [19.14; -]	47	8 (17.0)	Not reached [-; -]	1.93 [0.82; 4.57]	0.132	0.437
Absent	192	56 (29.2)	Not reached [98.00; -]	189	15 (7.9)	Not reached [-; -]	3.10 [1.73; 5.54]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: PD-L1 Expression									
High	138	44 (31.9)	Not reached [98.00; -]	138	15 (10.9)	Not reached [-; -]	2.60 [1.43; 4.72]	0.002	0.727
Low	101	29 (28.7)	Not reached [62.14; -]	98	8 (8.2)	Not reached [-; -]	2.91 [1.31; 6.48]	0.009	
Metastatic Disease Site									
Visceral metastases	169	47 (27.8)	Not reached [-; -]	157	18 (11.5)	Not reached [-; -]	2.07 [1.19; 3.60]	0.010	0.245
Lymph node only	60	21 (35.0)	98.00 [28.14; -]	65	5 (7.7)	Not reached [-; -]	3.80 [1.40; 10.31]	0.009	
Renal Function									
Normal	78	23 (29.5)	Not reached [-; -]	81	8 (9.9)	Not reached [-; -]	3.00 [1.33; 6.77]	0.008	0.981
Mild	115	36 (31.3)	98.00 [75.86; -]	118	12 (10.2)	Not reached [-; -]	2.52 [1.29; 4.92]	0.007	
Moderate/Severe	46	14 (30.4)	Not reached [62.14; -]	37	3 (8.1)	Not reached [-; -]	2.83 [0.79; 10.13]	0.111	
SOC: Investigations - PT ^g : White blood cell count decreased									
Age									
< 65	105	0 (0.0)	n.c.	102	7 (6.9)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	1 (0.7)	n.c.	134	7 (5.2)	n.c.	n.c.	n.c.	
Race									
White	166	0 (0.0)	Not reached [-; -]	147	4 (2.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.030	0.367
Non-white	73	1 (1.4)	Not reached [-; -]	89	10 (11.2)	Not reached [-; -]	0.12 [0.01; 0.91]	0.040	
Geographic Region									
North America	57	0 (0.0)	Not reached [-; -]	51	3 (5.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.065	0.659
Europe	97	0 (0.0)	Not reached [-; -]	101	2 (2.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.165	
Rest of World	85	1 (1.2)	Not reached [-; -]	84	9 (10.7)	Not reached [-; -]	0.10 [0.01; 0.81]	0.031	
Sex									
Male	197	1 (0.5)	Not reached [-; -]	181	11 (6.1)	Not reached [-; -]	0.08 [0.01; 0.62]	0.016	0.563
Female	42	0 (0.0)	Not reached [-; -]	55	3 (5.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.126	
ECOG at Baseline									
0	136	1 (0.7)	Not reached [-; -]	124	10 (8.1)	Not reached [-; -]	0.09 [0.01; 0.69]	0.020	0.452
1-2	103	0 (0.0)	Not reached [-; -]	111	4 (3.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.051	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	n.c.	44	5 (11.4)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	0 (0.0)	n.c.	192	9 (4.7)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	0.51 [0.05; 5.60]	0.580	0.057
Absent	192	0 (0.0)	Not reached [-; -]	189	12 (6.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	0 (0.0)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Low	101	1 (1.0)	n.c.	98	6 (6.1)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	1 (0.6)	n.c.	157	8 (5.1)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	0 (0.0)	n.c.	65	5 (7.7)	n.c.	n.c.	n.c.	
Renal Function									
Normal	78	0 (0.0)	n.c.	81	1 (1.2)	n.c.	n.c.	n.c.	n.c.
Mild	115	1 (0.9)	n.c.	118	7 (5.9)	n.c.	n.c.	n.c.	
Moderate/Severe	46	0 (0.0)	n.c.	37	6 (16.2)	n.c.	n.c.	n.c.	
SOC: Metabolism and nutrition disorders - PT^g: Hyperglycaemia									
Age									
< 65	105	21 (20.0)	Not reached [-; -]	102	5 (4.9)	Not reached [-; -]	3.37 [1.24; 9.15]	0.017	0.070
≥ 65	134	23 (17.2)	Not reached [-; -]	134	1 (0.7)	Not reached [-; -]	21.73 [2.92; 161.67]	0.003	
Race									
White	166	27 (16.3)	Not reached [-; -]	147	4 (2.7)	Not reached [-; -]	5.32 [1.84; 15.39]	0.002	0.504
Non-white	73	17 (23.3)	Not reached [-; -]	89	2 (2.2)	Not reached [-; -]	9.11 [2.07; 40.09]	0.003	
Geographic Region									
North America	57	6 (10.5)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	5.55 [0.67; 46.05]	0.113	0.456
Europe	97	19 (19.6)	Not reached [-; -]	101	4 (4.0)	Not reached [-; -]	4.52 [1.51; 13.53]	0.007	
Rest of World	85	19 (22.4)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	15.49 [2.05; 117.14]	0.008	
Sex									
Male	197	38 (19.3)	Not reached [-; -]	181	4 (2.2)	Not reached [-; -]	7.73 [2.73; 21.86]	< 0.001	0.432
Female	42	6 (14.3)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	3.65 [0.73; 18.37]	0.116	
ECOG at Baseline									
0	136	30 (22.1)	Not reached [-; -]	124	4 (3.2)	Not reached [-; -]	6.06 [2.11; 17.42]	< 0.001	0.962
1-2	103	14 (13.6)	Not reached [-; -]	111	2 (1.8)	Not reached [-; -]	6.91 [1.55; 30.72]	0.011	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]	Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Primary Disease Site of Origin									
Upper Tract	61 (14.8)	9 Not reached [-; -]	44 (0.0)	0 Not reached [-; -]	n.a. [n.a.; n.a.]	0.021	0.183		
Lower Tract	176 (19.9)	35 Not reached [-; -]	192 (3.1)	6 Not reached [-; -]	5.78 [2.41; 13.88]	< 0.001			
Stratification Factor: Liver Metastases									
Present	47 (17.0)	8 Not reached [-; -]	47 (0.0)	0 Not reached [-; -]	n.a. [n.a.; n.a.]	0.009	0.121		
Absent	192 (18.8)	36 Not reached [-; -]	189 (3.2)	6 Not reached [-; -]	5.31 [2.21; 12.73]	< 0.001			
Stratification Factor: PD-L1 Expression									
High	138 (18.1)	25 Not reached [-; -]	138 (3.6)	5 Not reached [-; -]	4.61 [1.74; 12.19]	0.002	0.195		
Low	101 (18.8)	19 Not reached [-; -]	98 (1.0)	1 Not reached [-; -]	15.58 [2.06; 117.70]	0.008			
Metastatic Disease Site									
Visceral metastases	169 (16.0)	27 Not reached [-; -]	157 (1.9)	3 Not reached [-; -]	7.29 [2.18; 24.31]	0.001	0.498		
Lymph node only	60 (21.7)	13 Not reached [-; -]	65 (4.6)	3 Not reached [-; -]	4.27 [1.19; 15.32]	0.026			
Renal Function									
Normal	78 (21.8)	17 Not reached [72.86; -]	81 (1.2)	1 Not reached [-; -]	16.04 [2.11; 121.98]	0.007	0.157		
Mild	115 (17.4)	20 Not reached [-; -]	118 (4.2)	5 Not reached [-; -]	3.79 [1.41; 10.24]	0.008			
Moderate/Severe	46 (15.2)	7 Not reached [-; -]	37 (0.0)	0 Not reached [-; -]	n.a. [n.a.; n.a.]	0.041			
SOC: Metabolism and nutrition disorders - PT^g: Hypomagnesaemia									
Age									
< 65	105 (4.8)	5 Not reached [-; -]	102 (7.8)	8 Not reached [-; -]	0.47 [0.14; 1.55]	0.213	0.485		
≥ 65	134 (3.0)	4 Not reached [-; -]	134 (9.0)	12 Not reached [-; -]	0.32 [0.10; 0.99]	0.049			
Race									
White	166 (3.0)	5 Not reached [-; -]	147 (8.8)	13 Not reached [-; -]	0.26 [0.08; 0.79]	0.018	0.374		
Non-white	73 (5.5)	4 Not reached [-; -]	89 (7.9)	7 Not reached [-; -]	0.70 [0.20; 2.38]	0.563			
Geographic Region									
North America	57 (7.0)	4 Not reached [-; -]	51 (21.6)	11 Not reached [-; -]	0.30 [0.09; 0.93]	0.037	0.656		
Europe	97 (3.1)	3 Not reached [-; -]	101 (6.9)	7 Not reached [-; -]	0.29 [0.06; 1.40]	0.124			
Rest of World	85 (2.4)	2 Not reached [-; -]	84 (2.4)	2 Not reached [-; -]	0.96 [0.14; 6.84]	0.970			
Sex									
Male	197 (4.6)	9 Not reached [-; -]	181 (8.3)	15 Not reached [-; -]	0.47 [0.20; 1.11]	0.087	0.079		
Female	42 (0.0)	0 Not reached [-; -]	55 (9.1)	5 Not reached [-; -]	n.a. [n.a.; n.a.]	0.047			

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
ECOG at Baseline									
0	136	5 (3.7)	Not reached [-; -]	124	12 (9.7)	Not reached [-; -]	0.30 [0.10; 0.92]	0.035	0.667
1-2	103	4 (3.9)	Not reached [-; -]	111	8 (7.2)	Not reached [-; -]	0.52 [0.16; 1.72]	0.283	
Primary Disease Site of Origin									
Upper Tract	61	3 (4.9)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	2.18 [0.23; 20.97]	0.499	0.099
Lower Tract	176	6 (3.4)	Not reached [-; -]	192	19 (9.9)	Not reached [-; -]	0.27 [0.10; 0.72]	0.009	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [63.57; -]	47	3 (6.4)	Not reached [-; -]	0.68 [0.11; 4.04]	0.668	0.232
Absent	192	6 (3.1)	Not reached [-; -]	189	17 (9.0)	Not reached [-; -]	0.33 [0.13; 0.84]	0.019	
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	Not reached [-; -]	138	14 (10.1)	Not reached [-; -]	0.27 [0.09; 0.82]	0.021	0.198
Low	101	5 (5.0)	Not reached [-; -]	98	6 (6.1)	Not reached [-; -]	0.63 [0.18; 2.24]	0.477	
Metastatic Disease Site									
Visceral metastases	169	7 (4.1)	Not reached [-; -]	157	11 (7.0)	Not reached [-; -]	0.49 [0.18; 1.34]	0.165	0.183
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	7 (10.8)	Not reached [-; -]	0.14 [0.02; 1.17]	0.070	
Renal Function									
Normal	78	4 (5.1)	Not reached [-; -]	81	10 (12.3)	Not reached [-; -]	0.40 [0.13; 1.29]	0.126	0.795
Mild	115	4 (3.5)	Not reached [-; -]	118	7 (5.9)	Not reached [-; -]	0.43 [0.11; 1.66]	0.222	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	0.25 [0.03; 2.38]	0.226	
SOC: Musculoskeletal and connective tissue disorders - PT^g: Arthralgia									
Age									
< 65	105	16 (15.2)	Not reached [-; -]	102	4 (3.9)	Not reached [-; -]	2.71 [0.86; 8.51]	0.087	0.702
≥ 65	134	20 (14.9)	Not reached [-; -]	134	7 (5.2)	Not reached [-; -]	2.21 [0.91; 5.40]	0.081	
Race									
White	166	31 (18.7)	Not reached [-; -]	147	9 (6.1)	Not reached [-; -]	2.24 [1.03; 4.84]	0.041	0.967
Non-white	73	5 (6.8)	Not reached [-; -]	89	2 (2.2)	Not reached [-; -]	2.46 [0.45; 13.46]	0.298	
Geographic Region									
North America	57	18 (31.6)	Not reached [43.71; -]	51	4 (7.8)	Not reached [-; -]	3.31 [1.09; 10.05]	0.035	0.685
Europe	97	14 (14.4)	Not reached [87.86; -]	101	6 (5.9)	Not reached [-; -]	1.64 [0.59; 4.55]	0.342	
Rest of World	85	4 (4.7)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	3.03 [0.32; 28.80]	0.334	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	197	31 (15.7)	Not reached [-; -]	181	9 (5.0)	Not reached [-; -]	2.31 [1.07; 5.00]	0.034	0.984
Female	42	5 (11.9)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	2.69 [0.50; 14.62]	0.251	
ECOG at Baseline									
0	136	20 (14.7)	Not reached [-; -]	124	4 (3.2)	Not reached [-; -]	2.63 [0.84; 8.21]	0.096	0.390
1-2	103	16 (15.5)	Not reached [-; -]	111	7 (6.3)	Not reached [-; -]	2.37 [0.97; 5.81]	0.059	
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	Not reached [87.86; -]	44	1 (2.3)	Not reached [-; -]	1.45 [0.13; 16.03]	0.760	0.810
Lower Tract	176	29 (16.5)	Not reached [-; -]	192	10 (5.2)	Not reached [-; -]	2.61 [1.25; 5.47]	0.011	
Stratification Factor: Liver Metastases									
Present	47	8 (17.0)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	6.37 [0.77; 52.88]	0.086	0.223
Absent	192	28 (14.6)	Not reached [-; -]	189	10 (5.3)	Not reached [-; -]	2.00 [0.94; 4.26]	0.072	
Stratification Factor: PD-L1 Expression									
High	138	20 (14.5)	Not reached [-; -]	138	5 (3.6)	Not reached [-; -]	2.94 [1.06; 8.12]	0.038	0.525
Low	101	16 (15.8)	Not reached [87.86; -]	98	6 (6.1)	Not reached [-; -]	1.93 [0.73; 5.14]	0.187	
Metastatic Disease Site									
Visceral metastases	169	26 (15.4)	Not reached [-; -]	157	9 (5.7)	Not reached [-; -]	2.01 [0.91; 4.44]	0.085	0.614
Lymph node only	60	8 (13.3)	Not reached [-; -]	65	2 (3.1)	Not reached [-; -]	3.35 [0.69; 16.38]	0.135	
Renal Function									
Normal	78	14 (17.9)	Not reached [87.86; -]	81	5 (6.2)	Not reached [-; -]	2.11 [0.72; 6.18]	0.173	0.831
Mild	115	16 (13.9)	Not reached [-; -]	118	4 (3.4)	Not reached [-; -]	3.22 [1.04; 9.95]	0.042	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	1.56 [0.29; 8.54]	0.606	
SOC: Nervous system disorders - PT^g: Paraesthesia									
Age									
< 65	105	10 (9.5)	Not reached [-; -]	102	4 (3.9)	Not reached [-; -]	1.77 [0.53; 5.90]	0.355	0.223
≥ 65	134	14 (10.4)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	4.57 [0.99; 21.08]	0.051	
Sex									
Male	197	21 (10.7)	Not reached [-; -]	181	4 (2.2)	Not reached [-; -]	3.49 [1.17; 10.46]	0.025	0.395
Female	42	3 (7.1)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	0.78 [0.09; 6.99]	0.821	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	136	16 (11.8)	Not reached [-; -]	124	3 (2.4)	Not reached [-; -]	3.33 [0.93; 11.94]	0.064	0.570
1-2	103	8 (7.8)	Not reached [-; -]	111	3 (2.7)	Not reached [-; -]	1.97 [0.49; 7.83]	0.337	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	4.09 [0.49; 34.11]	0.193	0.541
Lower Tract	176	15 (8.5)	Not reached [-; -]	192	5 (2.6)	Not reached [-; -]	2.12 [0.73; 6.18]	0.167	
Stratification Factor: Liver Metastases									
Present	47	6 (12.8)	Not reached [49.57; -]	47	2 (4.3)	Not reached [-; -]	1.16 [0.18; 7.64]	0.877	0.814
Absent	192	18 (9.4)	Not reached [-; -]	189	4 (2.1)	Not reached [-; -]	3.45 [1.14; 10.42]	0.028	
Stratification Factor: PD-L1 Expression									
High	138	11 (8.0)	Not reached [-; -]	138	5 (3.6)	Not reached [-; -]	1.45 [0.47; 4.43]	0.519	0.073
Low	101	13 (12.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	9.00 [1.14; 70.90]	0.037	
Metastatic Disease Site									
Visceral metastases	169	18 (10.7)	Not reached [-; -]	157	3 (1.9)	Not reached [-; -]	3.83 [1.09; 13.46]	0.036	0.944
Lymph node only	60	6 (10.0)	Not reached [-; -]	65	1 (1.5)	Not reached [-; -]	4.30 [0.48; 38.34]	0.192	
Renal Function									
Normal	78	6 (7.7)	Not reached [-; -]	81	2 (2.5)	Not reached [-; -]	2.11 [0.39; 11.42]	0.386	0.783
Mild	115	15 (13.0)	Not reached [-; -]	118	3 (2.5)	Not reached [-; -]	3.86 [1.09; 13.73]	0.037	
Moderate/Severe	46	3 (6.5)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	0.79 [0.06; 10.74]	0.863	
SOC: Nervous system disorders - PT^g: Peripheral sensory neuropathy									
Age									
< 65	105	56 (53.3)	28.57 [23.00; 57.43]	102	17 (16.7)	Not reached [-; -]	2.25 [1.27; 3.99]	0.005	0.436
≥ 65	134	70 (52.2)	26.14 [19.14; 36.86]	134	17 (12.7)	Not reached [-; -]	3.42 [1.98; 5.91]	< 0.001	
Race									
White	166	91 (54.8)	27.00 [21.00; 34.00]	147	18 (12.2)	Not reached [-; -]	3.42 [2.03; 5.77]	< 0.001	0.144
Non-white	73	35 (47.9)	28.43 [19.14; -]	89	16 (18.0)	Not reached [22.00; -]	2.13 [1.14; 3.97]	0.017	
Geographic Region									
North America	57	37 (64.9)	23.00 [14.43; 24.71]	51	13 (25.5)	Not reached [-; -]	1.70 [0.87; 3.33]	0.119	0.265

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Europe	50 (51.5)	27.71 [18.14; 38.14]	97	10 (9.9)	Not reached [-; -]	4.59 [2.28; 9.23]	< 0.001		
Rest of World	39 (45.9)	57.43 [24.43; -]	85	11 (13.1)	Not reached [-; -]	2.49 [1.24; 5.00]	0.011		
Sex									
Male	105 (53.3)	26.14 [21.29; 30.14]	197	27 (14.9)	Not reached [-; -]	2.76 [1.77; 4.28]	< 0.001	0.971	
Female	21 (50.0)	35.14 [16.29; 86.43]	42	7 (12.7)	Not reached [-; -]	2.95 [1.20; 7.23]	0.018		
ECOG at Baseline									
0	72 (52.9)	27.71 [20.86; 52.86]	136	21 (16.9)	Not reached [-; -]	2.52 [1.52; 4.19]	< 0.001	0.393	
1-2	54 (52.4)	26.14 [20.29; 36.14]	103	13 (11.7)	Not reached [-; -]	3.29 [1.76; 6.15]	< 0.001		
Primary Disease Site of Origin									
Upper Tract	31 (50.8)	24.71 [16.57; 87.86]	61	8 (18.2)	Not reached [22.00; -]	2.46 [1.10; 5.50]	0.028	0.474	
Lower Tract	94 (53.4)	27.71 [21.29; 34.00]	176	26 (13.5)	Not reached [-; -]	2.90 [1.84; 4.56]	< 0.001		
Stratification Factor: Liver Metastases									
Present	18 (38.3)	36.43 [19.14; -]	47	6 (12.8)	Not reached [-; -]	2.96 [1.15; 7.61]	0.025	0.961	
Absent	108 (56.3)	27.71 [21.29; 34.00]	192	28 (14.8)	Not reached [-; -]	2.79 [1.81; 4.30]	< 0.001		
Stratification Factor: PD-L1 Expression									
High	79 (57.2)	24.43 [18.29; 31.29]	138	20 (14.5)	Not reached [-; -]	3.21 [1.93; 5.33]	< 0.001	0.556	
Low	47 (46.5)	34.00 [23.57; 79.29]	101	14 (14.3)	Not reached [-; -]	2.31 [1.24; 4.33]	0.009		
Metastatic Disease Site									
Visceral metastases	86 (50.9)	27.14 [22.29; 36.86]	169	26 (16.6)	Not reached [-; -]	2.30 [1.46; 3.64]	< 0.001	0.392	
Lymph node only	34 (56.7)	31.29 [18.14; 62.86]	60	8 (12.3)	Not reached [-; -]	3.32 [1.48; 7.46]	0.004		
Renal Function									
Normal	45 (57.7)	19.43 [15.86; 32.00]	78	11 (13.6)	Not reached [-; -]	4.06 [2.07; 7.98]	< 0.001	0.446	
Mild	60 (52.2)	30.14 [24.71; 62.86]	115	19 (16.1)	Not reached [-; -]	1.97 [1.13; 3.43]	0.017		

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Moderate/Severe	46	21 (45.7)	30.14 [15.00; -]	37	4 (10.8)	Not reached [-; -]	3.88 [1.32; 11.46]	0.014	
SOC: Nervous system disorders - PT^g: Taste disorder									
Age									
< 65	105	2 (1.9)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.164	0.378
≥ 65	134	8 (6.0)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	4.08 [0.87; 19.22]	0.075	
Race									
White	166	6 (3.6)	n.c.	147	2 (1.4)	n.c.	n.c.	n.c.	n.c.
Non-white	73	4 (5.5)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	3 (5.3)	n.c.	51	1 (2.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	1 (1.0)	n.c.	101	1 (1.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	6 (7.1)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	9 (4.6)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	8.37 [1.06; 66.04]	0.044	0.293
Female	42	1 (2.4)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	1.36 [0.08; 21.71]	0.829	
ECOG at Baseline									
0	136	6 (4.4)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	4 (3.9)	n.c.	111	2 (1.8)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	7 (4.0)	n.c.	192	2 (1.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	192	7 (3.6)	n.c.	189	2 (1.1)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	138	7 (5.1)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	3 (3.0)	n.c.	98	2 (2.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	169	7 (4.1)	n.c.	157	1 (0.6)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	2 (3.3)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	1 (1.3)	n.c.	81	1 (1.2)	n.c.	n.c.	n.c.	n.c.
Mild	115	7 (6.1)	n.c.	118	1 (0.8)	n.c.	n.c.	n.c.	
Moderate/Severe	46	2 (4.3)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Renal and urinary disorders - PT^g: Acute kidney injury									
Age									
< 65	105	7 (6.7)	Not reached [-; -]	102	9 (8.8)	Not reached [-; -]	0.53 [0.18; 1.58]	0.255	0.122
≥ 65	134	4 (3.0)	Not reached [-; -]	134	16 (11.9)	Not reached [-; -]	0.13 [0.03; 0.50]	0.003	
Race									
White	166	7 (4.2)	Not reached [-; -]	147	20 (13.6)	Not reached [-; -]	0.21 [0.08; 0.55]	0.001	0.136
Non-white	73	4 (5.5)	Not reached [-; -]	89	5 (5.6)	Not reached [-; -]	0.49 [0.09; 2.51]	0.389	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	10 (19.6)	Not reached [-; -]	0.16 [0.04; 0.74]	0.019	0.393
Europe	97	3 (3.1)	Not reached [-; -]	101	9 (8.9)	Not reached [-; -]	0.23 [0.05; 1.03]	0.055	
Rest of World	85	5 (5.9)	Not reached [-; -]	84	6 (7.1)	Not reached [-; -]	0.48 [0.12; 1.94]	0.306	
Sex									
Male	197	10 (5.1)	Not reached [-; -]	181	19 (10.5)	Not reached [-; -]	0.28 [0.11; 0.69]	0.006	0.440
Female	42	1 (2.4)	Not reached [-; -]	55	6 (10.9)	Not reached [-; -]	0.21 [0.03; 1.75]	0.150	
ECOG at Baseline									
0	136	6 (4.4)	Not reached [-; -]	124	9 (7.3)	Not reached [-; -]	0.31 [0.09; 1.11]	0.072	0.404
1-2	103	5 (4.9)	Not reached [-; -]	111	16 (14.4)	Not reached [-; -]	0.25 [0.08; 0.75]	0.013	
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	Not reached [-; -]	44	4 (9.1)	Not reached [-; -]	0.36 [0.07; 1.95]	0.234	0.165
Lower Tract	176	6 (3.4)	Not reached [-; -]	192	21 (10.9)	Not reached [-; -]	0.25 [0.10; 0.66]	0.005	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	1.05 [0.15; 7.47]	0.960	0.094
Absent	192	8 (4.2)	Not reached [-; -]	189	23 (12.2)	Not reached [-; -]	0.20 [0.08; 0.53]	0.001	
Metastatic Disease Site									
Visceral metastases	169	9 (5.3)	Not reached [-; -]	157	17 (10.8)	Not reached [-; -]	0.27 [0.10; 0.72]	0.009	0.326
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	6 (9.2)	Not reached [-; -]	0.17 [0.02; 1.42]	0.102	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Epistaxis									
Age									
< 65	105	1 (1.0)	Not reached [-; -]	102	10 (9.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.992	0.080
≥ 65	134	5 (3.7)	Not reached [-; -]	134	9 (6.7)	Not reached [-; -]	0.50 [0.17; 1.49]	0.212	
Race									
White	166	5 (3.0)	Not reached [-; -]	147	12 (8.2)	Not reached [-; -]	0.26 [0.08; 0.81]	0.020	0.534
Non-white	73	1 (1.4)	Not reached [-; -]	89	7 (7.9)	Not reached [-; -]	0.17 [0.02; 1.40]	0.100	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	8 (15.7)	Not reached [-; -]	0.31 [0.08; 1.19]	0.088	0.745
Europe	97	3 (3.1)	Not reached [-; -]	101	10 (9.9)	Not reached [-; -]	0.18 [0.04; 0.84]	0.029	
Rest of World	85	0 (0.0)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.314	
Sex									
Male	197	3 (1.5)	Not reached [-; -]	181	14 (7.7)	Not reached [-; -]	0.17 [0.05; 0.61]	0.006	0.133
Female	42	3 (7.1)	Not reached [-; -]	55	5 (9.1)	Not reached [-; -]	0.53 [0.10; 2.73]	0.448	
ECOG at Baseline									
0	136	2 (1.5)	Not reached [-; -]	124	10 (8.1)	Not reached [-; -]	0.09 [0.01; 0.68]	0.020	0.310
1-2	103	4 (3.9)	Not reached [-; -]	111	9 (8.1)	Not reached [-; -]	0.43 [0.13; 1.39]	0.158	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	2 (4.5)	Not reached [-; -]	0.35 [0.03; 3.90]	0.397	0.905
Lower Tract	176	5 (2.8)	Not reached [-; -]	192	17 (8.9)	Not reached [-; -]	0.23 [0.08; 0.69]	0.009	
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.636
Absent	192	5 (2.6)	Not reached [-; -]	189	17 (9.0)	Not reached [-; -]	0.26 [0.10; 0.70]	0.008	
Stratification Factor: PD-L1 Expression									
High	138	5 (3.6)	Not reached [-; -]	138	13 (9.4)	Not reached [-; -]	0.27 [0.09; 0.84]	0.024	0.472
Low	101	1 (1.0)	Not reached [-; -]	98	6 (6.1)	Not reached [-; -]	0.16 [0.02; 1.30]	0.087	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	12 (7.6)	Not reached [-; -]	0.22 [0.06; 0.80]	0.021	0.958
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	7 (10.8)	Not reached [-; -]	0.25 [0.05; 1.23]	0.089	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Hiccups									
Age									
< 65	105	2 (1.9)	Not reached [-; -]	102	11 (10.8)	Not reached [-; -]	0.16 [0.04; 0.74]	0.019	0.287
≥ 65	134	5 (3.7)	Not reached [-; -]	134	11 (8.2)	Not reached [-; -]	0.30 [0.09; 0.98]	0.045	
Race									
White	166	5 (3.0)	Not reached [-; -]	147	8 (5.4)	Not reached [-; -]	0.37 [0.11; 1.26]	0.111	0.176
Non-white	73	2 (2.7)	Not reached [-; -]	89	14 (15.7)	Not reached [-; -]	0.16 [0.04; 0.70]	0.015	
Geographic Region									
North America	57	2 (3.5)	Not reached [-; -]	51	10 (19.6)	Not reached [-; -]	0.16 [0.04; 0.73]	0.018	0.106
Europe	97	3 (3.1)	Not reached [-; -]	101	2 (2.0)	Not reached [-; -]	0.69 [0.09; 5.54]	0.728	
Rest of World	85	2 (2.4)	Not reached [-; -]	84	10 (11.9)	Not reached [-; -]	0.18 [0.04; 0.84]	0.029	
Sex									
Male	197	7 (3.6)	Not reached [-; -]	181	22 (12.2)	Not reached [-; -]	0.21 [0.09; 0.53]	< 0.001	0.998
Female	42	0 (0.0)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
ECOG at Baseline									
0	136	4 (2.9)	Not reached [-; -]	124	12 (9.7)	Not reached [-; -]	0.22 [0.06; 0.77]	0.018	0.927
1-2	103	3 (2.9)	Not reached [-; -]	111	10 (9.0)	Not reached [-; -]	0.27 [0.07; 1.00]	0.049	
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	0.89 [0.07; 11.42]	0.932	0.162
Lower Tract	176	5 (2.8)	Not reached [-; -]	192	21 (10.9)	Not reached [-; -]	0.19 [0.07; 0.57]	0.003	
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	Not reached [-; -]	47	4 (8.5)	Not reached [-; -]	0.24 [0.03; 2.15]	0.203	0.860
Absent	192	6 (3.1)	Not reached [-; -]	189	18 (9.5)	Not reached [-; -]	0.23 [0.09; 0.64]	0.005	
Stratification Factor: PD-L1 Expression									
High	138	6 (4.3)	Not reached [-; -]	138	13 (9.4)	Not reached [-; -]	0.33 [0.11; 0.93]	0.036	0.170
Low	101	1 (1.0)	Not reached [-; -]	98	9 (9.2)	Not reached [-; -]	0.10 [0.01; 0.81]	0.030	
Metastatic Disease Site									
Visceral metastases	169	5 (3.0)	Not reached [-; -]	157	13 (8.3)	Not reached [-; -]	0.30 [0.11; 0.87]	0.027	0.344
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	8 (12.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.993	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	0 (0.0)	Not reached [-; -]	81	7 (8.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.008	0.110
Mild	115	6 (5.2)	Not reached [-; -]	118	13 (11.0)	Not reached [-; -]	0.32 [0.11; 0.94]	0.037	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	0.39 [0.04; 4.31]	0.443	
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Pneumonitis									
Age									
< 65	105	7 (6.7)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.055	0.309
≥ 65	134	10 (7.5)	Not reached [-; -]	134	1 (0.7)	Not reached [-; -]	6.64 [0.83; 53.42]	0.075	
Race									
White	166	9 (5.4)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	8 (11.0)	n.c.	89	1 (1.1)	n.c.	n.c.	n.c.	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.203	0.090
Europe	97	1 (1.0)	Not reached [-; -]	101	1 (1.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.997	
Rest of World	85	13 (15.3)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	
Sex									
Male	197	15 (7.6)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	7.84 [1.00; 61.50]	0.050 ⁱ	0.568
Female	42	2 (4.8)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.122	
ECOG at Baseline									
0	136	9 (6.6)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	8 (7.8)	n.c.	111	1 (0.9)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	3 (4.9)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.146	0.595
Lower Tract	176	14 (8.0)	Not reached [-; -]	192	1 (0.5)	Not reached [-; -]	8.24 [1.04; 65.37]	0.046	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	1.68 [0.15; 19.04]	0.677	0.056
Absent	192	15 (7.8)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	9 (6.5)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	5.39 [0.65; 44.86]	0.119	0.265
Low	101	8 (7.9)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.027	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	169	14 (8.3)	Not reached [-; -]	157	1 (0.6)	Not reached [-; -]	9.40 [1.21; 72.89]	0.032	0.595
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	1 (1.2)	Not reached [-; -]	1.11 [0.07; 17.71]	0.942	0.214
Mild	115	11 (9.6)	Not reached [-; -]	118	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Moderate/Severe	46	3 (6.5)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.247	
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Pulmonary embolism									
Age									
< 65	105	3 (2.9)	Not reached [91.43; -]	102	10 (9.8)	Not reached [-; -]	0.18 [0.04; 0.84]	0.028	0.175
≥ 65	134	5 (3.7)	Not reached [-; -]	134	5 (3.7)	Not reached [-; -]	0.78 [0.21; 2.89]	0.710	
Race									
White	166	6 (3.6)	Not reached [-; -]	147	12 (8.2)	Not reached [-; -]	0.28 [0.09; 0.86]	0.026	0.488
Non-white	73	2 (2.7)	Not reached [-; -]	89	3 (3.4)	Not reached [-; -]	0.79 [0.13; 4.73]	0.796	
Geographic Region									
North America	57	4 (7.0)	Not reached [91.43; -]	51	6 (11.8)	Not reached [-; -]	0.30 [0.06; 1.49]	0.141	0.611
Europe	97	2 (2.1)	Not reached [-; -]	101	7 (6.9)	Not reached [-; -]	0.28 [0.06; 1.37]	0.117	
Rest of World	85	2 (2.4)	Not reached [-; -]	84	2 (2.4)	Not reached [-; -]	0.91 [0.13; 6.48]	0.927	
Sex									
Male	197	7 (3.6)	Not reached [-; -]	181	14 (7.7)	Not reached [-; -]	0.31 [0.11; 0.86]	0.024	0.443
Female	42	1 (2.4)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	1.21 [0.08; 19.38]	0.893	
ECOG at Baseline									
0	136	4 (2.9)	Not reached [-; -]	124	7 (5.6)	Not reached [-; -]	0.50 [0.15; 1.71]	0.268	0.959
1-2	103	4 (3.9)	Not reached [-; -]	111	8 (7.2)	Not reached [-; -]	0.27 [0.06; 1.20]	0.086	
Primary Disease Site of Origin									
Upper Tract	61	4 (6.6)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	0.93 [0.21; 4.14]	0.920	0.298
Lower Tract	176	4 (2.3)	Not reached [-; -]	192	12 (6.3)	Not reached [-; -]	0.18 [0.04; 0.78]	0.021	
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	Not reached [91.43; -]	47	3 (6.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.732
Absent	192	7 (3.6)	Not reached [-; -]	189	12 (6.3)	Not reached [-; -]	0.47 [0.18; 1.23]	0.124	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	Not reached [-; -]	138	8 (5.8)	Not reached [-; -]	0.24 [0.05; 1.11]	0.068	0.878
Low	101	4 (4.0)	Not reached [-; -]	98	7 (7.1)	Not reached [-; -]	0.53 [0.15; 1.80]	0.305	
Metastatic Disease Site									
Visceral metastases	169	6 (3.6)	Not reached [-; -]	157	9 (5.7)	Not reached [-; -]	0.40 [0.12; 1.28]	0.121	0.698
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	5 (7.7)	Not reached [-; -]	0.42 [0.08; 2.14]	0.294	
Renal Function									
Normal	78	3 (3.8)	Not reached [91.43; -]	81	9 (11.1)	Not reached [-; -]	0.23 [0.05; 1.06]	0.059	0.672
Mild	115	4 (3.5)	Not reached [-; -]	118	5 (4.2)	Not reached [-; -]	0.57 [0.14; 2.39]	0.443	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	0.77 [0.05; 12.38]	0.856	
SOC: Skin and subcutaneous tissue disorders - PT^g: Alopecia									
Age									
< 65	105	38 (36.2)	Not reached [42.86; -]	102	11 (10.8)	Not reached [-; -]	3.36 [1.70; 6.63]	< 0.001	0.382
≥ 65	134	53 (39.6)	Not reached [27.00; -]	134	11 (8.2)	Not reached [-; -]	5.47 [2.85; 10.50]	< 0.001	
Race									
White	166	60 (36.1)	Not reached [-; -]	147	12 (8.2)	Not reached [-; -]	4.74 [2.55; 8.84]	< 0.001	0.915
Non-white	73	31 (42.5)	Not reached [8.86; -]	89	10 (11.2)	Not reached [-; -]	4.08 [1.98; 8.41]	< 0.001	
Geographic Region									
North America	57	28 (49.1)	24.00 [10.29; -]	51	4 (7.8)	Not reached [-; -]	7.60 [2.65; 21.75]	< 0.001	0.319
Europe	97	28 (28.9)	Not reached [-; -]	101	6 (5.9)	Not reached [-; -]	4.81 [1.97; 11.74]	< 0.001	
Rest of World	85	35 (41.2)	Not reached [18.57; -]	84	12 (14.3)	Not reached [-; -]	3.10 [1.60; 6.00]	< 0.001	
Sex									
Male	197	67 (34.0)	Not reached [-; -]	181	12 (6.6)	Not reached [-; -]	5.42 [2.92; 10.06]	< 0.001	0.429
Female	42	24 (57.1)	9.14 [5.71; -]	55	10 (18.2)	Not reached [-; -]	3.77 [1.79; 7.94]	< 0.001	
ECOG at Baseline									
0	136	51 (37.5)	Not reached [-; -]	124	13 (10.5)	Not reached [-; -]	3.81 [2.06; 7.04]	< 0.001	0.519
1-2	103	40 (38.8)	Not reached [26.43; -]	111	9 (8.1)	Not reached [-; -]	5.14 [2.48; 10.64]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	31 (50.8)	26.43 [5.71; -]	44	8 (18.2)	Not reached [-; -]	3.16 [1.44; 6.93]	0.004	0.425
Lower Tract	176	60 (34.1)	Not reached [-; -]	192	14 (7.3)	Not reached [-; -]	4.94 [2.75; 8.88]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	47	14 (29.8)	Not reached [-; -]	47	5 (10.6)	Not reached [-; -]	3.15 [1.13; 8.76]	0.028	0.432
Absent	192	77 (40.1)	Not reached [42.86; -]	189	17 (9.0)	Not reached [-; -]	4.77 [2.81; 8.10]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	57 (41.3)	Not reached [24.00; -]	138	12 (8.7)	Not reached [-; -]	5.12 [2.74; 9.58]	< 0.001	0.417
Low	101	34 (33.7)	Not reached [-; -]	98	10 (10.2)	Not reached [-; -]	3.55 [1.74; 7.22]	< 0.001	
Renal Function									
Normal	78	26 (33.3)	Not reached [-; -]	81	4 (4.9)	Not reached [-; -]	7.44 [2.59; 21.38]	< 0.001	0.228
Mild	115	47 (40.9)	Not reached [27.00; -]	118	16 (13.6)	Not reached [-; -]	3.07 [1.73; 5.46]	< 0.001	
Moderate/Severe	46	18 (39.1)	Not reached [8.14; -]	37	2 (5.4)	Not reached [-; -]	8.32 [1.93; 35.90]	0.004	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Blister									
Age									
< 65	105	6 (5.7)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	4 (3.0)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	
Race									
White	166	5 (3.0)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	5 (6.8)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	57	2 (3.5)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	4 (4.1)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	85	4 (4.7)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	197	10 (5.1)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.053	0.997
Female	42	0 (0.0)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
ECOG at Baseline									
0	136	7 (5.1)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	3 (2.9)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	4 (6.6)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	6 (3.4)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	192	7 (3.6)	n.c.	189	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	138	6 (4.3)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	4 (4.0)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	169	6 (3.6)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	3 (5.0)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	78	4 (5.1)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	2 (1.7)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	46	4 (8.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Skin and subcutaneous tissue disorders - PT^g: Dermatitis									
Age									
< 65	105	5 (4.8)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	8 (6.0)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	166	7 (4.2)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	6 (8.2)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	2 (3.5)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	5 (5.2)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	6 (7.1)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	9 (4.6)	n.c.	181	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	42	4 (9.5)	n.c.	55	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	136	9 (6.6)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	4 (3.9)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	7 (4.0)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.996
Absent	192	13 (6.8)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	10 (7.2)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
Low	101	3 (3.0)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.332	
Metastatic Disease Site									
Visceral metastases	169	8 (4.7)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	5 (8.3)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	78	5 (6.4)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	5 (4.3)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	46	3 (6.5)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Skin and subcutaneous tissue disorders - PT^g: Dermatitis bullous									
Age									
< 65	105	6 (5.7)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	8 (6.0)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	166	7 (4.2)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	7 (9.6)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	4 (7.0)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	5 (5.2)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	5 (5.9)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	13 (6.6)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
Female	42	1 (2.4)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.269	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	136	8 (5.9)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	6 (5.8)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	9 (5.1)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.142	0.997
Absent	192	11 (5.7)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	
Stratification Factor: PD-L1 Expression									
High	138	5 (3.6)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	9 (8.9)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	169	9 (5.3)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	5 (8.3)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	78	5 (6.4)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	5 (4.3)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	46	4 (8.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Skin and subcutaneous tissue disorders - PT^g: Dry skin									
Age									
< 65	105	14 (13.3)	Not reached [-; -]	102	1 (1.0)	Not reached [-; -]	12.09 [1.58; 92.73]	0.017	0.697
≥ 65	134	25 (18.7)	Not reached [-; -]	134	3 (2.2)	Not reached [-; -]	7.15 [2.13; 24.01]	0.001	
Race									
White	166	32 (19.3)	Not reached [-; -]	147	3 (2.0)	Not reached [-; -]	8.69 [2.65; 28.57]	< 0.001	0.896
Non-white	73	7 (9.6)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	5.45 [0.63; 47.43]	0.125	
Geographic Region									
North America	57	15 (26.3)	Not reached [-; -]	51	2 (3.9)	Not reached [-; -]	6.09 [1.37; 27.01]	0.017	0.788
Europe	97	15 (15.5)	Not reached [-; -]	101	1 (1.0)	Not reached [-; -]	13.72 [1.79; 104.98]	0.012	
Rest of World	85	9 (10.6)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	7.33 [0.91; 59.09]	0.061	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	197	35 (17.8)	Not reached [-; -]	181	4 (2.2)	Not reached [-; -]	7.07 [2.49; 20.07]	< 0.001	0.302
Female	42	4 (9.5)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.046	
ECOG at Baseline									
0	136	26 (19.1)	Not reached [-; -]	124	2 (1.6)	Not reached [-; -]	10.72 [2.52; 45.59]	0.001	0.584
1-2	103	13 (12.6)	Not reached [-; -]	111	2 (1.8)	Not reached [-; -]	5.87 [1.30; 26.41]	0.021	
Primary Disease Site of Origin									
Upper Tract	61	9 (14.8)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	5.38 [0.66; 43.77]	0.115	0.694
Lower Tract	176	30 (17.0)	Not reached [-; -]	192	3 (1.6)	Not reached [-; -]	9.64 [2.92; 31.83]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	5 (10.6)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.081	0.288
Absent	192	34 (17.7)	Not reached [-; -]	189	4 (2.1)	Not reached [-; -]	7.53 [2.65; 21.37]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	28 (16.6)	Not reached [-; -]	157	2 (1.3)	Not reached [-; -]	11.55 [2.73; 48.87]	< 0.001	0.285
Lymph node only	60	8 (13.3)	Not reached [-; -]	65	2 (3.1)	Not reached [-; -]	3.83 [0.79; 18.43]	0.094	
Renal Function									
Normal	78	13 (16.7)	Not reached [-; -]	81	1 (1.2)	Not reached [-; -]	12.34 [1.60; 95.23]	0.016	0.532
Mild	115	20 (17.4)	Not reached [-; -]	118	3 (2.5)	Not reached [-; -]	7.27 [2.16; 24.47]	0.001	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.285	
SOC: Skin and subcutaneous tissue disorders - PT^g: Eczema									
Age									
< 65	105	6 (5.7)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	6 (4.5)	n.c.	134	2 (1.5)	n.c.	n.c.	n.c.	
Race									
White	166	3 (1.8)	Not reached [-; -]	147	1 (0.7)	Not reached [-; -]	1.68 [0.15; 18.47]	0.670	0.342
Non-white	73	9 (12.3)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	11.71 [1.48; 92.42]	0.020	
Geographic Region									
North America	57	1 (1.8)	n.c.	51	1 (2.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	3 (3.1)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	85	8 (9.4)	n.c.	84	1 (1.2)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	197	8 (4.1)	Not reached [-; -]	181	2 (1.1)	Not reached [-; -]	3.15 [0.65; 15.18]	0.152	0.158
Female	42	4 (9.5)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	
ECOG at Baseline									
0	136	8 (5.9)	n.c.	124	1 (0.8)	n.c.	n.c.	n.c.	n.c.
1-2	103	4 (3.9)	n.c.	111	1 (0.9)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	1.47 [0.13; 16.17]	0.755	0.226
Lower Tract	176	10 (5.7)	Not reached [-; -]	192	1 (0.5)	Not reached [-; -]	9.85 [1.25; 77.72]	0.030	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	3.05 [0.32; 29.32]	0.334	0.512
Absent	192	9 (4.7)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	7.86 [0.98; 62.87]	0.052	
Stratification Factor: PD-L1 Expression									
High	138	7 (5.1)	n.c.	138	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Low	101	5 (5.0)	n.c.	98	1 (1.0)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	8 (4.7)	Not reached [-; -]	157	2 (1.3)	Not reached [-; -]	3.21 [0.67; 15.45]	0.146	0.194
Lymph node only	60	4 (6.7)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.036	
Renal Function									
Normal	78	3 (3.8)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	4 (3.5)	n.c.	118	2 (1.7)	n.c.	n.c.	n.c.	
Moderate/Severe	46	5 (10.9)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Skin and subcutaneous tissue disorders - PT^g: Pruritus									
Age									
< 65	105	48 (45.7)	Not reached [12.14; -]	102	7 (6.9)	Not reached [-; -]	8.37 [3.78; 18.56]	< 0.001	0.603
≥ 65	134	57 (42.5)	Not reached [29.71; -]	134	6 (4.5)	Not reached [-; -]	10.17 [4.36; 23.74]	< 0.001	
Race									
White	166	69 (41.6)	Not reached [31.43; -]	147	6 (4.1)	Not reached [-; -]	10.82 [4.68; 25.06]	< 0.001	0.556
Non-white	73	36 (49.3)	12.29 [4.14; -]	89	7 (7.9)	Not reached [-; -]	8.55 [3.80; 19.24]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	57	23 (40.4)	Not reached [9.00; -]	51	3 (5.9)	Not reached [-; -]	8.15 [2.43; 27.27]	< 0.001	0.421
Europe	97	41 (42.3)	Not reached [13.43; -]	101	3 (3.0)	Not reached [-; -]	16.65 [5.14; 53.99]	< 0.001	
Rest of World	85	41 (48.2)	45.14 [12.29; -]	84	7 (8.3)	Not reached [-; -]	6.42 [2.85; 14.43]	< 0.001	
Sex									
Male	197	90 (45.7)	Not reached [17.86; -]	181	10 (5.5)	Not reached [-; -]	9.68 [5.02; 18.67]	< 0.001	0.734
Female	42	15 (35.7)	Not reached [27.14; -]	55	3 (5.5)	Not reached [-; -]	6.80 [1.94; 23.86]	0.003	
ECOG at Baseline									
0	136	58 (42.6)	Not reached [26.00; -]	124	4 (3.2)	Not reached [-; -]	15.87 [5.75; 43.82]	< 0.001	0.131
1-2	103	47 (45.6)	38.14 [17.86; -]	111	9 (8.1)	Not reached [-; -]	6.05 [2.94; 12.45]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	17 (36.2)	Not reached [31.43; -]	47	1 (2.1)	Not reached [-; -]	16.67 [2.19; 126.83]	0.007	0.389
Absent	192	88 (45.8)	Not reached [17.86; -]	189	12 (6.3)	Not reached [-; -]	8.58 [4.68; 15.74]	< 0.001	
Renal Function									
Normal	78	34 (43.6)	Not reached [12.00; -]	81	4 (4.9)	Not reached [-; -]	10.79 [3.81; 30.56]	< 0.001	0.915
Mild	115	51 (44.3)	Not reached [17.86; -]	118	7 (5.9)	Not reached [-; -]	8.30 [3.75; 18.40]	< 0.001	
Moderate/Severe	46	20 (43.5)	Not reached [6.14; -]	37	2 (5.4)	Not reached [-; -]	8.91 [2.06; 38.41]	0.003	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Rash erythematous									
Age									
< 65	105	8 (7.6)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	4 (3.0)	n.c.	134	2 (1.5)	n.c.	n.c.	n.c.	n.c.
Race									
White	166	4 (2.4)	n.c.	147	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Non-white	73	8 (11.0)	n.c.	89	1 (1.1)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	2 (3.5)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	5 (5.2)	n.c.	101	2 (2.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	5 (5.9)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	11 (5.6)	Not reached [-; -]	181	2 (1.1)	Not reached [-; -]	5.03 [1.12; 22.70]	0.036	0.506

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Female	42	1 (2.4)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.252	
ECOG at Baseline									
0	136	9 (6.6)	Not reached [-; -]	124	1 (0.8)	Not reached [-; -]	8.36 [1.06; 65.96]	0.044	0.532
1-2	103	3 (2.9)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	3.13 [0.33; 30.08]	0.323	
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	n.c.	44	1 (2.3)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	7 (4.0)	n.c.	192	1 (0.5)	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	1 (2.1)	Not reached [-; -]	2.03 [0.18; 22.45]	0.562	0.332
Absent	192	10 (5.2)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	9.79 [1.25; 76.51]	0.030	
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	n.c.	138	2 (1.4)	n.c.	n.c.	n.c.	n.c.
Low	101	8 (7.9)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	7 (4.1)	n.c.	157	1 (0.6)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	3 (5.0)	n.c.	65	1 (1.5)	n.c.	n.c.	n.c.	
Renal Function									
Normal	78	5 (6.4)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	6 (5.2)	n.c.	118	2 (1.7)	n.c.	n.c.	n.c.	
Moderate/Severe	46	1 (2.2)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Skin and subcutaneous tissue disorders - PT^g: Rash macular									
Age									
< 65	105	14 (13.3)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.104
≥ 65	134	13 (9.7)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	4.95 [1.08; 22.61]	0.039	
Race									
White	166	20 (12.0)	Not reached [-; -]	147	1 (0.7)	Not reached [-; -]	14.32 [1.90; 107.96]	0.010	0.599
Non-white	73	7 (9.6)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	6.13 [0.72; 52.50]	0.098	
Geographic Region									
North America	57	6 (10.5)	Not reached [66.57; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.055	0.580
Europe	97	13 (13.4)	Not reached [-; -]	101	1 (1.0)	Not reached [-; -]	10.42 [1.33; 81.56]	0.026	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	85	8 (9.4)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	7.00 [0.86; 56.92]	0.069	
Sex									
Male	197	23 (11.7)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	15.54 [2.07; 116.76]	0.008	0.392
Female	42	4 (9.5)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	5.54 [0.62; 49.55]	0.126	
ECOG at Baseline									
0	136	14 (10.3)	Not reached [-; -]	124	1 (0.8)	Not reached [-; -]	8.80 [1.12; 68.95]	0.038	0.912
1-2	103	13 (12.6)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	12.51 [1.62; 96.73]	0.016	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	5.31 [0.65; 43.19]	0.118	0.404
Lower Tract	176	19 (10.8)	Not reached [-; -]	192	1 (0.5)	Not reached [-; -]	15.03 [1.97; 114.34]	0.009	
Stratification Factor: Liver Metastases									
Present	47	5 (10.6)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022	0.341
Absent	192	22 (11.5)	Not reached [-; -]	189	2 (1.1)	Not reached [-; -]	7.81 [1.79; 33.99]	0.006	
Stratification Factor: PD-L1 Expression									
High	138	14 (10.1)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	11.48 [1.48; 88.82]	0.019	0.960
Low	101	13 (12.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	9.41 [1.20; 73.70]	0.033	
Metastatic Disease Site									
Visceral metastases	169	22 (13.0)	Not reached [-; -]	157	2 (1.3)	Not reached [-; -]	8.26 [1.91; 35.72]	0.005	0.365
Lymph node only	60	5 (8.3)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.055	
Renal Function									
Normal	78	7 (9.0)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.017	0.441
Mild	115	14 (12.2)	Not reached [-; -]	118	1 (0.8)	Not reached [-; -]	9.60 [1.22; 75.72]	0.032	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	4.91 [0.59; 40.80]	0.141	
SOC: Skin and subcutaneous tissue disorders - PT^g: Rash maculo-papular									
Age									
< 65	105	29 (27.6)	Not reached [-; -]	102	4 (3.9)	Not reached [-; -]	5.33 [1.84; 15.47]	0.002	0.566
≥ 65	134	47 (35.1)	Not reached [65.00; -]	134	5 (3.7)	Not reached [-; -]	9.29 [3.67; 23.55]	< 0.001	
Race									
White	166	58 (34.9)	Not reached [55.00; -]	147	6 (4.1)	Not reached [-; -]	7.38 [3.15; 17.28]	< 0.001	0.823
Non-white	73	18 (24.7)	Not reached [89.43; -]	89	3 (3.4)	Not reached [-; -]	7.13 [2.08; 24.48]	0.002	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	57	30 (52.6)	22.43 [11.86; -]	51	4 (7.8)	Not reached [-; -]	7.02 [2.45; 20.12]	< 0.001	0.580
Europe	97	17 (17.5)	Not reached [-; -]	101	3 (3.0)	Not reached [-; -]	4.21 [1.19; 14.88]	0.026	
Rest of World	85	29 (34.1)	Not reached [89.43; -]	84	2 (2.4)	Not reached [-; -]	13.00 [3.07; 55.02]	< 0.001	
Sex									
Male	197	60 (30.5)	Not reached [-; -]	181	6 (3.3)	Not reached [-; -]	8.28 [3.55; 19.32]	< 0.001	0.764
Female	42	16 (38.1)	89.43 [28.00; -]	55	3 (5.5)	Not reached [-; -]	5.83 [1.65; 20.58]	0.006	
ECOG at Baseline									
0	136	47 (34.6)	Not reached [89.43; -]	124	4 (3.2)	Not reached [-; -]	10.67 [3.82; 29.77]	< 0.001	0.377
1-2	103	29 (28.2)	Not reached [65.00; -]	111	5 (4.5)	Not reached [-; -]	4.60 [1.73; 12.20]	0.002	
Stratification Factor: Liver Metastases									
Present	47	16 (34.0)	Not reached [29.57; -]	47	2 (4.3)	Not reached [-; -]	5.94 [1.32; 26.68]	0.020	0.998
Absent	192	60 (31.3)	Not reached [89.43; -]	189	7 (3.7)	Not reached [-; -]	7.85 [3.56; 17.30]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	48 (34.8)	Not reached [65.00; -]	138	3 (2.2)	Not reached [-; -]	15.35 [4.75; 49.58]	< 0.001	0.061
Low	101	28 (27.7)	Not reached [-; -]	98	6 (6.1)	Not reached [-; -]	3.56 [1.44; 8.79]	0.006	
Metastatic Disease Site									
Visceral metastases	169	53 (31.4)	Not reached [89.43; -]	157	5 (3.2)	Not reached [-; -]	8.38 [3.31; 21.19]	< 0.001	0.360
Lymph node only	60	19 (31.7)	Not reached [-; -]	65	4 (6.2)	Not reached [-; -]	5.02 [1.69; 14.91]	0.004	
Renal Function									
Normal	78	22 (28.2)	Not reached [-; -]	81	4 (4.9)	Not reached [-; -]	5.31 [1.81; 15.61]	0.002	0.686
Mild	115	41 (35.7)	Not reached [55.00; -]	118	4 (3.4)	Not reached [-; -]	8.96 [3.17; 25.35]	< 0.001	
Moderate/Severe	46	13 (28.3)	Not reached [31.86; -]	37	1 (2.7)	Not reached [-; -]	9.50 [1.23; 73.57]	0.031	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Rash papular									
Age									
< 65	105	11 (10.5)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.009	0.245
≥ 65	134	10 (7.5)	Not reached [-; -]	134	1 (0.7)	Not reached [-; -]	6.05 [0.73; 50.27]	0.095	
Race									
White	166	11 (6.6)	Not reached [-; -]	147	1 (0.7)	Not reached [-; -]	5.11 [0.62; 42.45]	0.131	0.199
Non-white	73	10 (13.7)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.344	0.416
Europe	97	8 (8.2)	Not reached [-; -]	101	1 (1.0)	Not reached [-; -]	3.16 [0.33; 30.40]	0.319	
Rest of World	85	12 (14.1)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Sex									
Male	197	16 (8.1)	Not reached [-; -]	181	1 (0.6)	Not reached [-; -]	8.13 [1.03; 64.21]	0.047	0.381
Female	42	5 (11.9)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	
ECOG at Baseline									
0	136	15 (11.0)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.137
1-2	103	6 (5.8)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	2.96 [0.31; 28.46]	0.348	
Primary Disease Site of Origin									
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	2.92 [0.33; 26.12]	0.338	0.125
Lower Tract	176	13 (7.4)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.559
Absent	192	18 (9.4)	Not reached [-; -]	189	1 (0.5)	Not reached [-; -]	12.75 [1.67; 97.46]	0.014	
Stratification Factor: PD-L1 Expression									
High	138	11 (8.0)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.009	0.232
Low	101	10 (9.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	5.87 [0.71; 48.75]	0.101	
Metastatic Disease Site									
Visceral metastases	169	14 (8.3)	Not reached [-; -]	157	1 (0.6)	Not reached [-; -]	7.38 [0.92; 59.00]	0.060	0.388
Lymph node only	60	6 (10.0)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.036	
Renal Function									
Normal	78	2 (2.6)	Not reached [-; -]	81	1 (1.2)	Not reached [-; -]	2.08 [0.19; 22.91]	0.550	0.115
Mild	115	14 (12.2)	Not reached [-; -]	118	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	
Moderate/Severe	46	5 (10.9)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.125	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Skin exfoliation									
Age									
< 65	105	2 (1.9)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	6 (4.5)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	166	6 (3.6)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	2 (2.7)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	1 (1.8)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	3 (3.1)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	4 (4.7)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	8 (4.1)	n.c.	181	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	42	0 (0.0)	n.c.	55	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	136	2 (1.5)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	6 (5.8)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	6 (3.4)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	47	1 (2.1)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	192	7 (3.6)	n.c.	189	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	4 (4.0)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	169	5 (3.0)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	3 (5.0)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	78	2 (2.6)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	6 (5.2)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	46	0 (0.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
SOC: Skin and subcutaneous tissue disorders - PT^g: Skin hyperpigmentation									
Age									
< 65	105	9 (8.6)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	8 (6.0)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	166	13 (7.8)	Not reached [-; -]	147	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.023	0.997
Non-white	73	4 (5.5)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.127	
Geographic Region									
North America	57	7 (12.3)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	6 (6.2)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	85	4 (4.7)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	197	13 (6.6)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.036	0.997
Female	42	4 (9.5)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.045	
ECOG at Baseline									
0	136	9 (6.6)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	8 (7.8)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.140	0.997
Lower Tract	176	11 (6.3)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.301	0.997
Absent	192	13 (6.8)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.010	
Stratification Factor: PD-L1 Expression									
High	138	9 (6.5)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	101	8 (7.9)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	14 (8.3)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	0.997
Lymph node only	60	3 (5.0)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.141	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	78	4 (5.1)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	9 (7.8)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	46	4 (8.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Vascular disorders - PT^g: Deep vein thrombosis									
Age									
< 65	105	1 (1.0)	n.c.	102	4 (3.9)	n.c.	n.c.	n.c.	n.c.
≥ 65	134	1 (0.7)	n.c.	134	4 (3.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	166	0 (0.0)	n.c.	147	6 (4.1)	n.c.	n.c.	n.c.	n.c.
Non-white	73	2 (2.7)	n.c.	89	2 (2.2)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	57	1 (1.8)	n.c.	51	2 (3.9)	n.c.	n.c.	n.c.	n.c.
Europe	97	0 (0.0)	n.c.	101	1 (1.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	85	1 (1.2)	n.c.	84	5 (6.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	197	2 (1.0)	n.c.	181	5 (2.8)	n.c.	n.c.	n.c.	n.c.
Female	42	0 (0.0)	n.c.	55	3 (5.5)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	136	2 (1.5)	n.c.	124	5 (4.0)	n.c.	n.c.	n.c.	n.c.
1-2	103	0 (0.0)	n.c.	111	3 (2.7)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	61	0 (0.0)	n.c.	44	2 (4.5)	n.c.	n.c.	n.c.	n.c.
Lower Tract	176	2 (1.1)	n.c.	192	6 (3.1)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	n.c.	47	2 (4.3)	n.c.	n.c.	n.c.	n.c.
Absent	192	2 (1.0)	n.c.	189	6 (3.2)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	138	2 (1.4)	n.c.	138	4 (2.9)	n.c.	n.c.	n.c.	n.c.
Low	101	0 (0.0)	n.c.	98	4 (4.1)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events		N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site										
Visceral metastases	169	1	(0.6)	n.c.	157	5	(3.2)	n.c.	n.c.	n.c.
Lymph node only	60	0	(0.0)	n.c.	65	3	(4.6)	n.c.	n.c.	n.c.
Renal Function										
Normal	78	1	(1.3)	n.c.	81	3	(3.7)	n.c.	n.c.	n.c.
Mild	115	1	(0.9)	n.c.	118	3	(2.5)	n.c.	n.c.	n.c.
Moderate/Severe	46	0	(0.0)	n.c.	37	2	(5.4)	n.c.	n.c.	n.c.
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A specific adverse event appears on this report only if its incidence $\geq 10\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>h: Unrounded p-value > 0.050</p> <p>i: Unrounded p-value < 0.050</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class</p>										

Tabelle 4G-89: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (SOC und PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events		N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC ^g : Blood and lymphatic system disorders										
Age										
< 65	105	2	(1.9)	Not reached [-; -]	102	6	(5.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994
≥ 65	134	3	(2.2)	Not reached [-; -]	134	10	(7.5)	Not reached [-; -]	0.25 [0.07; 0.92]	0.038
Geographic Region										
North America	57	0	(0.0)	Not reached [-; -]	51	1	(2.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.286
Europe	97	1	(1.0)	Not reached [-; -]	101	4	(4.0)	Not reached [-; -]	0.19 [0.02; 1.78]	0.146
Rest of World	85	4	(4.7)	Not reached [-; -]	84	11	(13.1)	Not reached [-; -]	0.16 [0.04; 0.74]	0.018

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Sex	
Male	197	3 (1.5)	Not reached [-; -]	181	12 (6.6)	Not reached [-; -]	0.19 [0.05; 0.70]	0.012	0.343	
Female	42	2 (4.8)	Not reached [-; -]	55	4 (7.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.995		
ECOG at Baseline										
0	136	2 (1.5)	Not reached [-; -]	124	4 (3.2)	Not reached [-; -]	0.43 [0.08; 2.35]	0.331	0.598	
1-2	103	3 (2.9)	Not reached [-; -]	111	12 (10.8)	Not reached [-; -]	0.07 [0.01; 0.55]	0.011		
Primary Disease Site of Origin										
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	0.23 [0.02; 2.20]	0.202	0.848	
Lower Tract	176	4 (2.3)	Not reached [-; -]	192	13 (6.8)	Not reached [-; -]	0.14 [0.03; 0.63]	0.010		
Stratification Factor: Liver Metastases										
Present	47	1 (2.1)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.067	
Absent	192	4 (2.1)	Not reached [-; -]	189	16 (8.5)	Not reached [-; -]	0.15 [0.04; 0.54]	0.003		
Stratification Factor: PD-L1 Expression										
High	138	3 (2.2)	Not reached [-; -]	138	8 (5.8)	Not reached [-; -]	0.12 [0.01; 0.95]	0.045	0.671	
Low	101	2 (2.0)	Not reached [-; -]	98	8 (8.2)	Not reached [-; -]	0.19 [0.04; 0.92]	0.039		
Metastatic Disease Site										
Visceral metastases	169	5 (3.0)	Not reached [-; -]	157	10 (6.4)	Not reached [-; -]	0.24 [0.06; 0.88]	0.031	0.075	
Lymph node only	60	0 (0.0)	Not reached [-; -]	65	5 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022		
SOC ^g : Gastrointestinal disorders										
Age										
< 65	105	9 (8.6)	Not reached [-; -]	102	2 (2.0)	Not reached [-; -]	3.29 [0.68; 15.84]	0.138	0.933	
≥ 65	134	15 (11.2)	Not reached [-; -]	134	4 (3.0)	Not reached [-; -]	3.17 [1.04; 9.70]	0.043		
Geographic Region										
North America	57	9 (15.8)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	7.25 [0.91; 57.96]	0.062	0.599	
Europe	97	10 (10.3)	Not reached [-; -]	101	3 (3.0)	Not reached [-; -]	3.04 [0.82; 11.23]	0.096		
Rest of World	85	5 (5.9)	Not reached [-; -]	84	2 (2.4)	Not reached [-; -]	1.46 [0.26; 8.27]	0.668		
Sex										
Male	197	21 (10.7)	Not reached [-; -]	181	3 (1.7)	Not reached [-; -]	5.34 [1.58; 18.11]	0.007	0.123	
Female	42	3 (7.1)	Not reached [-; -]	55	3 (5.5)	Not reached [-; -]	0.87 [0.15; 5.23]	0.883		

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									ECOG at Baseline	
0	136	12 (8.8)	Not reached [-; -]	124	2 (1.6)	Not reached [-; -]	4.85 [1.07; 21.90]	0.040	0.566	
1-2	103	12 (11.7)	Not reached [-; -]	111	4 (3.6)	Not reached [-; -]	2.38 [0.74; 7.64]	0.146		
Primary Disease Site of Origin										
Upper Tract	61	6 (9.8)	Not reached [-; -]	44	2 (4.5)	Not reached [21.71; -]	1.13 [0.20; 6.52]	0.888	0.426	
Lower Tract	176	18 (10.2)	Not reached [-; -]	192	4 (2.1)	Not reached [-; -]	4.46 [1.50; 13.25]	0.007		
Stratification Factor: PD-L1 Expression										
High	138	13 (9.4)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	5.21 [1.15; 23.52]	0.032	0.344	
Low	101	11 (10.9)	Not reached [-; -]	98	4 (4.1)	Not reached [-; -]	2.17 [0.67; 6.99]	0.194		
Metastatic Disease Site										
Visceral metastases	169	20 (11.8)	Not reached [-; -]	157	3 (1.9)	Not reached [-; -]	5.48 [1.61; 18.61]	0.006	0.072	
Lymph node only	60	3 (5.0)	Not reached [-; -]	65	3 (4.6)	Not reached [-; -]	0.46 [0.07; 2.98]	0.412		
Renal Function										
Normal	78	9 (11.5)	Not reached [-; -]	81	2 (2.5)	Not reached [-; -]	4.40 [0.94; 20.51]	0.059	0.798	
Mild	115	9 (7.8)	Not reached [-; -]	118	2 (1.7)	Not reached [-; -]	3.85 [0.81; 18.15]	0.089		
Moderate/Severe	46	6 (13.0)	Not reached [66.86; -]	37	2 (5.4)	Not reached [-; -]	1.43 [0.26; 7.83]	0.682		
SOC ^g : Hepatobiliary disorders										
Age										
< 65	105	1 (1.0)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
≥ 65	134	5 (3.7)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Race										
White	166	4 (2.4)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Non-white	73	2 (2.7)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Geographic Region										
North America	57	2 (3.5)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	97	3 (3.1)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Rest of World	85	1 (1.2)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	197	4 (2.0)	n.c.	181	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Female	42	2 (4.8)	n.c.	55	0 (0.0)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									ECOG at Baseline	
0	136	3 (2.2)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
1-2	103	3 (2.9)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	61	3 (4.9)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	176	3 (1.7)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases										
Present	47	2 (4.3)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Absent	192	4 (2.1)	n.c.	189	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression										
High	138	4 (2.9)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Low	101	2 (2.0)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	169	6 (3.6)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	60	0 (0.0)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	78	3 (3.8)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	115	2 (1.7)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	46	1 (2.2)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
SOC^g: Infections and infestations										
Age										
< 65	105	7 (6.7)	Not reached [-; -]	102	15 (14.7)	Not reached [-; -]	0.29 [0.11; 0.78]	0.015	0.379	
≥ 65	134	17 (12.7)	Not reached [-; -]	134	24 (17.9)	Not reached [-; -]	0.52 [0.27; 1.00]	0.052		
Race										
White	166	14 (8.4)	Not reached [-; -]	147	24 (16.3)	Not reached [-; -]	0.37 [0.18; 0.74]	0.005	0.296	
Non-white	73	10 (13.7)	Not reached [87.71; -]	89	15 (16.9)	Not reached [-; -]	0.57 [0.24; 1.35]	0.199		
Geographic Region										
North America	57	5 (8.8)	Not reached [-; -]	51	9 (17.6)	Not reached [-; -]	0.36 [0.11; 1.16]	0.086	0.640	
Europe	97	11 (11.3)	Not reached [-; -]	101	21 (20.8)	Not reached [-; -]	0.41 [0.19; 0.89]	0.024		
Rest of World	85	8 (9.4)	Not reached [-; -]	84	9 (10.7)	Not reached [-; -]	0.55 [0.19; 1.56]	0.261		

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Sex	
Male	197	19 (9.6)	Not reached [-; -]	181	30 (16.6)	Not reached [-; -]	0.37 [0.20; 0.70]	0.002	0.618	
Female	42	5 (11.9)	Not reached [-; -]	55	9 (16.4)	Not reached [-; -]	0.71 [0.24; 2.14]	0.548		
ECOG at Baseline										
0	136	12 (8.8)	Not reached [-; -]	124	17 (13.7)	Not reached [-; -]	0.55 [0.26; 1.18]	0.128	0.714	
1-2	103	12 (11.7)	Not reached [-; -]	111	22 (19.8)	Not reached [-; -]	0.33 [0.15; 0.73]	0.006		
Primary Disease Site of Origin										
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	5 (11.4)	Not reached [-; -]	0.12 [0.01; 1.03]	0.054	0.277	
Lower Tract	176	22 (12.5)	Not reached [-; -]	192	34 (17.7)	Not reached [-; -]	0.52 [0.29; 0.91]	0.023		
Stratification Factor: Liver Metastases										
Present	47	6 (12.8)	Not reached [-; -]	47	7 (14.9)	Not reached [-; -]	0.57 [0.18; 1.86]	0.352	0.428	
Absent	192	18 (9.4)	Not reached [-; -]	189	32 (16.9)	Not reached [-; -]	0.40 [0.21; 0.74]	0.003		
Stratification Factor: PD-L1 Expression										
High	138	15 (10.9)	Not reached [-; -]	138	25 (18.1)	Not reached [-; -]	0.47 [0.24; 0.92]	0.028	0.978	
Low	101	9 (8.9)	Not reached [-; -]	98	14 (14.3)	Not reached [-; -]	0.35 [0.14; 0.93]	0.034		
Metastatic Disease Site										
Visceral metastases	169	16 (9.5)	Not reached [-; -]	157	25 (15.9)	Not reached [-; -]	0.44 [0.23; 0.86]	0.016	0.966	
Lymph node only	60	7 (11.7)	Not reached [-; -]	65	12 (18.5)	Not reached [-; -]	0.37 [0.13; 1.07]	0.067		
Renal Function										
Normal	78	6 (7.7)	Not reached [-; -]	81	18 (22.2)	Not reached [-; -]	0.25 [0.10; 0.67]	0.006	0.287	
Mild	115	12 (10.4)	Not reached [-; -]	118	15 (12.7)	Not reached [-; -]	0.69 [0.32; 1.51]	0.358		
Moderate/Severe	46	6 (13.0)	Not reached [87.71; -]	37	6 (16.2)	Not reached [-; -]	0.35 [0.09; 1.34]	0.127		
SOC ^g : Respiratory, thoracic and mediastinal disorders										
Age										
< 65	105	8 (7.6)	Not reached [-; -]	102	2 (2.0)	Not reached [-; -]	2.30 [0.45; 11.85]	0.320	0.471	
≥ 65	134	17 (12.7)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	6.27 [1.42; 27.63]	0.015		
Race										
White	166	15 (9.0)	Not reached [-; -]	147	3 (2.0)	Not reached [-; -]	2.94 [0.82; 10.52]	0.097	0.341	
Non-white	73	10 (13.7)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	8.99 [1.12; 72.33]	0.039		

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Geographic Region	
North America	57	6 (10.5)	Not reached [91.43; -]	51	1 (2.0)	Not reached [-; -]	3.61 [0.40; 32.26]	0.251	0.750	
Europe	97	8 (8.2)	Not reached [-; -]	101	2 (2.0)	Not reached [-; -]	3.02 [0.61; 14.88]	0.175		
Rest of World	85	11 (12.9)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	7.48 [0.94; 59.27]	0.057		
Sex										
Male	197	22 (11.2)	Not reached [-; -]	181	3 (1.7)	Not reached [-; -]	4.32 [1.26; 14.85]	0.020	0.726	
Female	42	3 (7.1)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	3.99 [0.42; 38.38]	0.231		
Renal Function										
Normal	78	6 (7.7)	Not reached [-; -]	81	18 (22.2)	Not reached [-; -]	0.25 [0.10; 0.67]	0.006	0.287	
Mild	115	12 (10.4)	Not reached [-; -]	118	15 (12.7)	Not reached [-; -]	0.69 [0.32; 1.51]	0.358		
Moderate/Severe	46	6 (13.0)	Not reached [87.71; -]	37	6 (16.2)	Not reached [-; -]	0.35 [0.09; 1.34]	0.127		
SOC^g: Respiratory, thoracic and mediastinal disorders										
Age										
< 65	105	8 (7.6)	Not reached [-; -]	102	2 (2.0)	Not reached [-; -]	2.30 [0.45; 11.85]	0.320	0.471	
≥ 65	134	17 (12.7)	Not reached [-; -]	134	2 (1.5)	Not reached [-; -]	6.27 [1.42; 27.63]	0.015		
Race										
White	166	15 (9.0)	Not reached [-; -]	147	3 (2.0)	Not reached [-; -]	2.94 [0.82; 10.52]	0.097	0.341	
Non-white	73	10 (13.7)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	8.99 [1.12; 72.33]	0.039		
Geographic Region										
North America	57	6 (10.5)	Not reached [91.43; -]	51	1 (2.0)	Not reached [-; -]	3.61 [0.40; 32.26]	0.251	0.750	
Europe	97	8 (8.2)	Not reached [-; -]	101	2 (2.0)	Not reached [-; -]	3.02 [0.61; 14.88]	0.175		
Rest of World	85	11 (12.9)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	7.48 [0.94; 59.27]	0.057		
Sex										
Male	197	22 (11.2)	Not reached [-; -]	181	3 (1.7)	Not reached [-; -]	4.32 [1.26; 14.85]	0.020	0.726	
Female	42	3 (7.1)	Not reached [-; -]	55	1 (1.8)	Not reached [-; -]	3.99 [0.42; 38.38]	0.231		
ECOG at Baseline										
0	136	14 (10.3)	Not reached [-; -]	124	2 (1.6)	Not reached [-; -]	4.39 [0.97; 19.91]	0.055	0.925	
1-2	103	11 (10.7)	Not reached [-; -]	111	2 (1.8)	Not reached [-; -]	4.18 [0.89; 19.62]	0.069		

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Primary Disease Site of Origin	
Upper Tract	61	8 (13.1)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	5.08 [0.62; 41.30]	0.128	0.997	
Lower Tract	176	17 (9.7)	Not reached [-; -]	192	3 (1.6)	Not reached [-; -]	3.78 [1.06; 13.41]	0.040		
Stratification Factor: Liver Metastases										
Present	47	6 (12.8)	Not reached [91.43; -]	47	1 (2.1)	Not reached [-; -]	3.58 [0.40; 32.07]	0.254	0.956	
Absent	192	19 (9.9)	Not reached [-; -]	189	3 (1.6)	Not reached [-; -]	4.48 [1.30; 15.50]	0.018		
Stratification Factor: PD-L1 Expression										
High	138	13 (9.4)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	4.18 [0.90; 19.31]	0.067	0.928	
Low	101	12 (11.9)	Not reached [-; -]	98	2 (2.0)	Not reached [-; -]	4.34 [0.95; 19.88]	0.059		
Metastatic Disease Site										
Visceral metastases	169	19 (11.2)	Not reached [-; -]	157	3 (1.9)	Not reached [-; -]	4.00 [1.15; 13.94]	0.029	0.922	
Lymph node only	60	5 (8.3)	Not reached [-; -]	65	1 (1.5)	Not reached [-; -]	4.19 [0.47; 37.24]	0.198		
Renal Function										
Normal	78	6 (7.7)	Not reached [91.43; -]	81	1 (1.2)	Not reached [-; -]	4.22 [0.47; 37.72]	0.198	0.587	
Mild	115	15 (13.0)	Not reached [-; -]	118	3 (2.5)	Not reached [-; -]	3.51 [0.98; 12.51]	0.053		
Moderate/Severe	46	4 (8.7)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.136		
SOC^g: Skin and subcutaneous tissue disorders										
Age										
< 65	105	4 (3.8)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.052	0.997	
≥ 65	134	11 (8.2)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004		
Race										
White	166	6 (3.6)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Non-white	73	9 (12.3)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.		
Geographic Region										
North America	57	3 (5.3)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	97	5 (5.2)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.		
Rest of World	85	7 (8.2)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.		
Sex										
Male	197	12 (6.1)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.997	
Female	42	3 (7.1)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.045		

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									ECOG at Baseline	
0	136	7 (5.1)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
1-2	103	8 (7.8)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	61	5 (8.2)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.087	0.997	
Lower Tract	176	10 (5.7)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003		
Stratification Factor: Liver Metastases										
Present	47	4 (8.5)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.080	0.997	
Absent	192	11 (5.7)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003		
Stratification Factor: PD-L1 Expression										
High	138	7 (5.1)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Low	101	8 (7.9)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	169	10 (5.9)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	0.997	
Lymph node only	60	5 (8.3)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.040		
Renal Function										
Normal	78	3 (3.8)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	115	7 (6.1)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	46	5 (10.9)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A system organ class appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class</p>										

Tabelle 4G-90: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse (PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									SOC: Blood and lymphatic system disorders - PT^g: Anaemia	
Age										
< 65	105	0 (0.0)	n.c.	102	3 (2.9)	n.c.	n.c.	n.c.	n.c.	
≥ 65	134	0 (0.0)	n.c.	134	7 (5.2)	n.c.	n.c.	n.c.	n.c.	
Race										
White	166	0 (0.0)	n.c.	147	8 (5.4)	n.c.	n.c.	n.c.	n.c.	
Non-white	73	0 (0.0)	n.c.	89	2 (2.2)	n.c.	n.c.	n.c.	n.c.	
Geographic Region										
North America	57	0 (0.0)	n.c.	51	1 (2.0)	n.c.	n.c.	n.c.	n.c.	
Europe	97	0 (0.0)	n.c.	101	4 (4.0)	n.c.	n.c.	n.c.	n.c.	
Rest of World	85	0 (0.0)	n.c.	84	5 (6.0)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	197	0 (0.0)	n.c.	181	9 (5.0)	n.c.	n.c.	n.c.	n.c.	
Female	42	0 (0.0)	n.c.	55	1 (1.8)	n.c.	n.c.	n.c.	n.c.	
ECOG at Baseline										
0	136	0 (0.0)	n.c.	124	2 (1.6)	n.c.	n.c.	n.c.	n.c.	
1-2	103	0 (0.0)	n.c.	111	8 (7.2)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	61	0 (0.0)	n.c.	44	2 (4.5)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	176	0 (0.0)	n.c.	192	8 (4.2)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases										
Present	47	0 (0.0)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.996	
Absent	192	0 (0.0)	Not reached [-; -]	189	10 (5.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001		
Stratification Factor: PD-L1 Expression										
High	138	0 (0.0)	n.c.	138	6 (4.3)	n.c.	n.c.	n.c.	n.c.	
Low	101	0 (0.0)	n.c.	98	4 (4.1)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Metastatic Disease Site	
Visceral metastases	169	0 (0.0)	n.c.	157	6 (3.8)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	60	0 (0.0)	n.c.	65	3 (4.6)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	78	0 (0.0)	n.c.	81	1 (1.2)	n.c.	n.c.	n.c.	n.c.	
Mild	115	0 (0.0)	n.c.	118	6 (5.1)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	46	0 (0.0)	n.c.	37	3 (8.1)	n.c.	n.c.	n.c.	n.c.	
SOC: Blood and lymphatic system disorders - PT^g: Thrombocytopenia										
Age										
< 65	105	0 (0.0)	n.c.	102	2 (2.0)	n.c.	n.c.	n.c.	n.c.	
≥ 65	134	0 (0.0)	n.c.	134	3 (2.2)	n.c.	n.c.	n.c.	n.c.	
Race										
White	166	0 (0.0)	n.c.	147	4 (2.7)	n.c.	n.c.	n.c.	n.c.	
Non-white	73	0 (0.0)	n.c.	89	1 (1.1)	n.c.	n.c.	n.c.	n.c.	
Geographic Region										
North America	57	0 (0.0)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	97	0 (0.0)	n.c.	101	2 (2.0)	n.c.	n.c.	n.c.	n.c.	
Rest of World	85	0 (0.0)	n.c.	84	3 (3.6)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	197	0 (0.0)	n.c.	181	4 (2.2)	n.c.	n.c.	n.c.	n.c.	
Female	42	0 (0.0)	n.c.	55	1 (1.8)	n.c.	n.c.	n.c.	n.c.	
ECOG at Baseline										
0	136	0 (0.0)	n.c.	124	2 (1.6)	n.c.	n.c.	n.c.	n.c.	
1-2	103	0 (0.0)	n.c.	111	3 (2.7)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	61	0 (0.0)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	176	0 (0.0)	n.c.	192	5 (2.6)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases										
Present	47	0 (0.0)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Absent	192	0 (0.0)	n.c.	189	5 (2.6)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: PD-L1 Expression	
High	138	0 (0.0)	n.c.	138	4 (2.9)	n.c.	n.c.	n.c.	n.c.	
Low	101	0 (0.0)	n.c.	98	1 (1.0)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	169	0 (0.0)	n.c.	157	2 (1.3)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	60	0 (0.0)	n.c.	65	3 (4.6)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	78	0 (0.0)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	115	0 (0.0)	n.c.	118	5 (4.2)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	46	0 (0.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
SOC: Gastrointestinal disorders - PT ^g : Diarrhoea										
Age										
< 65	105	3 (2.9)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
≥ 65	134	4 (3.0)	n.c.	134	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Race										
White	166	7 (4.2)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Non-white	73	0 (0.0)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Geographic Region										
North America	57	5 (8.8)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	97	1 (1.0)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Rest of World	85	1 (1.2)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	197	5 (2.5)	n.c.	181	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Female	42	2 (4.8)	n.c.	55	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
ECOG at Baseline										
0	136	4 (2.9)	n.c.	124	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
1-2	103	3 (2.9)	n.c.	111	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	61	3 (4.9)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	176	4 (2.3)	n.c.	192	0 (0.0)	n.c.	n.c.	n.c.	n.c.	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: Liver Metastases	
Present	47	4 (8.5)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Absent	192	3 (1.6)	n.c.	189	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression										
High	138	5 (3.6)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Low	101	2 (2.0)	n.c.	98	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	169	7 (4.1)	n.c.	157	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	60	0 (0.0)	n.c.	65	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	78	5 (6.4)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	115	1 (0.9)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	46	1 (2.2)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
SOC: Infections and infestations - PT^g: Urinary tract infection										
Age										
< 65	105	2 (1.9)	Not reached [-; -]	102	4 (3.9)	26.71 [26.71; -]	0.07 [0.00; 1.31]	0.075	0.321	
≥ 65	134	2 (1.5)	Not reached [-; -]	134	13 (9.7)	Not reached [-; -]	0.13 [0.03; 0.57]	0.007		
Race										
White	166	2 (1.2)	Not reached [-; -]	147	10 (6.8)	26.71 [26.71; -]	0.09 [0.01; 0.58]	0.011	0.520	
Non-white	73	2 (2.7)	Not reached [-; -]	89	7 (7.9)	Not reached [-; -]	0.14 [0.02; 1.19]	0.073		
Geographic Region										
North America	57	0 (0.0)	Not reached [-; -]	51	3 (5.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.062	0.182	
Europe	97	1 (1.0)	Not reached [-; -]	101	9 (8.9)	Not reached [-; -]	0.11 [0.01; 0.84]	0.033		
Rest of World	85	3 (3.5)	Not reached [-; -]	84	5 (6.0)	26.71 [-; -]	0.17 [0.02; 1.29]	0.087		
Sex										
Male	197	3 (1.5)	Not reached [-; -]	181	11 (6.1)	Not reached [-; -]	0.14 [0.03; 0.64]	0.011	0.936	
Female	42	1 (2.4)	Not reached [-; -]	55	6 (10.9)	26.71 [26.71; -]	0.09 [0.01; 1.13]	0.062		
ECOG at Baseline										
0	136	3 (2.2)	Not reached [-; -]	124	6 (4.8)	Not reached [-; -]	0.30 [0.06; 1.46]	0.135	0.192	
1-2	103	1 (1.0)	Not reached [-; -]	111	11 (9.9)	26.71 [-; -]	0.03 [0.00; 0.38]	0.008		

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Primary Disease Site of Origin	
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	2 (4.5)	Not reached [-; -]	0.27 [0.02; 3.13]	0.297	0.188	
Lower Tract	176	2 (1.1)	Not reached [-; -]	192	15 (7.8)	26.71 [26.71; -]	0.08 [0.01; 0.46]	0.005		
Stratification Factor: Liver Metastases										
Present	47	2 (4.3)	Not reached [-; -]	47	4 (8.5)	Not reached [-; -]	0.46 [0.08; 2.54]	0.376	0.254	
Absent	192	2 (1.0)	Not reached [-; -]	189	13 (6.9)	26.71 [26.71; -]	0.02 [0.00; 0.31]	0.005		
Stratification Factor: PD-L1 Expression										
High	138	1 (0.7)	Not reached [-; -]	138	12 (8.7)	26.71 [-; -]	0.02 [0.00; 0.37]	0.008	0.094	
Low	101	3 (3.0)	Not reached [-; -]	98	5 (5.1)	Not reached [-; -]	0.33 [0.06; 1.72]	0.187		
Metastatic Disease Site										
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	11 (7.0)	Not reached [-; -]	0.24 [0.07; 0.85]	0.027	0.096	
Lymph node only	60	0 (0.0)	Not reached [-; -]	65	6 (9.2)	26.71 [-; -]	n.a. [n.a.; n.a.]	< 0.001		
Renal Function										
Normal	78	1 (1.3)	Not reached [-; -]	81	9 (11.1)	26.71 [26.71; -]	0.04 [0.00; 0.50]	0.012	0.527	
Mild	115	2 (1.7)	Not reached [-; -]	118	7 (5.9)	Not reached [-; -]	0.13 [0.02; 1.10]	0.061		
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	0.74 [0.05; 11.93]	0.835		
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A specific adverse event appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class</p>										

Tabelle 4G-91: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE Grad 3-5) (SOC und PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC^g: Blood and lymphatic system disorders									
Age									
< 65	105	6 (5.7)	Not reached [-; -]	102	43 (42.2)	Not reached [12.86; -]	0.05 [0.02; 0.17]	< 0.001	0.724
≥ 65	134	11 (8.2)	Not reached [-; -]	134	67 (50.0)	16.00 [12.00; -]	0.10 [0.05; 0.20]	< 0.001	
Race									
White	166	12 (7.2)	Not reached [-; -]	147	76 (51.7)	13.14 [9.86; -]	0.07 [0.04; 0.14]	< 0.001	0.476
Non-white	73	5 (6.8)	Not reached [-; -]	89	34 (38.2)	21.71 [21.43; -]	0.09 [0.03; 0.28]	< 0.001	
Geographic Region									
North America	57	2 (3.5)	Not reached [-; -]	51	23 (45.1)	Not reached [10.14; -]	0.03 [0.00; 0.21]	< 0.001	0.410
Europe	97	9 (9.3)	Not reached [-; -]	101	46 (45.5)	21.43 [12.14; -]	0.13 [0.06; 0.29]	< 0.001	
Rest of World	85	6 (7.1)	Not reached [-; -]	84	41 (48.8)	18.14 [11.43; -]	0.06 [0.02; 0.18]	< 0.001	
Sex									
Male	197	14 (7.1)	Not reached [-; -]	181	80 (44.2)	21.71 [14.00; -]	0.11 [0.06; 0.19]	< 0.001	0.637
Female	42	3 (7.1)	Not reached [-; -]	55	30 (54.5)	13.14 [9.00; -]	n.a. [n.a.; n.a.]	0.986	
ECOG at Baseline									
0	136	8 (5.9)	Not reached [-; -]	124	47 (37.9)	Not reached [-; -]	0.13 [0.06; 0.27]	< 0.001	0.713
1-2	103	9 (8.7)	Not reached [-; -]	111	62 (55.9)	12.29 [8.71; 21.43]	0.05 [0.02; 0.13]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	3 (4.9)	Not reached [-; -]	44	18 (40.9)	21.71 [12.71; -]	0.08 [0.02; 0.29]	< 0.001	0.776
Lower Tract	176	14 (8.0)	Not reached [-; -]	192	92 (47.9)	18.14 [12.14; -]	0.08 [0.04; 0.16]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	21 (44.7)	Not reached [10.14; -]	0.11 [0.03; 0.37]	< 0.001	0.461
Absent	192	13 (6.8)	Not reached [-; -]	189	89 (47.1)	21.43 [12.71; -]	0.08 [0.04; 0.15]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	11 (8.0)	Not reached [-; -]	138	66 (47.8)	18.14 [12.29; -]	0.08 [0.04; 0.17]	< 0.001	0.674
Low	101	6 (5.9)	Not reached [-; -]	98	44 (44.9)	21.71 [12.14; -]	0.09 [0.04; 0.21]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b			N ^b					
Metastatic Disease Site									
Visceral metastases	169	13 (7.7)	Not reached [-; -]	157	76 (48.4)	18.14 [12.29; -]	0.08 [0.04; 0.16]	< 0.001	0.652
Lymph node only	60	3 (5.0)	Not reached [-; -]	65	28 (43.1)	21.71 [11.43; -]	0.08 [0.02; 0.26]	< 0.001	
Renal Function									
Normal	78	5 (6.4)	Not reached [-; -]	81	34 (42.0)	Not reached [12.29; -]	0.05 [0.01; 0.19]	< 0.001	0.097
Mild	115	11 (9.6)	Not reached [-; -]	118	55 (46.6)	Not reached [12.57; -]	0.14 [0.07; 0.27]	< 0.001	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	21 (56.8)	12.71 [6.14; -]	0.02 [0.00; 0.17]	< 0.001	
SOC^g: General disorders and administration site conditions									
Age									
< 65	105	6 (5.7)	Not reached [-; -]	102	10 (9.8)	Not reached [-; -]	0.28 [0.08; 1.00]	0.050 ^h	0.864
≥ 65	134	7 (5.2)	Not reached [-; -]	134	14 (10.4)	Not reached [-; -]	0.32 [0.12; 0.90]	0.031	
Geographic Region									
North America	57	4 (7.0)	Not reached [-; -]	51	3 (5.9)	Not reached [-; -]	0.60 [0.10; 3.57]	0.572	0.097
Europe	97	3 (3.1)	Not reached [-; -]	101	15 (14.9)	Not reached [-; -]	0.07 [0.01; 0.50]	0.008	
Rest of World	85	6 (7.1)	Not reached [-; -]	84	6 (7.1)	Not reached [-; -]	0.72 [0.22; 2.38]	0.593	
Sex									
Male	197	11 (5.6)	Not reached [-; -]	181	17 (9.4)	Not reached [-; -]	0.34 [0.14; 0.83]	0.018	0.540
Female	42	2 (4.8)	Not reached [-; -]	55	7 (12.7)	Not reached [-; -]	0.18 [0.02; 1.47]	0.110	
ECOG at Baseline									
0	136	5 (3.7)	Not reached [-; -]	124	12 (9.7)	Not reached [-; -]	0.28 [0.09; 0.87]	0.028	0.341
1-2	103	8 (7.8)	Not reached [-; -]	111	12 (10.8)	Not reached [-; -]	0.33 [0.11; 1.03]	0.056	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994	0.070
Lower Tract	176	12 (6.8)	Not reached [-; -]	192	18 (9.4)	Not reached [-; -]	0.44 [0.19; 1.03]	0.058	
Stratification Factor: Liver Metastases									
Present	47	6 (12.8)	Not reached [-; -]	47	6 (12.8)	Not reached [-; -]	0.65 [0.18; 2.30]	0.502	0.117
Absent	192	7 (3.6)	Not reached [-; -]	189	18 (9.5)	Not reached [-; -]	0.20 [0.07; 0.58]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	5 (3.6)	Not reached [-; -]	138	13 (9.4)	Not reached [-; -]	0.20 [0.06; 0.72]	0.014	0.338

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
Low	101	8 (7.9)	Not reached [-; -]	98	11 (11.2)	Not reached [-; -]	0.42 [0.15; 1.21]	0.110	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	6 (7.4)	Not reached [-; -]	0.35 [0.07; 1.72]	0.194	0.816
Mild	115	6 (5.2)	Not reached [-; -]	118	10 (8.5)	Not reached [-; -]	0.26 [0.07; 0.96]	0.043	
Moderate/Severe	46	4 (8.7)	Not reached [-; -]	37	8 (21.6)	Not reached [-; -]	0.27 [0.07; 1.00]	0.050 ⁱ	
SOC ^g : Infections and infestations									
Age									
< 65	105	8 (7.6)	Not reached [-; -]	102	13 (12.7)	Not reached [-; -]	0.44 [0.17; 1.11]	0.083	0.630
≥ 65	134	20 (14.9)	Not reached [-; -]	134	26 (19.4)	Not reached [-; -]	0.56 [0.30; 1.05]	0.070	
Race									
White	166	18 (10.8)	Not reached [-; -]	147	26 (17.7)	Not reached [-; -]	0.46 [0.24; 0.87]	0.016	0.333
Non-white	73	10 (13.7)	Not reached [87.71; -]	89	13 (14.6)	Not reached [-; -]	0.65 [0.26; 1.60]	0.347	
Geographic Region									
North America	57	8 (14.0)	Not reached [-; -]	51	9 (17.6)	Not reached [-; -]	0.58 [0.21; 1.57]	0.282	0.416
Europe	97	10 (10.3)	Not reached [-; -]	101	21 (20.8)	Not reached [-; -]	0.38 [0.17; 0.85]	0.018	
Rest of World	85	10 (11.8)	Not reached [-; -]	84	9 (10.7)	Not reached [-; -]	0.74 [0.28; 1.95]	0.541	
Sex									
Male	197	21 (10.7)	Not reached [-; -]	181	29 (16.0)	Not reached [-; -]	0.48 [0.26; 0.88]	0.017	0.508
Female	42	7 (16.7)	Not reached [-; -]	55	10 (18.2)	Not reached [-; -]	0.70 [0.25; 1.95]	0.492	
ECOG at Baseline									
0	136	13 (9.6)	Not reached [-; -]	124	15 (12.1)	Not reached [-; -]	0.72 [0.34; 1.54]	0.398	0.587
1-2	103	15 (14.6)	Not reached [-; -]	111	24 (21.6)	Not reached [-; -]	0.40 [0.20; 0.82]	0.012	
Primary Disease Site of Origin									
Upper Tract	61	3 (4.9)	Not reached [-; -]	44	4 (9.1)	Not reached [-; -]	0.35 [0.06; 1.92]	0.227	0.651
Lower Tract	176	25 (14.2)	Not reached [-; -]	192	35 (18.2)	Not reached [-; -]	0.57 [0.33; 0.99]	0.045	
Stratification Factor: PD-L1 Expression									
High	138	17 (12.3)	Not reached [-; -]	138	23 (16.7)	Not reached [-; -]	0.55 [0.28; 1.06]	0.075	0.836
Low	101	11 (10.9)	Not reached [-; -]	98	16 (16.3)	Not reached [-; -]	0.48 [0.21; 1.09]	0.078	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
Metastatic Disease Site									
Visceral metastases	169	18 (10.7)	Not reached [-; -]	157	26 (16.6)	Not reached [-; -]	0.47 [0.25; 0.89]	0.021	0.993
Lymph node only	60	7 (11.7)	Not reached [87.71; -]	65	11 (16.9)	Not reached [-; -]	0.44 [0.15; 1.28]	0.133	
Renal Function									
Normal	78	10 (12.8)	Not reached [-; -]	81	16 (19.8)	Not reached [-; -]	0.57 [0.25; 1.29]	0.176	0.980
Mild	115	11 (9.6)	Not reached [-; -]	118	15 (12.7)	Not reached [-; -]	0.67 [0.31; 1.46]	0.315	
Moderate/Severe	46	7 (15.2)	Not reached [87.71; -]	37	8 (21.6)	Not reached [-; -]	0.24 [0.07; 0.87]	0.029	
SOC ^g : Investigations									
Age									
< 65	105	12 (11.4)	Not reached [-; -]	102	10 (9.8)	Not reached [-; -]	0.64 [0.24; 1.69]	0.370	0.630
≥ 65	134	21 (15.7)	Not reached [-; -]	134	24 (17.9)	Not reached [-; -]	0.52 [0.27; 1.01]	0.053	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	8 (15.7)	Not reached [-; -]	0.10 [0.01; 0.81]	0.031	0.157
Europe	97	15 (15.5)	Not reached [-; -]	101	12 (11.9)	Not reached [-; -]	0.79 [0.34; 1.82]	0.574	
Rest of World	85	15 (17.6)	Not reached [-; -]	84	14 (16.7)	Not reached [-; -]	0.66 [0.29; 1.48]	0.310	
Sex									
Male	197	29 (14.7)	Not reached [-; -]	181	28 (15.5)	Not reached [-; -]	0.57 [0.31; 1.01]	0.056	0.913
Female	42	4 (9.5)	Not reached [-; -]	55	6 (10.9)	Not reached [-; -]	0.40 [0.08; 1.97]	0.258	
ECOG at Baseline									
0	136	18 (13.2)	Not reached [-; -]	124	23 (18.5)	Not reached [-; -]	0.47 [0.24; 0.93]	0.031	0.100
1-2	103	15 (14.6)	Not reached [-; -]	111	11 (9.9)	Not reached [-; -]	0.70 [0.28; 1.76]	0.454	
Primary Disease Site of Origin									
Upper Tract	61	11 (18.0)	Not reached [-; -]	44	9 (20.5)	Not reached [-; -]	0.53 [0.20; 1.43]	0.213	0.913
Lower Tract	176	22 (12.5)	Not reached [-; -]	192	25 (13.0)	Not reached [-; -]	0.54 [0.28; 1.05]	0.069	
Stratification Factor: Liver Metastases									
Present	47	9 (19.1)	Not reached [46.86; -]	47	8 (17.0)	Not reached [-; -]	0.58 [0.19; 1.78]	0.345	0.559
Absent	192	24 (12.5)	Not reached [-; -]	189	26 (13.8)	Not reached [-; -]	0.55 [0.29; 1.02]	0.058	
Stratification Factor: PD-L1 Expression									
High	138	17 (12.3)	Not reached [-; -]	138	20 (14.5)	Not reached [-; -]	0.46 [0.21; 0.97]	0.042	0.571

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
Low	101	16 (15.8)	Not reached [-; -]	98	14 (14.3)	Not reached [-; -]	0.69 [0.31; 1.52]	0.356	
Metastatic Disease Site									
Visceral metastases	169	24 (14.2)	Not reached [-; -]	157	25 (15.9)	Not reached [-; -]	0.55 [0.29; 1.03]	0.060	0.981
Lymph node only	60	7 (11.7)	Not reached [-; -]	65	8 (12.3)	Not reached [-; -]	0.47 [0.14; 1.57]	0.222	
Renal Function									
Normal	78	10 (12.8)	Not reached [-; -]	81	7 (8.6)	Not reached [-; -]	1.13 [0.41; 3.13]	0.809	0.221
Mild	115	17 (14.8)	Not reached [-; -]	118	17 (14.4)	Not reached [-; -]	0.50 [0.22; 1.13]	0.096	
Moderate/Severe	46	6 (13.0)	Not reached [-; -]	37	10 (27.0)	Not reached [21.43; -]	0.25 [0.08; 0.82]	0.022	
SOC ^g : Skin and subcutaneous tissue disorders									
Age									
< 65	105	15 (14.3)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.997
≥ 65	134	24 (17.9)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Race									
White	166	20 (12.0)	Not reached [-; -]	147	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997
Non-white	73	19 (26.0)	Not reached [-; -]	89	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Geographic Region									
North America	57	7 (12.3)	Not reached [-; -]	51	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.055	> 0.999
Europe	97	14 (14.4)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Rest of World	85	18 (21.2)	Not reached [-; -]	84	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Sex									
Male	197	34 (17.3)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997
Female	42	5 (11.9)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.027	
ECOG at Baseline									
0	136	25 (18.4)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997
1-2	103	14 (13.6)	Not reached [-; -]	111	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	
Primary Disease Site of Origin									
Upper Tract	61	15 (24.6)	Not reached [65.00; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
Lower Tract	176	24 (13.6)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: Liver Metastases	
Present	47	6 (12.8)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022	0.997	
Absent	192	33 (17.2)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001		
Stratification Factor: PD-L1 Expression										
High	138	23 (16.7)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997	
Low	101	16 (15.8)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001		
Metastatic Disease Site										
Visceral metastases	169	28 (16.6)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997	
Lymph node only	60	11 (18.3)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.016		
Renal Function										
Normal	78	11 (14.1)	Not reached [-; -]	81	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	> 0.999	
Mild	115	19 (16.5)	Not reached [-; -]	118	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001		
Moderate/Severe	46	9 (19.6)	Not reached [57.00; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.044		
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin eligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A system organ class appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>h: Unrounded p-value < 0.050</p> <p>i: Unrounded p-value > 0.050</p> <p>CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class</p>										

Tabelle 4G-92: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE Grad 3-5) (PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Blood and lymphatic system disorders - PT^g: Anaemia									
Age									
< 65	105	2 (1.9)	Not reached [-; -]	102	26 (25.5)	Not reached [-; -]	0.03 [0.00; 0.24]	< 0.001	0.967
≥ 65	134	3 (2.2)	Not reached [-; -]	134	42 (31.3)	Not reached [21.71; -]	0.03 [0.01; 0.14]	< 0.001	
Race									
White	166	5 (3.0)	Not reached [-; -]	147	48 (32.7)	Not reached [-; -]	0.04 [0.01; 0.14]	< 0.001	0.123
Non-white	73	0 (0.0)	Not reached [-; -]	89	20 (22.5)	Not reached [21.71; -]	n.a. [n.a.; n.a.]	< 0.001	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	17 (33.3)	Not reached [13.86; -]	n.a. [n.a.; n.a.]	0.990	0.101
Europe	97	4 (4.1)	Not reached [-; -]	101	30 (29.7)	Not reached [-; -]	0.08 [0.03; 0.28]	< 0.001	
Rest of World	85	0 (0.0)	Not reached [-; -]	84	21 (25.0)	Not reached [21.71; -]	n.a. [n.a.; n.a.]	< 0.001	
Sex									
Male	197	4 (2.0)	Not reached [-; -]	181	48 (26.5)	Not reached [-; -]	0.04 [0.01; 0.14]	< 0.001	0.864
Female	42	1 (2.4)	Not reached [-; -]	55	20 (36.4)	Not reached [17.00; -]	n.a. [n.a.; n.a.]	0.989	
ECOG at Baseline									
0	136	1 (0.7)	Not reached [-; -]	124	28 (22.6)	Not reached [-; -]	0.03 [0.00; 0.21]	< 0.001	0.293
1-2	103	4 (3.9)	Not reached [-; -]	111	39 (35.1)	Not reached [21.43; -]	0.04 [0.01; 0.17]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	12 (27.3)	Not reached [21.71; -]	0.04 [0.00; 0.32]	0.002	0.867
Lower Tract	176	4 (2.3)	Not reached [-; -]	192	56 (29.2)	Not reached [-; -]	0.03 [0.01; 0.13]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	Not reached [-; -]	47	12 (25.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.222
Absent	192	5 (2.6)	Not reached [-; -]	189	56 (29.6)	Not reached [-; -]	0.04 [0.01; 0.13]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	4 (2.9)	Not reached [-; -]	138	41 (29.7)	Not reached [-; -]	0.04 [0.01; 0.17]	< 0.001	0.353
Low	101	1 (1.0)	Not reached [-; -]	98	27 (27.6)	Not reached [21.71; -]	0.02 [0.00; 0.18]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	45 (28.7)	Not reached [-; -]	0.03 [0.01; 0.14]	< 0.001	0.707
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	19 (29.2)	Not reached [21.71; -]	0.04 [0.01; 0.31]	0.002	
Renal Function									
Normal	78	2 (2.6)	Not reached [-; -]	81	21 (25.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.988	0.208
Mild	115	3 (2.6)	Not reached [-; -]	118	33 (28.0)	Not reached [-; -]	0.08 [0.02; 0.26]	< 0.001	
Moderate/Severe	46	0 (0.0)	Not reached [-; -]	37	14 (37.8)	Not reached [12.00; -]	n.a. [n.a.; n.a.]	< 0.001	
SOC: Blood and lymphatic system disorders - PT^g: Neutropenia									
Age									
< 65	105	1 (1.0)	Not reached [-; -]	102	22 (21.6)	Not reached [-; -]	0.04 [0.01; 0.29]	0.001	0.076
≥ 65	134	7 (5.2)	Not reached [-; -]	134	30 (22.4)	Not reached [-; -]	0.20 [0.09; 0.46]	< 0.001	
Race									
White	166	5 (3.0)	Not reached [-; -]	147	39 (26.5)	Not reached [-; -]	0.09 [0.04; 0.24]	< 0.001	0.216
Non-white	73	3 (4.1)	Not reached [-; -]	89	13 (14.6)	Not reached [-; -]	0.26 [0.07; 0.92]	0.036	
Geographic Region									
North America	57	0 (0.0)	Not reached [-; -]	51	8 (15.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.191
Europe	97	5 (5.2)	Not reached [-; -]	101	22 (21.8)	Not reached [-; -]	0.21 [0.08; 0.55]	0.002	
Rest of World	85	3 (3.5)	Not reached [-; -]	84	22 (26.2)	Not reached [-; -]	0.11 [0.03; 0.38]	< 0.001	
Sex									
Male	197	8 (4.1)	Not reached [-; -]	181	37 (20.4)	Not reached [-; -]	0.17 [0.08; 0.37]	< 0.001	0.050 ^h
Female	42	0 (0.0)	Not reached [-; -]	55	15 (27.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
ECOG at Baseline									
0	136	6 (4.4)	Not reached [-; -]	124	22 (17.7)	Not reached [-; -]	0.23 [0.09; 0.56]	0.001	0.090
1-2	103	2 (1.9)	Not reached [-; -]	111	30 (27.0)	Not reached [-; -]	0.06 [0.01; 0.25]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	7 (15.9)	Not reached [-; -]	0.19 [0.04; 0.93]	0.040	0.631
Lower Tract	176	6 (3.4)	Not reached [-; -]	192	45 (23.4)	Not reached [-; -]	0.12 [0.05; 0.29]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	3 (6.4)	Not reached [-; -]	47	12 (25.5)	Not reached [-; -]	0.22 [0.06; 0.80]	0.021	0.354

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Absent	192	5 (2.6)	Not reached [-; -]	189	40 (21.2)	Not reached [-; -]	0.11 [0.04; 0.27]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	138	5 (3.6)	Not reached [-; -]	138	32 (23.2)	Not reached [-; -]	0.13 [0.05; 0.35]	< 0.001	0.906
Low	101	3 (3.0)	Not reached [-; -]	98	20 (20.4)	Not reached [-; -]	0.13 [0.04; 0.43]	< 0.001	
Metastatic Disease Site									
Visceral metastases	169	6 (3.6)	Not reached [-; -]	157	37 (23.6)	Not reached [-; -]	0.13 [0.06; 0.31]	< 0.001	0.674
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	10 (15.4)	Not reached [-; -]	0.19 [0.04; 0.88]	0.034	
Renal Function									
Normal	78	2 (2.6)	Not reached [-; -]	81	18 (22.2)	Not reached [-; -]	0.10 [0.02; 0.43]	0.002	0.860
Mild	115	5 (4.3)	Not reached [-; -]	118	28 (23.7)	Not reached [-; -]	0.16 [0.06; 0.42]	< 0.001	
Moderate/Severe	46	1 (2.2)	Not reached [-; -]	37	6 (16.2)	Not reached [-; -]	0.12 [0.01; 0.97]	0.047	
SOC: Blood and lymphatic system disorders - PT ^g : Thrombocytopenia									
Age									
< 65	105	1 (1.0)	Not reached [-; -]	102	7 (6.9)	Not reached [-; -]	0.13 [0.02; 1.07]	0.058	0.457
≥ 65	134	1 (0.7)	Not reached [-; -]	134	21 (15.7)	Not reached [-; -]	0.04 [0.01; 0.31]	0.002	
Race									
White	166	2 (1.2)	Not reached [-; -]	147	23 (15.6)	Not reached [-; -]	0.07 [0.02; 0.28]	< 0.001	0.469
Non-white	73	0 (0.0)	Not reached [-; -]	89	5 (5.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.041	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	5 (9.8)	Not reached [-; -]	0.16 [0.02; 1.34]	0.091	0.340
Europe	97	1 (1.0)	Not reached [-; -]	101	12 (11.9)	Not reached [-; -]	0.08 [0.01; 0.61]	0.015	
Rest of World	85	0 (0.0)	Not reached [-; -]	84	11 (13.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Sex									
Male	197	2 (1.0)	Not reached [-; -]	181	21 (11.6)	Not reached [-; -]	0.08 [0.02; 0.34]	< 0.001	0.360
Female	42	0 (0.0)	Not reached [-; -]	55	7 (12.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.017	
ECOG at Baseline									
0	136	1 (0.7)	Not reached [-; -]	124	10 (8.1)	Not reached [-; -]	0.09 [0.01; 0.67]	0.019	0.759
1-2	103	1 (1.0)	Not reached [-; -]	111	17 (15.3)	Not reached [-; -]	0.06 [0.01; 0.41]	0.005	

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Primary Disease Site of Origin										
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	0.23 [0.02; 2.21]	0.203	0.263	
Lower Tract	176	1 (0.6)	Not reached [-; -]	192	25 (13.0)	Not reached [-; -]	0.04 [0.01; 0.29]	0.002		
Stratification Factor: Liver Metastases										
Present	47	0 (0.0)	Not reached [-; -]	47	6 (12.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.012	0.347	
Absent	192	2 (1.0)	Not reached [-; -]	189	22 (11.6)	Not reached [-; -]	0.08 [0.02; 0.34]	< 0.001		
Stratification Factor: PD-L1 Expression										
High	138	1 (0.7)	Not reached [-; -]	138	17 (12.3)	Not reached [-; -]	0.05 [0.01; 0.40]	0.005	0.770	
Low	101	1 (1.0)	Not reached [-; -]	98	11 (11.2)	Not reached [-; -]	0.08 [0.01; 0.62]	0.016		
Metastatic Disease Site										
Visceral metastases	169	0 (0.0)	Not reached [-; -]	157	21 (13.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.074	
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	6 (9.2)	Not reached [-; -]	0.16 [0.02; 1.36]	0.093		
Renal Function										
Normal	78	0 (0.0)	Not reached [-; -]	81	8 (9.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.193	
Mild	115	2 (1.7)	Not reached [-; -]	118	13 (11.0)	Not reached [-; -]	0.14 [0.03; 0.64]	0.011		
Moderate/Severe	46	0 (0.0)	Not reached [-; -]	37	7 (18.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002		
SOC: General disorders and administration site conditions - PT^g: Fatigue										
Age										
< 65	105	3 (2.9)	Not reached [-; -]	102	5 (4.9)	Not reached [-; -]	0.39 [0.08; 1.90]	0.242	0.764	
≥ 65	134	3 (2.2)	Not reached [-; -]	134	7 (5.2)	Not reached [-; -]	0.24 [0.05; 1.20]	0.082		
Geographic Region										
North America	57	3 (5.3)	n.c.	51	3 (5.9)	n.c.	n.c.	n.c.	n.c.	
Europe	97	0 (0.0)	n.c.	101	6 (5.9)	n.c.	n.c.	n.c.		
Rest of World	85	3 (3.5)	n.c.	84	3 (3.6)	n.c.	n.c.	n.c.		
Sex										
Male	197	6 (3.0)	Not reached [-; -]	181	8 (4.4)	Not reached [-; -]	0.40 [0.12; 1.36]	0.143	0.081	
Female	42	0 (0.0)	Not reached [-; -]	55	4 (7.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.077		
ECOG at Baseline										
0	136	2 (1.5)	n.c.	124	7 (5.6)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
1-2	103	4 (3.9)	n.c.	111	5 (4.5)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	3 (6.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.467
Lower Tract	176	5 (2.8)	Not reached [-; -]	192	9 (4.7)	Not reached [-; -]	0.44 [0.13; 1.43]	0.171	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	2 (4.3)	Not reached [-; -]	1.01 [0.14; 7.18]	0.991	0.337
Absent	192	4 (2.1)	Not reached [-; -]	189	10 (5.3)	Not reached [-; -]	0.17 [0.04; 0.76]	0.020	
Stratification Factor: PD-L1 Expression									
High	138	2 (1.4)	Not reached [-; -]	138	8 (5.8)	Not reached [-; -]	0.21 [0.04; 1.03]	0.054	0.173
Low	101	4 (4.0)	Not reached [-; -]	98	4 (4.1)	Not reached [-; -]	0.47 [0.09; 2.51]	0.377	
Metastatic Disease Site									
Visceral metastases	169	4 (2.4)	Not reached [-; -]	157	8 (5.1)	Not reached [-; -]	0.23 [0.05; 1.07]	0.061	0.112
Lymph node only	60	0 (0.0)	Not reached [-; -]	65	4 (6.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.045	
Renal Function									
Normal	78	2 (2.6)	n.c.	81	3 (3.7)	n.c.	n.c.	n.c.	n.c.
Mild	115	2 (1.7)	n.c.	118	5 (4.2)	n.c.	n.c.	n.c.	
Moderate/Severe	46	2 (4.3)	n.c.	37	4 (10.8)	n.c.	n.c.	n.c.	
SOC: Infections and infestations - PT^g: Urinary tract infection									
Age									
< 65	105	3 (2.9)	Not reached [-; -]	102	3 (2.9)	26.71 [26.71; -]	0.51 [0.08; 3.12]	0.465	0.227
≥ 65	134	5 (3.7)	Not reached [-; -]	134	16 (11.9)	Not reached [-; -]	0.28 [0.10; 0.76]	0.013	
Race									
White	166	5 (3.0)	Not reached [-; -]	147	14 (9.5)	26.71 [26.71; -]	0.23 [0.08; 0.69]	0.009	0.335
Non-white	73	3 (4.1)	Not reached [-; -]	89	5 (5.6)	Not reached [-; -]	0.59 [0.13; 2.65]	0.487	
Geographic Region									
North America	57	1 (1.8)	Not reached [-; -]	51	4 (7.8)	Not reached [-; -]	0.15 [0.02; 1.47]	0.104	0.217
Europe	97	2 (2.1)	Not reached [-; -]	101	10 (9.9)	Not reached [-; -]	0.20 [0.04; 0.93]	0.039	
Rest of World	85	5 (5.9)	Not reached [-; -]	84	5 (6.0)	26.71 [-; -]	0.65 [0.17; 2.49]	0.532	

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Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Sex										
Male	197	6 (3.0)	Not reached [-; -]	181	12 (6.6)	Not reached [-; -]	0.41 [0.15; 1.11]	0.080	0.849	
Female	42	2 (4.8)	Not reached [-; -]	55	7 (12.7)	26.71 [26.71; -]	0.19 [0.03; 1.14]	0.070		
ECOG at Baseline										
0	136	4 (2.9)	Not reached [-; -]	124	6 (4.8)	Not reached [-; -]	0.62 [0.17; 2.18]	0.454	0.446	
1-2	103	4 (3.9)	Not reached [-; -]	111	13 (11.7)	26.71 [-; -]	0.20 [0.06; 0.69]	0.011		
Primary Disease Site of Origin										
Upper Tract	61	2 (3.3)	Not reached [-; -]	44	1 (2.3)	Not reached [-; -]	1.45 [0.13; 15.96]	0.763	0.260	
Lower Tract	176	6 (3.4)	Not reached [-; -]	192	18 (9.4)	26.71 [26.71; -]	0.26 [0.09; 0.69]	0.007		
Stratification Factor: PD-L1 Expression										
High	138	4 (2.9)	Not reached [-; -]	138	12 (8.7)	26.71 [-; -]	0.22 [0.06; 0.79]	0.020	0.545	
Low	101	4 (4.0)	Not reached [-; -]	98	7 (7.1)	Not reached [-; -]	0.47 [0.13; 1.65]	0.238		
Metastatic Disease Site										
Visceral metastases	169	6 (3.6)	Not reached [-; -]	157	13 (8.3)	Not reached [-; -]	0.36 [0.13; 0.96]	0.042	0.415	
Lymph node only	60	1 (1.7)	Not reached [-; -]	65	6 (9.2)	26.71 [-; -]	0.05 [0.00; 0.88]	0.040		
Renal Function										
Normal	78	3 (3.8)	Not reached [-; -]	81	7 (8.6)	26.71 [26.71; -]	0.32 [0.07; 1.44]	0.138	0.898	
Mild	115	3 (2.6)	Not reached [-; -]	118	9 (7.6)	Not reached [-; -]	0.29 [0.08; 1.07]	0.064		
Moderate/Severe	46	2 (4.3)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	0.40 [0.06; 2.51]	0.330		
SOC: Investigations - PT ^g : Neutrophil count decreased										
Age										
< 65	105	2 (1.9)	Not reached [-; -]	102	8 (7.8)	Not reached [-; -]	0.23 [0.05; 1.07]	0.062	0.666	
≥ 65	134	2 (1.5)	Not reached [-; -]	134	13 (9.7)	Not reached [-; -]	0.14 [0.03; 0.63]	0.010		
Race										
White	166	3 (1.8)	Not reached [-; -]	147	7 (4.8)	Not reached [-; -]	0.36 [0.09; 1.40]	0.140	0.193	
Non-white	73	1 (1.4)	Not reached [-; -]	89	14 (15.7)	Not reached [-; -]	0.08 [0.01; 0.59]	0.014		
Geographic Region										
North America	57	0 (0.0)	Not reached [-; -]	51	5 (9.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.014	0.312	
Europe	97	2 (2.1)	Not reached [-; -]	101	7 (6.9)	Not reached [-; -]	0.28 [0.06; 1.37]	0.116		

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	85	2 (2.4)	Not reached [-; -]	84	9 (10.7)	Not reached [-; -]	0.20 [0.04; 0.93]	0.040	
Sex									
Male	197	3 (1.5)	Not reached [-; -]	181	16 (8.8)	Not reached [-; -]	0.16 [0.05; 0.55]	0.004	0.760
Female	42	1 (2.4)	Not reached [-; -]	55	5 (9.1)	Not reached [-; -]	0.23 [0.03; 2.00]	0.184	
ECOG at Baseline									
0	136	2 (1.5)	Not reached [-; -]	124	16 (12.9)	Not reached [-; -]	0.10 [0.02; 0.45]	0.003	0.237
1-2	103	2 (1.9)	Not reached [-; -]	111	5 (4.5)	Not reached [-; -]	0.42 [0.08; 2.16]	0.298	
Primary Disease Site of Origin									
Upper Tract	61	1 (1.6)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	0.11 [0.01; 0.95]	0.045	0.620
Lower Tract	176	3 (1.7)	Not reached [-; -]	192	15 (7.8)	Not reached [-; -]	0.20 [0.06; 0.69]	0.011	
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	Not reached [-; -]	47	4 (8.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.043	0.227
Absent	192	4 (2.1)	Not reached [-; -]	189	17 (9.0)	Not reached [-; -]	0.21 [0.07; 0.63]	0.005	
Stratification Factor: PD-L1 Expression									
High	138	3 (2.2)	Not reached [-; -]	138	11 (8.0)	Not reached [-; -]	0.25 [0.07; 0.89]	0.032	0.371
Low	101	1 (1.0)	Not reached [-; -]	98	10 (10.2)	Not reached [-; -]	0.09 [0.01; 0.71]	0.022	
Metastatic Disease Site									
Visceral metastases	169	2 (1.2)	Not reached [-; -]	157	14 (8.9)	Not reached [-; -]	0.13 [0.03; 0.56]	0.006	0.370
Lymph node only	60	2 (3.3)	Not reached [-; -]	65	6 (9.2)	Not reached [-; -]	0.32 [0.06; 1.57]	0.158	
Renal Function									
Normal	78	3 (3.8)	Not reached [-; -]	81	5 (6.2)	Not reached [-; -]	0.58 [0.14; 2.41]	0.451	0.074
Mild	115	1 (0.9)	Not reached [-; -]	118	11 (9.3)	Not reached [-; -]	0.09 [0.01; 0.68]	0.020	
Moderate/Severe	46	0 (0.0)	Not reached [-; -]	37	5 (13.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
SOC: Investigations - PT ^g : Platelet count decreased									
Age									
< 65	105	0 (0.0)	Not reached [-; -]	102	1 (1.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.289	0.997
≥ 65	134	0 (0.0)	Not reached [-; -]	134	11 (8.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Race									
White	166	0 (0.0)	n.c.	147	5 (3.4)	n.c.	n.c.	n.c.	n.c.

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Non-white	73	0 (0.0)	n.c.	89	7 (7.9)	n.c.	n.c.	n.c.	
Geographic Region									
North America	57	0 (0.0)	n.c.	51	4 (7.8)	n.c.	n.c.	n.c.	n.c.
Europe	97	0 (0.0)	n.c.	101	4 (4.0)	n.c.	n.c.	n.c.	
Rest of World	85	0 (0.0)	n.c.	84	4 (4.8)	n.c.	n.c.	n.c.	
Sex									
Male	197	0 (0.0)	Not reached [-; -]	181	10 (5.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.997
Female	42	0 (0.0)	Not reached [-; -]	55	2 (3.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.195	
ECOG at Baseline									
0	136	0 (0.0)	n.c.	124	9 (7.3)	n.c.	n.c.	n.c.	n.c.
1-2	103	0 (0.0)	n.c.	111	3 (2.7)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	61	0 (0.0)	Not reached [-; -]	44	2 (4.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.095	0.997
Lower Tract	176	0 (0.0)	Not reached [-; -]	192	10 (5.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Stratification Factor: Liver Metastases									
Present	47	0 (0.0)	n.c.	47	3 (6.4)	n.c.	n.c.	n.c.	n.c.
Absent	192	0 (0.0)	n.c.	189	9 (4.8)	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression									
High	138	0 (0.0)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Low	101	0 (0.0)	n.c.	98	4 (4.1)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	169	0 (0.0)	n.c.	157	7 (4.5)	n.c.	n.c.	n.c.	n.c.
Lymph node only	60	0 (0.0)	n.c.	65	4 (6.2)	n.c.	n.c.	n.c.	
Renal Function									
Normal	78	0 (0.0)	n.c.	81	1 (1.2)	n.c.	n.c.	n.c.	n.c.
Mild	115	0 (0.0)	n.c.	118	5 (4.2)	n.c.	n.c.	n.c.	
Moderate/Severe	46	0 (0.0)	n.c.	37	6 (16.2)	n.c.	n.c.	n.c.	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Metabolism and nutrition disorders - PT^g: Hyperglycaemia									
Age									
< 65	105	13 (12.4)	Not reached [-; -]	102	2 (2.0)	Not reached [-; -]	4.16 [0.89; 19.40]	0.070	0.191
≥ 65	134	7 (5.2)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.008	
Race									
White	166	10 (6.0)	Not reached [-; -]	147	1 (0.7)	Not reached [-; -]	7.13 [0.89; 57.05]	0.064	0.801
Non-white	73	10 (13.7)	Not reached [-; -]	89	1 (1.1)	Not reached [-; -]	9.14 [1.13; 73.88]	0.038	
Geographic Region									
North America	57	3 (5.3)	Not reached [-; -]	51	1 (2.0)	Not reached [-; -]	2.74 [0.28; 26.34]	0.383	0.302
Europe	97	7 (7.2)	Not reached [-; -]	101	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.011	
Rest of World	85	10 (11.8)	Not reached [-; -]	84	1 (1.2)	Not reached [-; -]	6.25 [0.76; 51.30]	0.088	
Sex									
Male	197	15 (7.6)	Not reached [-; -]	181	2 (1.1)	Not reached [-; -]	5.57 [1.25; 24.88]	0.025	0.218
Female	42	5 (11.9)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.039	
ECOG at Baseline									
0	136	14 (10.3)	Not reached [-; -]	124	1 (0.8)	Not reached [-; -]	11.38 [1.48; 87.48]	0.019	0.652
1-2	103	6 (5.8)	Not reached [-; -]	111	1 (0.9)	Not reached [-; -]	3.66 [0.40; 33.59]	0.251	
Primary Disease Site of Origin									
Upper Tract	61	5 (8.2)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.228	0.384
Lower Tract	176	15 (8.5)	Not reached [-; -]	192	2 (1.0)	Not reached [-; -]	7.38 [1.67; 32.58]	0.008	
Stratification Factor: Liver Metastases									
Present	47	4 (8.5)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.243	0.338
Absent	192	16 (8.3)	Not reached [-; -]	189	2 (1.1)	Not reached [-; -]	7.02 [1.60; 30.90]	0.010	
Stratification Factor: PD-L1 Expression									
High	138	9 (6.5)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	8.24 [1.03; 65.89]	0.047	0.888
Low	101	11 (10.9)	Not reached [-; -]	98	1 (1.0)	Not reached [-; -]	7.12 [0.88; 57.39]	0.065	
Renal Function									
Normal	78	8 (10.3)	Not reached [-; -]	81	1 (1.2)	Not reached [-; -]	7.67 [0.94; 62.34]	0.057	0.782
Mild	115	9 (7.8)	Not reached [-; -]	118	1 (0.8)	Not reached [-; -]	6.28 [0.76; 52.10]	0.089	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Moderate/Severe	46	3 (6.5)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.190	
SOC: Skin and subcutaneous tissue disorders - PT^g: Rash maculo-papular									
Age									
< 65	105	4 (3.8)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.167	0.997
≥ 65	134	12 (9.0)	Not reached [-; -]	134	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Race									
White	166	9 (5.4)	n.c.	147	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	73	7 (9.6)	n.c.	89	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	57	5 (8.8)	n.c.	51	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	97	3 (3.1)	n.c.	101	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	85	8 (9.4)	n.c.	84	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	197	14 (7.1)	Not reached [-; -]	181	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.997
Female	42	2 (4.8)	Not reached [-; -]	55	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.254	
ECOG at Baseline									
0	136	12 (8.8)	Not reached [-; -]	124	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
1-2	103	4 (3.9)	Not reached [-; -]	111	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.141	
Primary Disease Site of Origin									
Upper Tract	61	6 (9.8)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.088	0.997
Lower Tract	176	10 (5.7)	Not reached [-; -]	192	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Stratification Factor: Liver Metastases									
Present	47	2 (4.3)	Not reached [-; -]	47	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.155	0.997
Absent	192	14 (7.3)	Not reached [-; -]	189	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	138	11 (8.0)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.015	0.997
Low	101	5 (5.0)	Not reached [-; -]	98	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.027	
Metastatic Disease Site									
Visceral metastases	169	13 (7.7)	Not reached [-; -]	157	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Lymph node only	60	3 (5.0)	Not reached [-; -]	65	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.142	
Renal Function									
Normal	78	4 (5.1)	n.c.	81	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	115	9 (7.8)	n.c.	118	0 (0.0)	n.c.	n.c.	n.c.	
Moderate/Severe	46	3 (6.5)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	

a: Database Cutoff Date: 08AUG2023
b: Number of participants: all-participants-as-treated population, cisplatin eligible
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
g: A specific adverse event appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated
h: Unrounded p-value > 0.050
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class

Cisplatin ungeeignet

Nebenwirkungen

Unerwünschte Ereignisse gesamt

Tabelle 4G-93: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Age									
< 65	39	39 (100.0)	1.1 [1.0; 1.6]	28	27 (96.4)	1.0 [0.4; 1.1]	0.83 [0.50; 1.37]	0.470	0.965
≥ 65	162	161 (99.4)	1.0 [0.7; 1.1]	169	166 (98.2)	0.9 [0.6; 1.0]	0.83 [0.67; 1.03]	0.092	
Sex									
Male	145	144 (99.3)	1.1 [0.9; 1.1]	148	144 (97.3)	1.0 [0.9; 1.1]	0.88 [0.70; 1.11]	0.286	0.057
Female	56	56 (100.0)	1.0 [0.6; 1.1]	49	49 (100.0)	0.6 [0.4; 0.7]	0.56 [0.38; 0.84]	0.005	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	46 (100.0)	0.8 [0.6; 1.1]	33	32 (97.0)	0.4 [0.3; 0.7]	0.88 [0.55; 1.40]	0.580	0.754
Europe	73	72 (98.6)	1.1 [0.9; 1.3]	94	92 (97.9)	1.0 [0.7; 1.0]	0.75 [0.55; 1.03]	0.072	
Rest of World	82	82 (100.0)	1.1 [0.7; 1.3]	70	69 (98.6)	1.1 [0.6; 1.1]	0.80 [0.58; 1.10]	0.174	
ECOG at Baseline									
0	87	87 (100.0)	1.1 [0.7; 1.1]	85	85 (100.0)	0.9 [0.6; 1.0]	0.83 [0.61; 1.12]	0.219	0.781
1-2	114	113 (99.1)	1.0 [0.7; 1.1]	112	108 (96.4)	1.0 [0.4; 1.1]	0.81 [0.62; 1.05]	0.116	
Race									
White	141	140 (99.3)	1.1 [0.9; 1.1]	138	135 (97.8)	0.9 [0.6; 1.0]	0.76 [0.60; 0.96]	0.024	0.217
Non-white	60	60 (100.0)	1.0 [0.6; 1.1]	59	58 (98.3)	1.0 [0.4; 1.1]	0.98 [0.68; 1.41]	0.918	
Metastatic Disease Site									
Visceral metastases	147	146 (99.3)	1.0 [0.7; 1.1]	152	150 (98.7)	1.0 [0.6; 1.0]	0.84 [0.67; 1.06]	0.141	0.973
Lymph node only	43	43 (100.0)	1.1 [0.9; 1.4]	37	35 (94.6)	0.9 [0.4; 1.1]	0.85 [0.54; 1.33]	0.479	
Primary Disease Site of Origin									
Upper Tract	74	74 (100.0)	1.0 [0.6; 1.1]	53	51 (96.2)	0.7 [0.4; 1.1]	0.91 [0.64; 1.30]	0.611	0.529
Lower Tract	127	126 (99.2)	1.1 [0.9; 1.1]	143	141 (98.6)	1.0 [0.6; 1.0]	0.78 [0.61; 1.00]	0.048	
Renal Function									
Normal	6	6 (100.0)	0.9 [0.3; -]	13	12 (92.3)	1.1 [0.4; 2.1]	1.91 [0.66; 5.51]	0.230	0.169
Mild	49	49 (100.0)	1.1 [0.7; 1.3]	40	39 (97.5)	0.9 [0.4; 1.1]	0.79 [0.52; 1.22]	0.290	
Moderate/Severe	146	145 (99.3)	1.0 [0.7; 1.1]	144	142 (98.6)	0.9 [0.6; 1.0]	0.77 [0.61; 0.97]	0.029	
Stratification Factor: Liver Metastases									
Present	50	50 (100.0)	1.1 [0.7; 1.1]	49	48 (98.0)	1.0 [0.4; 1.1]	0.83 [0.56; 1.25]	0.376	0.908
Absent	151	150 (99.3)	1.1 [0.9; 1.1]	148	145 (98.0)	0.9 [0.6; 1.0]	0.82 [0.65; 1.03]	0.085	
Stratification Factor: PD-L1 Expression									
High	117	117 (100.0)	1.0 [0.7; 1.1]	114	112 (98.2)	0.7 [0.4; 1.0]	0.77 [0.59; 1.00]	0.052	0.479
Low	84	83 (98.8)	1.1 [0.7; 1.1]	83	81 (97.6)	1.0 [0.9; 1.1]	0.87 [0.64; 1.18]	0.368	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: all-participants-as-treated population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1									

*Schwerwiegende unerwünschte Ereignisse*Tabelle 4G-94: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro		Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
									Age
< 65	39	18 (46.2)	81.1 [24.3; -]	28	11 (39.3)	23.3 [18.3; -]	0.67 [0.29; 1.53]	0.345	0.603
≥ 65	162	95 (58.6)	26.9 [16.1; 48.0]	169	75 (44.4)	Not reached [14.4; -]	0.97 [0.71; 1.34]	0.870	
Sex									
Male	145	87 (60.0)	26.9 [15.3; 48.0]	148	65 (43.9)	23.3 [18.3; -]	1.00 [0.71; 1.41]	> 0.999	0.225
Female	56	26 (46.4)	Not reached [23.7; -]	49	21 (42.9)	Not reached [5.4; -]	0.71 [0.38; 1.31]	0.269	
Geographic Region									
North America	46	27 (58.7)	23.0 [2.9; -]	33	14 (42.4)	Not reached [8.6; -]	1.11 [0.57; 2.17]	0.760	0.779
Europe	73	45 (61.6)	30.6 [17.4; 48.0]	94	42 (44.7)	22.0 [10.9; -]	0.84 [0.53; 1.33]	0.446	
Rest of World	82	41 (50.0)	57.1 [15.9; -]	70	30 (42.9)	23.3 [16.3; -]	0.87 [0.53; 1.43]	0.576	
ECOG at Baseline									
0	87	47 (54.0)	35.4 [20.7; -]	85	34 (40.0)	Not reached [14.4; -]	0.92 [0.57; 1.48]	0.732	0.690
1-2	114	66 (57.9)	24.6 [11.3; 56.3]	112	52 (46.4)	22.0 [12.1; -]	0.89 [0.61; 1.31]	0.561	
Race									
White	141	81 (57.4)	24.3 [15.3; 48.0]	138	60 (43.5)	Not reached [12.1; -]	1.01 [0.71; 1.43]	0.953	0.463
Non-white	60	32 (53.3)	57.1 [24.3; -]	59	26 (44.1)	23.3 [16.3; -]	0.67 [0.38; 1.20]	0.182	
Metastatic Disease Site									
Visceral metastases	147	87 (59.2)	26.9 [15.9; 41.3]	152	70 (46.1)	22.0 [12.1; -]	0.91 [0.65; 1.27]	0.572	0.825
Lymph node only	43	22 (51.2)	48.0 [13.1; -]	37	14 (37.8)	Not reached [6.7; -]	0.94 [0.46; 1.89]	0.858	
Primary Disease Site of Origin									
Upper Tract	74	36 (48.6)	65.0 [19.4; -]	53	19 (35.8)	Not reached [18.3; -]	1.02 [0.57; 1.82]	0.947	0.850
Lower Tract	127	77 (60.6)	28.6 [13.4; 41.3]	143	66 (46.2)	22.0 [10.9; -]	0.92 [0.64; 1.31]	0.634	
Renal Function									
Normal	6	6 (100.0)	2.9 [1.0; -]	13	5 (38.5)	Not reached [2.0; -]	2.36 [0.63; 8.88]	0.203	0.181
Mild	49	23 (46.9)	65.0 [9.3; -]	40	12 (30.0)	Not reached [-; -]	1.50 [0.74; 3.04]	0.265	
Moderate/Severe	146	84 (57.5)	30.6 [20.9; 48.0]	144	69 (47.9)	20.1 [12.1; -]	0.77 [0.54; 1.08]	0.133	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: Liver Metastases	
Present	50	34 (68.0)	19.4 [7.9; 30.6]	49	24 (49.0)	19.3 [8.3; -]	1.01 [0.58; 1.77]	0.970	0.439	
Absent	151	79 (52.3)	39.1 [23.7; -]	148	62 (41.9)	23.3 [18.3; -]	0.87 [0.61; 1.24]	0.440		
Stratification Factor: PD-L1 Expression										
High	117	67 (57.3)	30.1 [17.4; 76.9]	114	44 (38.6)	23.3 [19.3; -]	1.09 [0.73; 1.63]	0.667	0.237	
Low	84	46 (54.8)	35.4 [15.3; -]	83	42 (50.6)	16.3 [8.9; -]	0.71 [0.45; 1.12]	0.143		
a: Database Cutoff Date: 08AUG2023										
b: Number of participants: all-participants-as-treated population, cisplatin ineligible										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1										

*Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)*Tabelle 4G-95: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Events (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Age	
< 65	39	26 (66.7)	30.1 [9.3; 45.7]	28	21 (75.0)	5.9 [2.1; 13.0]	0.41 [0.22; 0.78]	0.007	0.666	
≥ 65	162	131 (80.9)	9.4 [6.1; 13.0]	169	145 (85.8)	3.0 [2.1; 4.0]	0.48 [0.37; 0.61]	< 0.001		
Sex										
Male	145	117 (80.7)	10.0 [6.0; 15.3]	148	123 (83.1)	3.1 [2.1; 4.1]	0.52 [0.40; 0.69]	< 0.001	0.072	
Female	56	40 (71.4)	17.1 [9.0; 26.1]	49	43 (87.8)	3.1 [2.1; 4.0]	0.30 [0.19; 0.49]	< 0.001		
ECOG at Baseline										
0	87	69 (79.3)	13.1 [6.1; 20.1]	85	72 (84.7)	3.1 [2.1; 4.3]	0.43 [0.30; 0.62]	< 0.001	0.834	
1-2	114	88 (77.2)	9.8 [6.1; 16.1]	112	94 (83.9)	3.1 [2.1; 4.1]	0.48 [0.35; 0.66]	< 0.001		
Race										
White	141	109 (77.3)	8.7 [4.7; 13.1]	138	116 (84.1)	3.3 [2.1; 4.1]	0.52 [0.40; 0.69]	< 0.001	0.300	
Non-white	60	48 (80.0)	19.6 [10.4; 33.1]	59	50 (84.7)	2.6 [2.1; 4.1]	0.34 [0.22; 0.54]	< 0.001		

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Events (CTCAE-Grade 3-5)	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Metastatic Disease Site									
Visceral metastases	147	118 (80.3)	9.3 [6.0; 15.3]	152	130 (85.5)	2.9 [2.1; 3.6]	0.48 [0.37; 0.63]	< 0.001	0.959
Lymph node only	43	31 (72.1)	18.0 [6.1; 38.7]	37	29 (78.4)	4.1 [2.4; 6.7]	0.46 [0.26; 0.80]	0.006	
Primary Disease Site of Origin									
Upper Tract	74	55 (74.3)	17.1 [9.3; 24.6]	53	42 (79.2)	3.0 [2.1; 4.1]	0.43 [0.28; 0.66]	< 0.001	0.649
Lower Tract	127	102 (80.3)	9.1 [4.1; 15.3]	143	123 (86.0)	3.3 [2.1; 4.1]	0.49 [0.37; 0.66]	< 0.001	
Renal Function									
Normal	6	6 (100.0)	3.1 [1.6; -]	13	9 (69.2)	4.1 [1.6; -]	1.22 [0.41; 3.66]	0.720	0.358
Mild	49	38 (77.6)	8.6 [3.1; 12.3]	40	35 (87.5)	3.1 [2.1; 4.1]	0.53 [0.33; 0.86]	0.010	
Moderate/Severe	146	113 (77.4)	15.3 [9.1; 20.1]	144	122 (84.7)	3.0 [2.1; 4.1]	0.41 [0.31; 0.55]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	43 (86.0)	4.4 [3.0; 10.7]	49	42 (85.7)	2.3 [2.0; 3.9]	0.57 [0.36; 0.90]	0.015	0.592
Absent	151	114 (75.5)	14.3 [9.3; 20.1]	148	124 (83.8)	3.6 [2.4; 4.3]	0.43 [0.32; 0.56]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	91 (77.8)	11.3 [8.6; 18.1]	114	94 (82.5)	3.9 [2.3; 4.3]	0.46 [0.34; 0.63]	< 0.001	0.929
Low	84	66 (78.6)	10.9 [4.1; 24.1]	83	72 (86.7)	2.6 [2.1; 4.0]	0.45 [0.31; 0.65]	< 0.001	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: all-participants-as-treated population, cisplatin ineligible									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1									

Therapieabbruch wegen unerwünschter Ereignisse

Tabelle 4G-96: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events Leading to Treatment Discontinuation	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Age									
< 65	39	21 (53.8)	42.9 [15.9; -]	28	4 (14.3)	Not reached [-; -]	2.88 [0.95; 8.72]	0.061	0.215
≥ 65	162	62 (38.3)	Not reached [44.6; -]	169	31 (18.3)	Not reached [-; -]	1.60 [1.03; 2.51]	0.038	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events Leading to Treatment Discontinuation	Participants with Event n (%)	Median Time ^e in Weeks [95 %-CI]	Participants with Event n (%)	Median Time ^e in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
Sex									
Male	145	62 (42.8)	61.0 [29.6; -]	148	25 (16.9)	Not reached [-; -]	2.06 [1.28; 3.34]	0.003	0.242
Female	56	21 (37.5)	88.4 [38.7; -]	49	10 (20.4)	Not reached [-; -]	1.10 [0.50; 2.44]	0.814	
Geographic Region									
North America	46	20 (43.5)	88.4 [19.1; -]	33	7 (21.2)	Not reached [-; -]	1.58 [0.65; 3.83]	0.313	0.892
Europe	73	35 (47.9)	45.9 [18.0; -]	94	18 (19.1)	Not reached [-; -]	1.97 [1.09; 3.56]	0.025	
Rest of World	82	28 (34.1)	Not reached [44.6; -]	70	10 (14.3)	Not reached [23.3; -]	1.69 [0.79; 3.59]	0.176	
ECOG at Baseline									
0	87	38 (43.7)	61.0 [24.9; -]	85	11 (12.9)	Not reached [-; -]	2.80 [1.41; 5.56]	0.003	0.079
1-2	114	45 (39.5)	88.4 [42.9; -]	112	24 (21.4)	Not reached [-; -]	1.29 [0.77; 2.18]	0.337	
Race									
White	141	59 (41.8)	88.4 [38.7; -]	138	27 (19.6)	Not reached [-; -]	1.69 [1.05; 2.70]	0.030	0.618
Non-white	60	24 (40.0)	Not reached [30.6; -]	59	8 (13.6)	Not reached [-; -]	2.05 [0.89; 4.75]	0.093	
Metastatic Disease Site									
Visceral metastases	147	56 (38.1)	Not reached [42.9; -]	152	24 (15.8)	Not reached [-; -]	1.85 [1.13; 3.04]	0.015	0.834
Lymph node only	43	25 (58.1)	24.1 [16.3; 88.4]	37	11 (29.7)	Not reached [23.3; -]	1.58 [0.76; 3.31]	0.221	
Primary Disease Site of Origin									
Upper Tract	74	29 (39.2)	Not reached [24.3; -]	53	5 (9.4)	Not reached [-; -]	3.25 [1.24; 8.53]	0.016	0.137
Lower Tract	127	54 (42.5)	88.4 [38.7; -]	143	30 (21.0)	Not reached [-; -]	1.53 [0.96; 2.45]	0.075	
Renal Function									
Normal	6	3 (50.0)	88.4 [2.4; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.041	0.139
Mild	49	24 (49.0)	42.9 [16.3; -]	40	8 (20.0)	Not reached [-; -]	2.16 [0.95; 4.90]	0.065	
Moderate/Severe	146	56 (38.4)	Not reached [44.6; -]	144	27 (18.8)	Not reached [-; -]	1.48 [0.92; 2.40]	0.108	
Stratification Factor: Liver Metastases									
Present	50	19 (38.0)	Not reached [29.6; -]	49	10 (20.4)	Not reached [-; -]	1.37 [0.61; 3.06]	0.444	0.451
Absent	151	64 (42.4)	88.4 [39.1; -]	148	25 (16.9)	Not reached [-; -]	1.93 [1.20; 3.12]	0.007	
Stratification Factor: PD-L1 Expression									
High	117	57 (48.7)	44.6 [21.9; -]	114	19 (16.7)	Not reached [-; -]	2.32 [1.36; 3.96]	0.002	0.107
Low	84	26 (31.0)	88.4 [88.4; -]	83	16 (19.3)	Not reached [-; -]	1.14 [0.59; 2.21]	0.694	
a: Database Cutoff Date: 08AUG2023									
b: Number of participants: all-participants-as-treated population, cisplatin ineligible									

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events Leading to Treatment Discontinuation	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1									

Unerwünschte Ereignisse gesamt (SOC und PT)*Unerwünschte Ereignisse gesamt*

Tabelle 4G-97: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC^g: Blood and lymphatic system disorders									
Age									
< 65	39 (33.3)	Not reached [39.14; -]	28 (78.6)	22 (78.6)	4.07 [1.57; 6.71]	0.16 [0.07; 0.35]	< 0.001	0.701	
≥ 65	162 (46.3)	50.14 [31.14; 76.14]	169 (87.6)	148 (87.6)	2.14 [2.14; 3.00]	0.19 [0.14; 0.26]	< 0.001		
Geographic Region									
North America	46 (30.4)	Not reached [-; -]	33 (72.7)	24 (72.7)	4.00 [2.14; 7.00]	0.22 [0.11; 0.44]	< 0.001	0.963	
Europe	73 (47.9)	43.71 [18.14; -]	94 (89.4)	84 (89.4)	2.14 [2.00; 3.00]	0.19 [0.12; 0.29]	< 0.001		
Rest of World	82 (47.6)	52.57 [27.14; 76.14]	70 (88.6)	62 (88.6)	2.14 [2.00; 3.00]	0.18 [0.11; 0.28]	< 0.001		
Sex									
Male	145 (45.5)	46.71 [28.14; -]	148 (85.8)	127 (85.8)	2.14 [2.14; 3.29]	0.21 [0.15; 0.29]	< 0.001	0.087	
Female	56 (39.3)	76.14 [38.71; -]	49 (87.8)	43 (87.8)	2.14 [2.00; 3.00]	0.14 [0.07; 0.25]	< 0.001		
ECOG at Baseline									
0	87 (44.8)	46.71 [20.14; -]	85 (88.2)	75 (88.2)	2.14 [2.14; 4.14]	0.19 [0.12; 0.29]	< 0.001	0.628	
1-2	114 (43.0)	59.86 [38.71; -]	112 (84.8)	95 (84.8)	2.14 [2.00; 3.00]	0.18 [0.12; 0.27]	< 0.001		
Primary Disease Site of Origin									
Upper Tract	74 (41.9)	65.71 [31.14; -]	53 (84.9)	45 (84.9)	3.00 [2.14; 4.00]	0.18 [0.11; 0.30]	< 0.001	0.975	
Lower Tract	127 (44.9)	50.14 [36.14; -]	143 (86.7)	124 (86.7)	2.14 [2.14; 3.00]	0.19 [0.13; 0.27]	< 0.001		

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	50	22 (44.0)	43.71 [9.14; -]	49	40 (81.6)	2.14 [1.71; 3.14]	0.28 [0.16; 0.48]	< 0.001	0.359
Absent	151	66 (43.7)	59.86 [43.86; -]	148	130 (87.8)	2.29 [2.14; 3.14]	0.16 [0.11; 0.22]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	52 (44.4)	52.57 [39.14; -]	114	98 (86.0)	2.86 [2.14; 4.14]	0.18 [0.12; 0.27]	< 0.001	0.600
Low	84	36 (42.9)	59.86 [21.14; -]	83	72 (86.7)	2.14 [1.43; 3.00]	0.18 [0.12; 0.29]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	60 (40.8)	65.71 [43.71; -]	152	128 (84.2)	2.14 [2.14; 3.14]	0.19 [0.13; 0.26]	< 0.001	0.841
Lymph node only	43	21 (48.8)	43.86 [10.43; -]	37	35 (94.6)	2.86 [2.14; 4.14]	0.18 [0.10; 0.33]	< 0.001	
Renal Function									
Normal	6	2 (33.3)	Not reached [2.00; -]	13	10 (76.9)	4.14 [1.14; 12.14]	0.25 [0.05; 1.16]	0.077	0.916
Mild	49	20 (40.8)	Not reached [12.29; -]	40	35 (87.5)	3.36 [2.14; 6.71]	0.20 [0.11; 0.36]	< 0.001	
Moderate/Severe	146	66 (45.2)	50.14 [38.71; 76.14]	144	125 (86.8)	2.14 [2.00; 3.00]	0.18 [0.12; 0.25]	< 0.001	
SOC ^g : Endocrine disorders									
Age									
< 65	39	7 (17.9)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.138	0.285
≥ 65	162	29 (17.9)	Not reached [-; -]	169	4 (2.4)	Not reached [-; -]	5.03 [1.72; 14.70]	0.003	
Race									
White	141	21 (14.9)	Not reached [-; -]	138	4 (2.9)	Not reached [-; -]	3.49 [1.16; 10.54]	0.026	0.058
Non-white	60	15 (25.0)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Sex									
Male	145	25 (17.2)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	7.89 [1.81; 34.37]	0.006	0.290
Female	56	11 (19.6)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	2.75 [0.58; 12.98]	0.201	
ECOG at Baseline									
0	87	11 (12.6)	Not reached [-; -]	85	2 (2.4)	Not reached [-; -]	4.11 [0.89; 19.07]	0.071	0.437
1-2	114	25 (21.9)	Not reached [-; -]	112	2 (1.8)	Not reached [-; -]	6.76 [1.54; 29.65]	0.011	
Primary Disease Site of Origin									
Upper Tract	74	13 (17.6)	Not reached [-; -]	53	2 (3.8)	Not reached [-; -]	4.45 [1.00; 19.88]	0.051	0.351
Lower Tract	127	23 (18.1)	Not reached [-; -]	143	2 (1.4)	Not reached [-; -]	5.72 [1.28; 25.65]	0.023	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [57.00; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.337	0.288
Absent	151	31 (20.5)	Not reached [-; -]	148	4 (2.7)	Not reached [-; -]	5.27 [1.82; 15.24]	0.002	
Stratification Factor: PD-L1 Expression									
High	117	19 (16.2)	Not reached [-; -]	114	2 (1.8)	Not reached [-; -]	5.58 [1.25; 24.97]	0.025	0.942
Low	84	17 (20.2)	Not reached [-; -]	83	2 (2.4)	Not reached [-; -]	5.34 [1.19; 23.90]	0.029	
Metastatic Disease Site									
Visceral metastases	147	23 (15.6)	Not reached [-; -]	152	2 (1.3)	Not reached [-; -]	7.38 [1.69; 32.31]	0.008	0.334
Lymph node only	43	10 (23.3)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	2.58 [0.53; 12.50]	0.240	
Renal Function									
Normal	6	2 (33.3)	57.00 [29.29; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.655	0.181
Mild	49	11 (22.4)	Not reached [49.86; -]	40	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.017	
Moderate/Severe	146	23 (15.8)	Not reached [-; -]	144	4 (2.8)	Not reached [-; -]	3.83 [1.28; 11.42]	0.016	
SOC ^g : Eye disorders									
Age									
< 65	39	15 (38.5)	Not reached [32.14; -]	28	1 (3.6)	Not reached [-; -]	5.94 [0.74; 47.55]	0.093	0.400
≥ 65	162	49 (30.2)	Not reached [65.14; -]	169	11 (6.5)	Not reached [-; -]	3.70 [1.90; 7.23]	< 0.001	
Race									
White	141	45 (31.9)	Not reached [56.86; -]	138	6 (4.3)	Not reached [-; -]	5.83 [2.45; 13.86]	< 0.001	0.113
Non-white	60	19 (31.7)	Not reached [56.00; -]	59	6 (10.2)	Not reached [-; -]	1.87 [0.70; 4.97]	0.212	
Geographic Region									
North America	46	17 (37.0)	Not reached [17.14; -]	33	2 (6.1)	Not reached [-; -]	5.04 [1.15; 22.19]	0.032	0.810
Europe	73	23 (31.5)	76.29 [37.29; -]	94	7 (7.4)	Not reached [-; -]	2.98 [1.24; 7.20]	0.015	
Rest of World	82	24 (29.3)	Not reached [65.14; -]	70	3 (4.3)	Not reached [-; -]	4.60 [1.34; 15.78]	0.015	
Sex									
Male	145	45 (31.0)	Not reached [56.86; -]	148	9 (6.1)	Not reached [-; -]	4.27 [2.05; 8.88]	< 0.001	0.845
Female	56	19 (33.9)	72.14 [37.29; -]	49	3 (6.1)	Not reached [-; -]	2.85 [0.80; 10.16]	0.107	
ECOG at Baseline									
0	87	35 (40.2)	65.14 [32.14; -]	85	6 (7.1)	Not reached [-; -]	4.25 [1.75; 10.37]	0.001	0.666
1-2	114	29 (25.4)	Not reached [72.14; -]	112	6 (5.4)	Not reached [-; -]	3.45 [1.40; 8.54]	0.007	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	74	23 (31.1)	76.29 [65.14; -]	53	6 (11.3)	Not reached [-; -]	1.94 [0.76; 4.94]	0.163	0.092
Lower Tract	127	41 (32.3)	Not reached [56.86; -]	143	6 (4.2)	Not reached [-; -]	5.80 [2.42; 13.93]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	11 (22.0)	76.29 [76.29; -]	49	2 (4.1)	Not reached [-; -]	3.45 [0.72; 16.62]	0.122	0.981
Absent	151	53 (35.1)	Not reached [56.86; -]	148	10 (6.8)	Not reached [-; -]	3.97 [1.98; 7.94]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	35 (29.9)	Not reached [72.14; -]	114	7 (6.1)	Not reached [-; -]	3.59 [1.55; 8.29]	0.003	0.782
Low	84	29 (34.5)	76.29 [35.29; -]	83	5 (6.0)	Not reached [-; -]	4.19 [1.59; 11.06]	0.004	
Metastatic Disease Site									
Visceral metastases	147	44 (29.9)	Not reached [65.14; -]	152	9 (5.9)	Not reached [-; -]	3.64 [1.73; 7.65]	< 0.001	0.652
Lymph node only	43	17 (39.5)	Not reached [23.29; -]	37	2 (5.4)	Not reached [-; -]	5.62 [1.27; 24.86]	0.023	
Renal Function									
Normal	6	2 (33.3)	Not reached [5.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.138	0.318
Mild	49	19 (38.8)	76.29 [24.14; -]	40	5 (12.5)	Not reached [-; -]	2.40 [0.87; 6.63]	0.090	
Moderate/Severe	146	43 (29.5)	Not reached [65.14; -]	144	7 (4.9)	Not reached [-; -]	4.47 [1.97; 10.13]	< 0.001	
SOC^g: General disorders and administration site conditions									
Age									
< 65	39	26 (66.7)	20.29 [4.14; 37.29]	28	17 (60.7)	7.14 [3.14; -]	0.79 [0.41; 1.52]	0.484	0.386
≥ 65	162	110 (67.9)	11.14 [6.43; 20.71]	169	119 (70.4)	3.57 [2.29; 5.57]	0.62 [0.47; 0.81]	< 0.001	
Geographic Region									
North America	46	37 (80.4)	4.14 [1.86; 9.57]	33	23 (69.7)	3.14 [1.14; 10.57]	0.93 [0.55; 1.58]	0.780	0.278
Europe	73	59 (80.8)	5.29 [2.57; 10.43]	94	77 (81.9)	2.86 [1.86; 4.43]	0.67 [0.47; 0.95]	0.026	
Rest of World	82	40 (48.8)	42.86 [26.14; -]	70	36 (51.4)	14.00 [4.57; -]	0.51 [0.31; 0.84]	0.008	
Sex									
Male	145	100 (69.0)	10.43 [6.14; 21.57]	148	98 (66.2)	5.14 [3.00; 6.71]	0.72 [0.54; 0.96]	0.028	0.099
Female	56	36 (64.3)	19.29 [5.29; 32.00]	49	38 (77.6)	3.14 [1.14; 7.00]	0.42 [0.26; 0.69]	< 0.001	
ECOG at Baseline									
0	87	54 (62.1)	9.57 [6.14; 26.29]	85	57 (67.1)	4.14 [1.86; 7.71]	0.69 [0.47; 1.01]	0.056	0.746
1-2	114	82 (71.9)	12.29 [5.29; 25.71]	112	79 (70.5)	4.57 [2.86; 6.71]	0.59 [0.42; 0.83]	0.002	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Primary Disease Site of Origin									
Upper Tract	74	45 (60.8)	26.29 [11.14; 39.29]	53	36 (67.9)	4.71 [1.43; 11.14]	0.50 [0.31; 0.81]	0.004	0.282
Lower Tract	127	91 (71.7)	9.14 [5.29; 12.29]	143	100 (69.9)	4.29 [2.86; 6.43]	0.73 [0.54; 0.97]	0.033	
Stratification Factor: Liver Metastases									
Present	50	39 (78.0)	5.29 [3.14; 12.29]	49	37 (75.5)	3.57 [2.43; 5.57]	0.77 [0.48; 1.23]	0.273	0.307
Absent	151	97 (64.2)	20.29 [9.57; 28.29]	148	99 (66.9)	4.86 [2.43; 7.14]	0.60 [0.44; 0.80]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	82 (70.1)	13.29 [6.43; 25.71]	114	80 (70.2)	3.14 [2.00; 5.57]	0.58 [0.42; 0.81]	0.001	0.667
Low	84	54 (64.3)	11.14 [4.00; 26.71]	83	56 (67.5)	5.71 [3.00; 10.29]	0.73 [0.50; 1.07]	0.110	
Metastatic Disease Site									
Visceral metastases	147	101 (68.7)	9.57 [6.14; 20.71]	152	105 (69.1)	4.43 [3.00; 6.00]	0.67 [0.50; 0.89]	0.006	0.644
Lymph node only	43	28 (65.1)	20.29 [2.14; 32.14]	37	25 (67.6)	2.14 [1.00; 12.43]	0.57 [0.32; 1.02]	0.058	
Renal Function									
Normal	6	6 (100.0)	6.14 [0.57; -]	13	7 (53.8)	6.71 [0.57; -]	1.14 [0.33; 3.91]	0.836	0.351
Mild	49	38 (77.6)	9.57 [5.29; 12.29]	40	31 (77.5)	3.07 [1.43; 5.86]	0.64 [0.39; 1.05]	0.076	
Moderate/Severe	146	92 (63.0)	20.29 [6.43; 28.86]	144	98 (68.1)	4.86 [2.86; 7.00]	0.59 [0.44; 0.80]	< 0.001	
SOC ^c : Hepatobiliary disorders									
Age									
< 65	39	8 (20.5)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	4.72 [0.58; 38.67]	0.148	0.293
≥ 65	162	24 (14.8)	Not reached [-; -]	169	12 (7.1)	Not reached [-; -]	1.90 [0.94; 3.83]	0.074	
Race									
White	141	22 (15.6)	Not reached [-; -]	138	9 (6.5)	Not reached [-; -]	2.06 [0.93; 4.55]	0.073	0.982
Non-white	60	10 (16.7)	Not reached [-; -]	59	4 (6.8)	Not reached [-; -]	2.25 [0.70; 7.24]	0.175	
Geographic Region									
North America	46	3 (6.5)	Not reached [-; -]	33	1 (3.0)	Not reached [-; -]	1.33 [0.12; 14.69]	0.815	0.930
Europe	73	15 (20.5)	Not reached [-; -]	94	8 (8.5)	Not reached [-; -]	2.11 [0.87; 5.07]	0.097	
Rest of World	82	14 (17.1)	Not reached [-; -]	70	4 (5.7)	Not reached [-; -]	2.91 [0.95; 8.90]	0.061	
Sex									
Male	145	26 (17.9)	Not reached [-; -]	148	11 (7.4)	Not reached [-; -]	2.09 [1.02; 4.30]	0.045	0.993
Female	56	6 (10.7)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	2.39 [0.48; 11.87]	0.285	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	22 (25.3)	Not reached [-; -]	85	7 (8.2)	Not reached [-; -]	2.81 [1.19; 6.67]	0.019	0.277
1-2	114	10 (8.8)	Not reached [-; -]	112	6 (5.4)	Not reached [-; -]	1.42 [0.50; 3.98]	0.509	
Primary Disease Site of Origin									
Upper Tract	74	14 (18.9)	Not reached [-; -]	53	4 (7.5)	Not reached [-; -]	2.44 [0.80; 7.49]	0.118	0.817
Lower Tract	127	18 (14.2)	Not reached [-; -]	143	9 (6.3)	Not reached [-; -]	1.86 [0.82; 4.24]	0.137	
Stratification Factor: Liver Metastases									
Present	50	4 (8.0)	Not reached [-; -]	49	5 (10.2)	Not reached [-; -]	0.78 [0.21; 2.90]	0.710	0.060
Absent	151	28 (18.5)	Not reached [-; -]	148	8 (5.4)	Not reached [-; -]	2.96 [1.33; 6.58]	0.008	
Stratification Factor: PD-L1 Expression									
High	117	21 (17.9)	Not reached [-; -]	114	7 (6.1)	Not reached [-; -]	2.74 [1.15; 6.49]	0.022	0.431
Low	84	11 (13.1)	Not reached [-; -]	83	6 (7.2)	Not reached [-; -]	1.42 [0.51; 4.00]	0.504	
Metastatic Disease Site									
Visceral metastases	147	25 (17.0)	Not reached [-; -]	152	10 (6.6)	Not reached [-; -]	2.29 [1.09; 4.83]	0.029	0.572
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	1.68 [0.42; 6.72]	0.463	
Renal Function									
Normal	6	2 (33.3)	Not reached [2.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.033	0.101
Mild	49	8 (16.3)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	6.80 [0.85; 54.35]	0.071	
Moderate/Severe	146	22 (15.1)	Not reached [-; -]	144	12 (8.3)	Not reached [-; -]	1.47 [0.71; 3.03]	0.300	
SOC^g: Injury, poisoning and procedural complications									
Age									
< 65	39	7 (17.9)	Not reached [68.71; -]	28	3 (10.7)	Not reached [-; -]	0.24 [0.02; 2.28]	0.212	0.698
≥ 65	162	20 (12.3)	Not reached [-; -]	169	19 (11.2)	Not reached [-; -]	0.57 [0.28; 1.16]	0.118	
Race									
White	141	21 (14.9)	Not reached [-; -]	138	16 (11.6)	Not reached [-; -]	0.60 [0.28; 1.29]	0.188	0.388
Non-white	60	6 (10.0)	Not reached [-; -]	59	6 (10.2)	Not reached [-; -]	0.29 [0.07; 1.24]	0.095	
Geographic Region									
North America	46	11 (23.9)	Not reached [41.29; -]	33	4 (12.1)	Not reached [-; -]	0.89 [0.25; 3.19]	0.859	0.332
Europe	73	6 (8.2)	Not reached [-; -]	94	11 (11.7)	Not reached [-; -]	0.31 [0.09; 1.11]	0.072	
Rest of World	82	10 (12.2)	Not reached [-; -]	70	7 (10.0)	Not reached [-; -]	0.42 [0.13; 1.36]	0.148	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	145	18 (12.4)	Not reached [-; -]	148	13 (8.8)	Not reached [-; -]	0.66 [0.29; 1.53]	0.336	0.260
Female	56	9 (16.1)	Not reached [-; -]	49	9 (18.4)	Not reached [-; -]	0.28 [0.08; 0.94]	0.040	
ECOG at Baseline									
0	87	11 (12.6)	Not reached [-; -]	85	10 (11.8)	Not reached [-; -]	0.59 [0.22; 1.57]	0.291	0.796
1-2	114	16 (14.0)	Not reached [-; -]	112	12 (10.7)	Not reached [-; -]	0.43 [0.17; 1.12]	0.084	
Primary Disease Site of Origin									
Upper Tract	74	10 (13.5)	Not reached [-; -]	53	5 (9.4)	Not reached [-; -]	0.79 [0.25; 2.55]	0.699	0.623
Lower Tract	127	17 (13.4)	Not reached [-; -]	143	17 (11.9)	Not reached [-; -]	0.39 [0.16; 0.94]	0.035	
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [-; -]	49	8 (16.3)	Not reached [-; -]	0.40 [0.12; 1.36]	0.144	0.242
Absent	151	22 (14.6)	Not reached [-; -]	148	14 (9.5)	Not reached [-; -]	0.57 [0.25; 1.29]	0.176	
Stratification Factor: PD-L1 Expression									
High	117	16 (13.7)	Not reached [-; -]	114	10 (8.8)	Not reached [-; -]	0.57 [0.21; 1.51]	0.257	0.416
Low	84	11 (13.1)	Not reached [-; -]	83	12 (14.5)	Not reached [-; -]	0.45 [0.17; 1.16]	0.097	
Metastatic Disease Site									
Visceral metastases	147	15 (10.2)	Not reached [-; -]	152	14 (9.2)	Not reached [-; -]	0.63 [0.28; 1.44]	0.277	0.988
Lymph node only	43	9 (20.9)	Not reached [68.71; -]	37	6 (16.2)	Not reached [21.57; -]	0.33 [0.08; 1.36]	0.125	
Renal Function									
Normal	6	2 (33.3)	Not reached [35.43; -]	13	1 (7.7)	Not reached [8.71; -]	n.a. [n.a.; n.a.]	0.998	0.625
Mild	49	6 (12.2)	Not reached [-; -]	40	5 (12.5)	Not reached [-; -]	0.30 [0.06; 1.56]	0.153	
Moderate/Severe	146	19 (13.0)	Not reached [-; -]	144	16 (11.1)	Not reached [-; -]	0.58 [0.27; 1.25]	0.164	
SOC^g: Metabolism and nutrition disorders									
Age									
< 65	39	20 (51.3)	39.14 [4.86; -]	28	10 (35.7)	Not reached [9.29; -]	1.57 [0.73; 3.39]	0.246	0.910
≥ 65	162	102 (63.0)	8.14 [5.14; 11.43]	169	76 (45.0)	Not reached [12.00; -]	1.44 [1.07; 1.94]	0.017	
Race									
White	141	88 (62.4)	6.29 [4.71; 10.00]	138	58 (42.0)	Not reached [13.43; -]	1.69 [1.21; 2.36]	0.002	0.102
Non-white	60	34 (56.7)	14.14 [8.14; -]	59	28 (47.5)	Not reached [5.00; -]	0.99 [0.59; 1.64]	0.962	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	33 (71.7)	3.00 [2.00; 7.71]	33	14 (42.4)	Not reached [1.57; -]	1.76 [0.94; 3.32]	0.078	0.434
Europe	73	44 (60.3)	8.57 [5.86; 79.00]	94	46 (48.9)	19.86 [9.43; -]	1.22 [0.80; 1.85]	0.352	
Rest of World	82	45 (54.9)	14.14 [8.14; -]	70	26 (37.1)	Not reached [14.14; -]	1.46 [0.90; 2.38]	0.124	
ECOG at Baseline									
0	87	52 (59.8)	9.14 [5.86; 39.14]	85	34 (40.0)	Not reached [13.00; -]	1.56 [1.01; 2.42]	0.044	0.581
1-2	114	70 (61.4)	8.14 [4.71; 14.14]	112	52 (46.4)	19.86 [10.00; -]	1.34 [0.93; 1.92]	0.116	
Primary Disease Site of Origin									
Upper Tract	74	41 (55.4)	12.14 [6.29; -]	53	21 (39.6)	Not reached [9.29; -]	1.36 [0.80; 2.31]	0.253	0.741
Lower Tract	127	81 (63.8)	7.00 [4.71; 10.14]	143	65 (45.5)	Not reached [12.00; -]	1.50 [1.08; 2.09]	0.016	
Stratification Factor: Liver Metastases									
Present	50	27 (54.0)	10.14 [6.14; -]	49	17 (34.7)	Not reached [14.14; -]	1.59 [0.86; 2.94]	0.136	0.668
Absent	151	95 (62.9)	8.14 [4.71; 12.14]	148	69 (46.6)	20.00 [10.29; -]	1.38 [1.01; 1.89]	0.041	
Stratification Factor: PD-L1 Expression									
High	117	68 (58.1)	9.00 [5.86; 79.00]	114	50 (43.9)	Not reached [12.14; -]	1.35 [0.94; 1.95]	0.106	0.574
Low	84	54 (64.3)	8.14 [4.29; 14.14]	83	36 (43.4)	Not reached [9.29; -]	1.53 [1.00; 2.35]	0.050 ^h	
Metastatic Disease Site									
Visceral metastases	147	89 (60.5)	8.57 [5.86; 12.14]	152	68 (44.7)	Not reached [10.43; -]	1.39 [1.01; 1.91]	0.042	0.693
Lymph node only	43	25 (58.1)	7.00 [4.14; -]	37	17 (45.9)	19.86 [5.00; -]	1.21 [0.65; 2.26]	0.543	
SOC ^g : Nervous system disorders									
Age									
< 65	39	27 (69.2)	16.29 [12.29; 22.14]	28	9 (32.1)	Not reached [16.00; -]	2.02 [0.93; 4.38]	0.075	0.298
≥ 65	162	116 (71.6)	14.29 [11.71; 16.29]	169	39 (23.1)	Not reached [23.29; -]	2.85 [1.96; 4.15]	< 0.001	
Race									
White	141	99 (70.2)	14.29 [11.71; 16.29]	138	34 (24.6)	Not reached [23.29; -]	2.84 [1.91; 4.24]	< 0.001	0.753
Non-white	60	44 (73.3)	15.71 [11.14; 24.14]	59	14 (23.7)	Not reached [-; -]	2.41 [1.29; 4.51]	0.006	
Geographic Region									
North America	46	33 (71.7)	10.14 [6.00; 15.14]	33	12 (36.4)	Not reached [10.00; -]	1.90 [0.97; 3.74]	0.062	0.233

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Europe	73	54 (74.0)	12.29 [10.86; 16.29]	94	26 (27.7)	Not reached [-; -]	2.63 [1.62; 4.25]	< 0.001	
Rest of World	82	56 (68.3)	19.57 [14.43; 24.57]	70	10 (14.3)	Not reached [23.29; -]	3.77 [1.89; 7.54]	< 0.001	
Sex									
Male	145	101 (69.7)	14.14 [11.14; 16.00]	148	36 (24.3)	Not reached [23.29; -]	2.93 [1.98; 4.34]	< 0.001	0.492
Female	56	42 (75.0)	16.29 [12.29; 28.43]	49	12 (24.5)	Not reached [-; -]	2.16 [1.11; 4.19]	0.023	
Primary Disease Site of Origin									
Upper Tract	74	49 (66.2)	15.71 [12.14; 24.57]	53	10 (18.9)	Not reached [-; -]	3.12 [1.55; 6.26]	0.001	0.659
Lower Tract	127	94 (74.0)	14.00 [10.14; 16.29]	143	38 (26.6)	Not reached [23.29; -]	2.67 [1.81; 3.93]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	30 (60.0)	14.43 [10.14; 19.86]	49	14 (28.6)	Not reached [-; -]	1.98 [1.04; 3.77]	0.037	0.148
Absent	151	113 (74.8)	15.00 [12.00; 18.00]	148	34 (23.0)	Not reached [23.29; -]	2.97 [2.00; 4.41]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	87 (74.4)	15.14 [12.14; 19.14]	114	30 (26.3)	Not reached [-; -]	2.45 [1.60; 3.76]	< 0.001	0.429
Low	84	56 (66.7)	12.14 [8.57; 21.43]	83	18 (21.7)	Not reached [23.29; -]	3.04 [1.76; 5.25]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	100 (68.0)	14.86 [11.71; 19.14]	152	34 (22.4)	Not reached [-; -]	2.84 [1.90; 4.23]	< 0.001	0.828
Lymph node only	43	34 (79.1)	14.86 [9.14; 18.00]	37	10 (27.0)	23.29 [21.43; -]	3.05 [1.48; 6.28]	0.003	
Renal Function									
Normal	6	5 (83.3)	10.86 [2.00; -]	13	3 (23.1)	21.43 [8.71; -]	2.84 [0.62; 12.90]	0.177	0.900
Mild	49	39 (79.6)	12.00 [8.29; 16.29]	40	12 (30.0)	Not reached [17.43; -]	2.60 [1.34; 5.04]	0.005	
Moderate/Severe	146	99 (67.8)	15.57 [12.57; 19.29]	144	33 (22.9)	Not reached [23.29; -]	2.67 [1.78; 4.00]	< 0.001	
SOC ^g : Skin and subcutaneous tissue disorders									
Age									
< 65	39	27 (69.2)	3.57 [1.43; 20.29]	28	6 (21.4)	Not reached [-; -]	4.57 [1.86; 11.19]	< 0.001	0.961
≥ 65	162	135 (83.3)	2.14 [1.86; 3.14]	169	45 (26.6)	Not reached [-; -]	5.14 [3.65; 7.24]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	110 (78.0)	3.29 [2.57; 5.14]	138	33 (23.9)	Not reached [-; -]	4.85 [3.27; 7.18]	< 0.001	0.324
Non-white	60	52 (86.7)	1.29 [1.14; 1.71]	59	18 (30.5)	Not reached [-; -]	5.34 [3.08; 9.26]	< 0.001	
Geographic Region									
North America	46	42 (91.3)	2.00 [1.43; 3.14]	33	12 (36.4)	Not reached [10.00; -]	5.91 [3.01; 11.62]	< 0.001	0.787
Europe	73	57 (78.1)	4.14 [2.29; 6.00]	94	19 (20.2)	Not reached [-; -]	5.62 [3.33; 9.51]	< 0.001	
Rest of World	82	63 (76.8)	2.14 [1.57; 3.43]	70	20 (28.6)	Not reached [-; -]	3.92 [2.36; 6.53]	< 0.001	
Sex									
Male	145	116 (80.0)	2.86 [2.00; 3.43]	148	34 (23.0)	Not reached [-; -]	5.63 [3.82; 8.30]	< 0.001	0.189
Female	56	46 (82.1)	1.86 [1.43; 3.14]	49	17 (34.7)	Not reached [9.14; -]	3.55 [2.03; 6.22]	< 0.001	
ECOG at Baseline									
0	87	74 (85.1)	1.86 [1.43; 2.71]	85	22 (25.9)	Not reached [-; -]	5.72 [3.52; 9.27]	< 0.001	0.357
1-2	114	88 (77.2)	3.14 [2.14; 3.57]	112	29 (25.9)	Not reached [-; -]	4.40 [2.88; 6.73]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	58 (78.4)	1.86 [1.43; 3.29]	53	13 (24.5)	Not reached [-; -]	5.59 [3.04; 10.28]	< 0.001	0.526
Lower Tract	127	104 (81.9)	2.57 [2.00; 3.57]	143	38 (26.6)	Not reached [-; -]	4.64 [3.18; 6.77]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	94 (80.3)	2.57 [1.86; 3.29]	114	32 (28.1)	Not reached [-; -]	4.58 [3.05; 6.89]	< 0.001	0.475
Low	84	68 (81.0)	2.14 [1.86; 3.57]	83	19 (22.9)	Not reached [-; -]	5.52 [3.30; 9.22]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	114 (77.6)	2.14 [1.86; 3.14]	152	42 (27.6)	Not reached [-; -]	4.31 [3.01; 6.16]	< 0.001	0.117
Lymph node only	43	38 (88.4)	2.14 [1.71; 3.71]	37	7 (18.9)	Not reached [-; -]	10.31 [4.53; 23.49]	< 0.001	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A system organ class appears on this report only if its incidence $\geq 10\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>h: Unrounded p-value < 0.050</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class</p>									

Tabelle 4G-98: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC: Blood and lymphatic system disorders - PT^g: Anaemia									
Age									
< 65	39	8 (20.5)	Not reached [-; -]	28	18 (64.3)	6.57 [3.14; -]	0.17 [0.07; 0.44]	< 0.001	0.212
≥ 65	162	59 (36.4)	76.14 [52.57; -]	169	117 (69.2)	6.00 [4.14; 7.14]	0.26 [0.19; 0.37]	< 0.001	
Race									
White	141	52 (36.9)	Not reached [39.14; -]	138	95 (68.8)	6.14 [4.43; 8.14]	0.30 [0.21; 0.43]	< 0.001	0.065
Non-white	60	15 (25.0)	Not reached [76.14; -]	59	40 (67.8)	5.14 [4.00; 10.00]	0.14 [0.07; 0.28]	< 0.001	
Geographic Region									
North America	46	11 (23.9)	Not reached [-; -]	33	17 (51.5)	9.00 [3.14; -]	0.29 [0.14; 0.64]	0.002	0.708
Europe	73	29 (39.7)	59.86 [32.86; -]	94	68 (72.3)	6.14 [4.43; 10.00]	0.27 [0.16; 0.43]	< 0.001	
Rest of World	82	27 (32.9)	Not reached [66.86; -]	70	50 (71.4)	5.14 [4.00; 6.43]	0.23 [0.14; 0.38]	< 0.001	
Sex									
Male	145	49 (33.8)	Not reached [59.86; -]	148	100 (67.6)	6.14 [4.43; 9.00]	0.27 [0.19; 0.39]	< 0.001	0.282
Female	56	18 (32.1)	Not reached [66.86; -]	49	35 (71.4)	4.86 [2.14; 6.43]	0.20 [0.10; 0.37]	< 0.001	
ECOG at Baseline									
0	87	29 (33.3)	Not reached [66.86; -]	85	61 (71.8)	7.14 [4.14; 9.71]	0.24 [0.15; 0.39]	< 0.001	0.913
1-2	114	38 (33.3)	Not reached [52.57; -]	112	74 (66.1)	5.14 [4.00; 6.29]	0.26 [0.17; 0.40]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	25 (33.8)	Not reached [66.86; -]	53	36 (67.9)	6.00 [3.57; 10.00]	0.27 [0.16; 0.48]	< 0.001	0.644
Lower Tract	127	42 (33.1)	Not reached [52.57; -]	143	99 (69.2)	5.86 [4.14; 7.29]	0.24 [0.16; 0.35]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	17 (34.0)	Not reached [21.14; -]	49	31 (63.3)	6.14 [3.14; 11.71]	0.36 [0.19; 0.66]	0.001	0.391
Absent	151	50 (33.1)	Not reached [66.86; -]	148	104 (70.3)	6.00 [4.43; 7.14]	0.22 [0.15; 0.32]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	41 (35.0)	Not reached [50.14; -]	114	77 (67.5)	6.14 [5.14; 8.00]	0.26 [0.17; 0.39]	< 0.001	0.471
Low	84	26 (31.0)	Not reached [59.86; -]	83	58 (69.9)	4.71 [3.29; 10.00]	0.23 [0.14; 0.38]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	147	44 (29.9)	Not reached [76.14; -]	152	106 (69.7)	5.14 [4.14; 7.14]	0.23 [0.15; 0.33]	< 0.001	0.156
Lymph node only	43	17 (39.5)	Not reached [24.00; -]	37	23 (62.2)	6.29 [4.86; -]	0.36 [0.18; 0.71]	0.003	
Renal Function									
Normal	6	1 (16.7)	Not reached [4.57; -]	13	5 (38.5)	Not reached [4.14; -]	0.36 [0.04; 3.11]	0.354	0.542
Mild	49	14 (28.6)	Not reached [59.86; -]	40	21 (52.5)	13.86 [8.00; -]	0.35 [0.17; 0.71]	0.004	
Moderate/Severe	146	52 (35.6)	Not reached [50.14; -]	144	109 (75.7)	4.71 [3.57; 6.00]	0.21 [0.15; 0.31]	< 0.001	
SOC: Blood and lymphatic system disorders - PT^g: Febrile neutropenia									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.238	0.601
≥ 65	162	1 (0.6)	Not reached [-; -]	169	9 (5.3)	Not reached [-; -]	0.10 [0.01; 0.83]	0.032	
Race									
White	141	1 (0.7)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	2 (3.4)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	0 (0.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	1 (1.4)	n.c.	94	8 (8.5)	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	2 (2.9)	n.c.	n.c.	n.c.	
Sex									
Male	145	1 (0.7)	n.c.	148	7 (4.7)	n.c.	n.c.	n.c.	n.c.
Female	56	0 (0.0)	n.c.	49	3 (6.1)	n.c.	n.c.	n.c.	
ECOG at Baseline									
0	87	0 (0.0)	n.c.	85	3 (3.5)	n.c.	n.c.	n.c.	n.c.
1-2	114	1 (0.9)	n.c.	112	7 (6.3)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	n.c.	53	2 (3.8)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	1 (0.8)	n.c.	143	8 (5.6)	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	n.c.	49	6 (12.2)	n.c.	n.c.	n.c.	n.c.
Absent	151	0 (0.0)	n.c.	148	4 (2.7)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: PD-L1 Expression									
High	117	0 (0.0)	n.c.	114	4 (3.5)	n.c.	n.c.	n.c.	n.c.
Low	84	1 (1.2)	n.c.	83	6 (7.2)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	1 (0.7)	Not reached [-; -]	152	9 (5.9)	Not reached [-; -]	0.10 [0.01; 0.83]	0.032	0.622
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.281	
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	1 (2.0)	n.c.	40	3 (7.5)	n.c.	n.c.	n.c.	
Moderate/Severe	146	0 (0.0)	n.c.	144	7 (4.9)	n.c.	n.c.	n.c.	
SOC: Blood and lymphatic system disorders - PT ^g : Leukopenia									
Age									
< 65	39	2 (5.1)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	0.73 [0.05; 11.73]	0.827	0.232
≥ 65	162	6 (3.7)	Not reached [-; -]	169	20 (11.8)	Not reached [-; -]	0.20 [0.07; 0.57]	0.003	
Race									
White	141	7 (5.0)	Not reached [-; -]	138	17 (12.3)	Not reached [-; -]	0.27 [0.10; 0.73]	0.010	0.590
Non-white	60	1 (1.7)	Not reached [-; -]	59	4 (6.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.995	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	1 (3.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.223	0.604
Europe	73	1 (1.4)	Not reached [-; -]	94	6 (6.4)	Not reached [-; -]	0.21 [0.03; 1.74]	0.148	
Rest of World	82	7 (8.5)	Not reached [-; -]	70	14 (20.0)	Not reached [-; -]	0.22 [0.07; 0.67]	0.008	
Sex									
Male	145	5 (3.4)	Not reached [-; -]	148	16 (10.8)	Not reached [-; -]	0.24 [0.08; 0.73]	0.012	0.622
Female	56	3 (5.4)	Not reached [-; -]	49	5 (10.2)	Not reached [-; -]	0.16 [0.02; 1.38]	0.095	
ECOG at Baseline									
0	87	3 (3.4)	Not reached [-; -]	85	11 (12.9)	Not reached [-; -]	0.17 [0.04; 0.75]	0.020	0.440
1-2	114	5 (4.4)	Not reached [-; -]	112	10 (8.9)	Not reached [-; -]	0.29 [0.08; 1.02]	0.054	
Primary Disease Site of Origin									
Upper Tract	74	1 (1.4)	Not reached [-; -]	53	3 (5.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.619
Lower Tract	127	7 (5.5)	Not reached [-; -]	143	18 (12.6)	Not reached [-; -]	0.29 [0.11; 0.79]	0.015	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	Not reached [-; -]	49	5 (10.2)	Not reached [-; -]	0.20 [0.02; 1.67]	0.136	0.582
Absent	151	7 (4.6)	Not reached [-; -]	148	16 (10.8)	Not reached [-; -]	0.23 [0.08; 0.68]	0.008	
Stratification Factor: PD-L1 Expression									
High	117	4 (3.4)	Not reached [-; -]	114	7 (6.1)	Not reached [-; -]	0.40 [0.10; 1.56]	0.189	0.379
Low	84	4 (4.8)	Not reached [-; -]	83	14 (16.9)	Not reached [-; -]	0.13 [0.03; 0.57]	0.007	
Metastatic Disease Site									
Visceral metastases	147	6 (4.1)	Not reached [-; -]	152	18 (11.8)	Not reached [-; -]	0.27 [0.10; 0.73]	0.010	0.868
Lymph node only	43	1 (2.3)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	0.11 [0.00; 2.56]	0.168	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	1 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.497	0.325
Mild	49	4 (8.2)	Not reached [-; -]	40	4 (10.0)	Not reached [-; -]	0.61 [0.14; 2.71]	0.513	
Moderate/Severe	146	4 (2.7)	Not reached [-; -]	144	16 (11.1)	Not reached [-; -]	0.12 [0.03; 0.50]	0.004	
SOC: Blood and lymphatic system disorders - PT^g: Neutropenia									
Age									
< 65	39	3 (7.7)	Not reached [-; -]	28	12 (42.9)	Not reached [7.86; -]	0.04 [0.01; 0.33]	0.003	0.700
≥ 65	162	19 (11.7)	Not reached [-; -]	169	83 (49.1)	15.71 [7.00; -]	0.14 [0.08; 0.23]	< 0.001	
Race									
White	141	19 (13.5)	Not reached [-; -]	138	69 (50.0)	13.86 [7.14; -]	0.14 [0.08; 0.25]	< 0.001	0.070
Non-white	60	3 (5.0)	Not reached [-; -]	59	26 (44.1)	Not reached [3.00; -]	0.06 [0.01; 0.24]	< 0.001	
Geographic Region									
North America	46	1 (2.2)	Not reached [-; -]	33	12 (36.4)	Not reached [7.00; -]	0.04 [0.01; 0.34]	0.003	0.250
Europe	73	7 (9.6)	Not reached [-; -]	94	45 (47.9)	15.71 [7.14; -]	0.12 [0.05; 0.28]	< 0.001	
Rest of World	82	14 (17.1)	Not reached [-; -]	70	38 (54.3)	9.14 [4.00; -]	0.14 [0.07; 0.29]	< 0.001	
Sex									
Male	145	17 (11.7)	Not reached [-; -]	148	67 (45.3)	Not reached [7.86; -]	0.14 [0.08; 0.26]	< 0.001	0.164
Female	56	5 (8.9)	Not reached [-; -]	49	28 (57.1)	7.14 [3.00; -]	0.07 [0.03; 0.21]	< 0.001	
ECOG at Baseline									
0	87	11 (12.6)	Not reached [-; -]	85	36 (42.4)	Not reached [7.71; -]	0.16 [0.07; 0.35]	< 0.001	0.200
1-2	114	11 (9.6)	Not reached [-; -]	112	59 (52.7)	8.29 [6.29; -]	0.09 [0.05; 0.19]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]		Participants with Event n (%) ^b	Median Time ^c in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	74	9 (12.2)	Not reached [-; -]	53	26 (49.1)	16.14 [4.00; -]	0.11 [0.05; 0.27]	< 0.001	0.776
Lower Tract	127	13 (10.2)	Not reached [-; -]	143	68 (47.6)	13.86 [7.00; -]	0.13 [0.07; 0.24]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	6 (12.0)	Not reached [-; -]	49	20 (40.8)	Not reached [7.71; -]	0.19 [0.07; 0.51]	0.001	0.308
Absent	151	16 (10.6)	Not reached [-; -]	148	75 (50.7)	13.14 [6.71; -]	0.10 [0.06; 0.19]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	13 (11.1)	Not reached [-; -]	114	55 (48.2)	13.86 [7.14; -]	0.12 [0.06; 0.24]	< 0.001	0.919
Low	84	9 (10.7)	Not reached [-; -]	83	40 (48.2)	15.71 [5.00; -]	0.12 [0.05; 0.26]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	17 (11.6)	Not reached [-; -]	152	68 (44.7)	Not reached [8.14; -]	0.15 [0.09; 0.27]	< 0.001	0.123
Lymph node only	43	3 (7.0)	Not reached [-; -]	37	22 (59.5)	7.00 [4.14; -]	0.05 [0.01; 0.20]	< 0.001	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	7 (53.8)	4.14 [2.14; -]	n.a. [n.a.; n.a.]	0.043	0.182
Mild	49	9 (18.4)	Not reached [-; -]	40	21 (52.5)	8.29 [5.00; -]	0.21 [0.09; 0.48]	< 0.001	
Moderate/Severe	146	13 (8.9)	Not reached [-; -]	144	67 (46.5)	16.14 [7.86; -]	0.09 [0.05; 0.19]	< 0.001	
SOC: Blood and lymphatic system disorders - PT^g: Thrombocytopenia									
Age									
< 65	39	1 (2.6)	Not reached [-; -]	28	13 (46.4)	Not reached [5.14; -]	0.04 [0.01; 0.33]	0.002	0.513
≥ 65	162	9 (5.6)	Not reached [-; -]	169	83 (49.1)	14.00 [8.43; -]	0.06 [0.03; 0.13]	< 0.001	
Race									
White	141	7 (5.0)	Not reached [-; -]	138	71 (51.4)	11.14 [6.29; -]	0.07 [0.03; 0.15]	< 0.001	0.802
Non-white	60	3 (5.0)	Not reached [-; -]	59	25 (42.4)	Not reached [10.00; -]	0.03 [0.00; 0.22]	< 0.001	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	11 (33.3)	Not reached [12.00; -]	n.a. [n.a.; n.a.]	< 0.001	0.141
Europe	73	6 (8.2)	Not reached [-; -]	94	47 (50.0)	12.14 [5.86; -]	0.12 [0.05; 0.27]	< 0.001	
Rest of World	82	4 (4.9)	Not reached [-; -]	70	38 (54.3)	12.00 [6.14; -]	0.03 [0.01; 0.13]	< 0.001	
Sex									
Male	145	9 (6.2)	Not reached [-; -]	148	74 (50.0)	13.00 [7.71; -]	0.07 [0.03; 0.15]	< 0.001	0.211
Female	56	1 (1.8)	Not reached [-; -]	49	22 (44.9)	Not reached [6.14; -]	0.03 [0.00; 0.22]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	5 (5.7)	Not reached [-; -]	85	38 (44.7)	Not reached [9.86; -]	0.07 [0.03; 0.21]	< 0.001	0.437
1-2	114	5 (4.4)	Not reached [-; -]	112	58 (51.8)	10.43 [5.86; -]	0.05 [0.02; 0.13]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	3 (4.1)	Not reached [-; -]	53	24 (45.3)	Not reached [5.14; -]	0.04 [0.01; 0.18]	< 0.001	0.795
Lower Tract	127	7 (5.5)	Not reached [-; -]	143	71 (49.7)	12.14 [7.71; -]	0.07 [0.03; 0.16]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	Not reached [-; -]	49	21 (42.9)	Not reached [5.00; -]	0.11 [0.03; 0.38]	< 0.001	0.473
Absent	151	7 (4.6)	Not reached [-; -]	148	75 (50.7)	13.00 [8.29; -]	0.05 [0.02; 0.11]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	6 (5.1)	Not reached [-; -]	114	52 (45.6)	Not reached [10.00; -]	0.05 [0.02; 0.15]	< 0.001	0.618
Low	84	4 (4.8)	Not reached [-; -]	83	44 (53.0)	10.00 [5.00; -]	0.06 [0.02; 0.17]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	7 (4.8)	Not reached [-; -]	152	69 (45.4)	Not reached [9.14; -]	0.06 [0.02; 0.14]	< 0.001	0.929
Lymph node only	43	3 (7.0)	Not reached [-; -]	37	22 (59.5)	12.14 [6.14; -]	0.08 [0.02; 0.26]	< 0.001	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	7 (53.8)	12.14 [2.14; -]	n.a. [n.a.; n.a.]	0.026	0.467
Mild	49	3 (6.1)	Not reached [-; -]	40	15 (37.5)	Not reached [7.14; -]	0.13 [0.04; 0.46]	0.001	
Moderate/Severe	146	7 (4.8)	Not reached [-; -]	144	74 (51.4)	12.00 [7.71; -]	0.05 [0.02; 0.11]	< 0.001	
SOC: Endocrine disorders - PT^g: Hypothyroidism									
Age									
< 65	39	4 (10.3)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.349	0.472
≥ 65	162	19 (11.7)	Not reached [-; -]	169	2 (1.2)	Not reached [-; -]	5.61 [1.26; 25.01]	0.024	
Race									
White	141	13 (9.2)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	3.85 [0.83; 17.93]	0.086	0.172
Non-white	60	10 (16.7)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.048	
Sex									
Male	145	19 (13.1)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	8.77 [1.12; 68.75]	0.039	0.223
Female	56	4 (7.1)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	2.73 [0.30; 24.43]	0.370	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
ECOG at Baseline									
0	87	7 (8.0)	Not reached [-; -]	85	1 (1.2)	Not reached [-; -]	4.48 [0.53; 38.12]	0.170	0.603
1-2	114	16 (14.0)	Not reached [-; -]	112	1 (0.9)	Not reached [-; -]	7.24 [0.91; 57.55]	0.061	
Primary Disease Site of Origin									
Upper Tract	74	10 (13.5)	Not reached [-; -]	53	1 (1.9)	Not reached [-; -]	5.94 [0.75; 47.04]	0.092	0.634
Lower Tract	127	13 (10.2)	Not reached [-; -]	143	1 (0.7)	Not reached [-; -]	4.37 [0.51; 37.46]	0.179	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.337	0.452
Absent	151	20 (13.2)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	5.45 [1.23; 24.22]	0.026	
Stratification Factor: PD-L1 Expression									
High	117	12 (10.3)	Not reached [-; -]	114	1 (0.9)	Not reached [-; -]	5.73 [0.70; 46.96]	0.104	0.955
Low	84	11 (13.1)	Not reached [-; -]	83	1 (1.2)	Not reached [-; -]	5.99 [0.74; 48.81]	0.094	
Metastatic Disease Site									
Visceral metastases	147	12 (8.2)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	5.90 [0.71; 48.79]	0.100	0.685
Lymph node only	43	8 (18.6)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	3.74 [0.44; 31.60]	0.225	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.463
Mild	49	8 (16.3)	Not reached [-; -]	40	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.080	
Moderate/Severe	146	15 (10.3)	Not reached [-; -]	144	2 (1.4)	Not reached [-; -]	4.16 [0.90; 19.11]	0.067	
SOC: Eye disorders - PT^g: Dry eye									
Age									
< 65	39	4 (10.3)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.123	0.444
≥ 65	162	17 (10.5)	Not reached [-; -]	169	2 (1.2)	Not reached [-; -]	6.48 [1.46; 28.77]	0.014	
Race									
White	141	13 (9.2)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	8.95 [1.14; 70.46]	0.037	0.707
Non-white	60	8 (13.3)	Not reached [-; -]	59	1 (1.7)	Not reached [-; -]	6.31 [0.77; 51.69]	0.086	
Geographic Region									
North America	46	8 (17.4)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	5 (6.8)	n.c.	94	2 (2.1)	n.c.	n.c.	n.c.	
Rest of World	82	8 (9.8)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	145	17 (11.7)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	14.62 [1.92; 111.18]	0.010	0.254
Female	56	4 (7.1)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	1.61 [0.15; 17.85]	0.697	
ECOG at Baseline									
0	87	12 (13.8)	Not reached [-; -]	85	1 (1.2)	Not reached [-; -]	9.62 [1.23; 75.17]	0.031	0.793
1-2	114	9 (7.9)	Not reached [-; -]	112	1 (0.9)	Not reached [-; -]	5.80 [0.70; 48.12]	0.103	
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [60.14; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.143	0.289
Absent	151	16 (10.6)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	6.59 [1.50; 29.03]	0.013	
Stratification Factor: PD-L1 Expression									
High	117	10 (8.5)	Not reached [-; -]	114	1 (0.9)	Not reached [-; -]	8.40 [1.06; 66.54]	0.044	0.926
Low	84	11 (13.1)	Not reached [-; -]	83	1 (1.2)	Not reached [-; -]	6.92 [0.86; 55.93]	0.070	
Metastatic Disease Site									
Visceral metastases	147	13 (8.8)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	8.40 [1.05; 66.98]	0.044	0.490
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	4.55 [0.54; 38.03]	0.162	
Renal Function									
Normal	6	1 (16.7)	Not reached [5.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.138	0.103
Mild	49	8 (16.3)	Not reached [-; -]	40	2 (5.0)	Not reached [-; -]	2.12 [0.42; 10.75]	0.363	
Moderate/Severe	146	12 (8.2)	Not reached [-; -]	144	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	
SOC: Gastrointestinal disorders - PT^g: Abdominal pain									
Age									
< 65	39	7 (17.9)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	3.14 [0.35; 27.92]	0.305	0.745
≥ 65	162	17 (10.5)	Not reached [-; -]	169	5 (3.0)	Not reached [-; -]	2.69 [0.96; 7.53]	0.060	
Race									
White	141	20 (14.2)	Not reached [-; -]	138	6 (4.3)	Not reached [-; -]	2.66 [1.04; 6.80]	0.040	0.193
Non-white	60	4 (6.7)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.321	
Geographic Region									
North America	46	6 (13.0)	Not reached [-; -]	33	2 (6.1)	Not reached [-; -]	1.01 [0.17; 6.02]	0.996	0.346
Europe	73	14 (19.2)	Not reached [-; -]	94	4 (4.3)	Not reached [-; -]	3.70 [1.18; 11.60]	0.025	
Rest of World	82	4 (4.9)	Not reached [-; -]	70	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.103	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	145	18 (12.4)	Not reached [-; -]	148	4 (2.7)	Not reached [-; -]	3.27 [1.06; 10.10]	0.039	0.503
Female	56	6 (10.7)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	1.84 [0.35; 9.64]	0.469	
ECOG at Baseline									
0	87	12 (13.8)	Not reached [-; -]	85	2 (2.4)	Not reached [-; -]	3.87 [0.82; 18.28]	0.088	0.419
1-2	114	12 (10.5)	Not reached [-; -]	112	4 (3.6)	Not reached [-; -]	2.25 [0.70; 7.28]	0.174	
Primary Disease Site of Origin									
Upper Tract	74	8 (10.8)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.032	0.080
Lower Tract	127	16 (12.6)	Not reached [-; -]	143	6 (4.2)	Not reached [-; -]	2.00 [0.74; 5.43]	0.172	
Stratification Factor: Liver Metastases									
Present	50	11 (22.0)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	11.32 [1.45; 88.49]	0.021	0.111
Absent	151	13 (8.6)	Not reached [-; -]	148	5 (3.4)	Not reached [-; -]	1.33 [0.43; 4.13]	0.626	
Stratification Factor: PD-L1 Expression									
High	117	16 (13.7)	Not reached [-; -]	114	4 (3.5)	Not reached [-; -]	2.48 [0.78; 7.92]	0.124	0.971
Low	84	8 (9.5)	Not reached [-; -]	83	2 (2.4)	Not reached [-; -]	3.35 [0.70; 16.05]	0.131	
Metastatic Disease Site									
Visceral metastases	147	18 (12.2)	Not reached [-; -]	152	5 (3.3)	Not reached [-; -]	2.81 [1.01; 7.86]	0.049	0.184
Lymph node only	43	5 (11.6)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.155	
Renal Function									
Normal	6	3 (50.0)	32.86 [2.57; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.031	0.083
Mild	49	10 (20.4)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	6.77 [0.85; 54.17]	0.071	
Moderate/Severe	146	11 (7.5)	Not reached [-; -]	144	5 (3.5)	Not reached [-; -]	1.32 [0.42; 4.15]	0.630	
SOC: Gastrointestinal disorders - PT^g: Constipation									
Age									
< 65	39	11 (28.2)	Not reached [71.43; -]	28	11 (39.3)	Not reached [5.00; -]	0.44 [0.18; 1.09]	0.075	0.948
≥ 65	162	38 (23.5)	106.43 [83.00; -]	169	60 (35.5)	Not reached [-; -]	0.45 [0.29; 0.69]	< 0.001	
Race									
White	141	37 (26.2)	106.43 [83.00; -]	138	51 (37.0)	Not reached [-; -]	0.51 [0.33; 0.80]	0.004	0.354
Non-white	60	12 (20.0)	Not reached [-; -]	59	20 (33.9)	Not reached [-; -]	0.30 [0.13; 0.68]	0.004	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	15 (32.6)	71.43 [56.43; -]	33	12 (36.4)	Not reached [7.14; -]	0.57 [0.25; 1.29]	0.178	0.655
Europe	73	19 (26.0)	Not reached [83.00; -]	94	38 (40.4)	Not reached [8.14; -]	0.44 [0.24; 0.79]	0.006	
Rest of World	82	15 (18.3)	Not reached [-; -]	70	21 (30.0)	Not reached [-; -]	0.41 [0.20; 0.83]	0.014	
ECOG at Baseline									
0	87	20 (23.0)	Not reached [-; -]	85	24 (28.2)	Not reached [-; -]	0.67 [0.36; 1.24]	0.199	0.299
1-2	114	29 (25.4)	106.43 [71.43; -]	112	47 (42.0)	Not reached [10.43; -]	0.34 [0.20; 0.56]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	20 (27.0)	Not reached [68.57; -]	53	22 (41.5)	Not reached [7.14; -]	0.44 [0.23; 0.84]	0.012	0.978
Lower Tract	127	29 (22.8)	106.43 [83.00; -]	143	49 (34.3)	Not reached [-; -]	0.44 [0.27; 0.72]	0.001	
Stratification Factor: Liver Metastases									
Present	50	12 (24.0)	Not reached [41.14; -]	49	20 (40.8)	Not reached [5.71; -]	0.43 [0.20; 0.92]	0.029	0.765
Absent	151	37 (24.5)	106.43 [106.43; -]	148	51 (34.5)	Not reached [-; -]	0.46 [0.29; 0.72]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	27 (23.1)	106.43 [106.43; -]	114	48 (42.1)	Not reached [8.43; -]	0.34 [0.20; 0.57]	< 0.001	0.065
Low	84	22 (26.2)	Not reached [71.43; -]	83	23 (27.7)	Not reached [-; -]	0.68 [0.37; 1.27]	0.229	
Metastatic Disease Site									
Visceral metastases	147	36 (24.5)	Not reached [-; -]	152	51 (33.6)	Not reached [-; -]	0.52 [0.33; 0.81]	0.004	0.323
Lymph node only	43	9 (20.9)	106.43 [71.43; -]	37	16 (43.2)	Not reached [6.71; -]	0.26 [0.10; 0.66]	0.005	
Renal Function									
Normal	6	3 (50.0)	71.43 [3.14; -]	13	4 (30.8)	Not reached [4.14; -]	0.55 [0.06; 4.91]	0.590	0.482
Mild	49	12 (24.5)	Not reached [83.00; -]	40	14 (35.0)	Not reached [10.14; -]	0.49 [0.22; 1.11]	0.086	
Moderate/Severe	146	34 (23.3)	Not reached [106.43; -]	144	53 (36.8)	Not reached [-; -]	0.43 [0.27; 0.69]	< 0.001	
SOC: Gastrointestinal disorders - PT ^g : Diarrhoea									
Age									
< 65	39	19 (48.7)	48.43 [11.86; -]	28	4 (14.3)	Not reached [-; -]	2.59 [0.85; 7.92]	0.096	0.577
≥ 65	162	58 (35.8)	Not reached [-; -]	169	25 (14.8)	Not reached [-; -]	2.23 [1.38; 3.61]	0.001	
Race									
White	141	61 (43.3)	Not reached [23.71; -]	138	22 (15.9)	Not reached [-; -]	2.60 [1.58; 4.28]	< 0.001	0.446
Non-white	60	16 (26.7)	Not reached [-; -]	59	7 (11.9)	Not reached [-; -]	1.49 [0.58; 3.86]	0.408	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	22 (47.8)	23.71 [5.43; -]	33	7 (21.2)	Not reached [-; -]	2.16 [0.91; 5.14]	0.082	0.858
Europe	73	33 (45.2)	48.43 [19.00; -]	94	17 (18.1)	Not reached [-; -]	2.25 [1.22; 4.12]	0.009	
Rest of World	82	22 (26.8)	Not reached [-; -]	70	5 (7.1)	Not reached [-; -]	2.99 [1.11; 8.07]	0.031	
Sex									
Male	145	52 (35.9)	Not reached [48.43; -]	148	24 (16.2)	Not reached [-; -]	1.86 [1.13; 3.08]	0.015	0.196
Female	56	25 (44.6)	Not reached [17.00; -]	49	5 (10.2)	Not reached [-; -]	4.16 [1.58; 10.96]	0.004	
ECOG at Baseline									
0	87	38 (43.7)	Not reached [23.29; -]	85	16 (18.8)	Not reached [-; -]	2.18 [1.20; 3.97]	0.011	0.718
1-2	114	39 (34.2)	Not reached [49.29; -]	112	13 (11.6)	Not reached [-; -]	2.46 [1.29; 4.69]	0.006	
Stratification Factor: Liver Metastases									
Present	50	23 (46.0)	27.43 [8.00; -]	49	6 (12.2)	Not reached [-; -]	3.76 [1.51; 9.40]	0.005	0.214
Absent	151	54 (35.8)	Not reached [-; -]	148	23 (15.5)	Not reached [-; -]	1.95 [1.18; 3.23]	0.009	
Stratification Factor: PD-L1 Expression									
High	117	43 (36.8)	Not reached [41.00; -]	114	13 (11.4)	Not reached [-; -]	2.77 [1.47; 5.24]	0.002	0.360
Low	84	34 (40.5)	Not reached [23.71; -]	83	16 (19.3)	Not reached [-; -]	1.94 [1.05; 3.57]	0.033	
Metastatic Disease Site									
Visceral metastases	147	57 (38.8)	Not reached [41.00; -]	152	21 (13.8)	Not reached [-; -]	2.56 [1.53; 4.28]	< 0.001	0.349
Lymph node only	43	16 (37.2)	Not reached [28.86; -]	37	7 (18.9)	Not reached [-; -]	1.55 [0.62; 3.85]	0.349	
Renal Function									
Normal	6	4 (66.7)	16.14 [1.71; -]	13	1 (7.7)	Not reached [-; -]	8.33 [0.89; 78.13]	0.063	0.299
Mild	49	21 (42.9)	Not reached [23.29; -]	40	9 (22.5)	Not reached [-; -]	1.58 [0.70; 3.56]	0.272	
Moderate/Severe	146	52 (35.6)	Not reached [-; -]	144	19 (13.2)	Not reached [-; -]	2.46 [1.44; 4.20]	0.001	
SOC: Gastrointestinal disorders - PT ^g : Dry mouth									
Age									
< 65	39	4 (10.3)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	2.24 [0.23; 21.51]	0.486	0.069
≥ 65	162	13 (8.0)	Not reached [-; -]	169	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Geographic Region									
North America	46	9 (19.6)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	7 (9.6)	n.c.	94	1 (1.1)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
Rest of World	82	1 (1.2)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	13 (9.0)	Not reached [-; -]	148	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	0.076
Female	56	4 (7.1)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	3.05 [0.34; 27.27]	0.319	
ECOG at Baseline									
0	87	7 (8.0)	Not reached [-; -]	85	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.028	0.308
1-2	114	10 (8.8)	Not reached [-; -]	112	1 (0.9)	Not reached [-; -]	8.83 [1.12; 69.67]	0.039	
Primary Disease Site of Origin									
Upper Tract	74	3 (4.1)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.146	0.617
Lower Tract	127	14 (11.0)	Not reached [-; -]	143	1 (0.7)	Not reached [-; -]	12.42 [1.60; 96.13]	0.016	
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	5.32 [0.62; 45.56]	0.127	0.139
Absent	151	12 (7.9)	Not reached [-; -]	148	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Stratification Factor: PD-L1 Expression									
High	117	9 (7.7)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	8 (9.5)	n.c.	83	1 (1.2)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	12 (8.2)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	10.50 [1.34; 81.96]	0.025	0.455
Lymph node only	43	5 (11.6)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.069	
Renal Function									
Normal	6	1 (16.7)	Not reached [5.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.138	0.580
Mild	49	11 (22.4)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	7.63 [0.97; 60.26]	0.054	
Moderate/Severe	146	5 (3.4)	Not reached [-; -]	144	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.046	
SOC: Gastrointestinal disorders - PT ^g : Dysphagia									
Age									
< 65	39	2 (5.1)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	5 (3.1)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	
Race									
White	141	5 (3.5)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	2 (3.3)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	4 (8.7)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	3 (4.1)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	0 (0.0)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	5 (3.4)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	2 (3.6)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	87	3 (3.4)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	4 (3.5)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	7 (5.5)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	2 (1.3)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	3 (2.6)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	4 (4.8)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	7 (4.8)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	0 (0.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	4 (8.2)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	3 (2.1)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: General disorders and administration site conditions - PT*: Asthenia									
Age									
< 65	39	6 (15.4)	Not reached [-; -]	28	5 (17.9)	Not reached [23.57; -]	0.49 [0.13; 1.91]	0.302	0.799
≥ 65	162	28 (17.3)	Not reached [-; -]	169	38 (22.5)	Not reached [-; -]	0.57 [0.34; 0.96]	0.033	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	31 (22.0)	Not reached [-; -]	138	38 (27.5)	Not reached [23.57; -]	0.63 [0.38; 1.03]	0.064	0.589
Non-white	60	3 (5.0)	Not reached [-; -]	59	5 (8.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994	
Sex									
Male	145	26 (17.9)	Not reached [-; -]	148	31 (20.9)	Not reached [23.57; -]	0.62 [0.35; 1.08]	0.093	0.310
Female	56	8 (14.3)	Not reached [-; -]	49	12 (24.5)	Not reached [-; -]	0.40 [0.16; 1.03]	0.059	
ECOG at Baseline									
0	87	15 (17.2)	Not reached [-; -]	85	17 (20.0)	Not reached [-; -]	0.79 [0.39; 1.58]	0.506	0.656
1-2	114	19 (16.7)	Not reached [-; -]	112	26 (23.2)	23.57 [23.57; -]	0.40 [0.20; 0.80]	0.009	
Stratification Factor: Liver Metastases									
Present	50	8 (16.0)	Not reached [-; -]	49	11 (22.4)	Not reached [-; -]	0.63 [0.25; 1.60]	0.334	0.931
Absent	151	26 (17.2)	Not reached [-; -]	148	32 (21.6)	Not reached [-; -]	0.53 [0.30; 0.93]	0.026	
Stratification Factor: PD-L1 Expression									
High	117	18 (15.4)	Not reached [-; -]	114	23 (20.2)	Not reached [-; -]	0.56 [0.29; 1.09]	0.086	0.969
Low	84	16 (19.0)	Not reached [-; -]	83	20 (24.1)	Not reached [23.57; -]	0.55 [0.27; 1.12]	0.100	
Metastatic Disease Site									
Visceral metastases	147	24 (16.3)	Not reached [-; -]	152	32 (21.1)	Not reached [-; -]	0.58 [0.33; 1.01]	0.054	0.937
Lymph node only	43	8 (18.6)	Not reached [-; -]	37	8 (21.6)	23.57 [23.57; -]	0.61 [0.22; 1.74]	0.357	
Renal Function									
Normal	6	1 (16.7)	Not reached [3.14; -]	13	3 (23.1)	23.57 [5.14; -]	0.36 [0.03; 4.57]	0.431	0.225
Mild	49	12 (24.5)	Not reached [-; -]	40	7 (17.5)	Not reached [-; -]	1.29 [0.50; 3.32]	0.603	
Moderate/Severe	146	21 (14.4)	Not reached [-; -]	144	33 (22.9)	Not reached [-; -]	0.41 [0.23; 0.75]	0.004	
SOC: General disorders and administration site conditions - PT*: Gait disturbance									
Age									
< 65	39	2 (5.1)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	7 (4.3)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	
Race									
White	141	9 (6.4)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Geographic Region									
North America	46	6 (13.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	3 (4.1)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	0 (0.0)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	8 (5.5)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	1 (1.8)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	87	5 (5.7)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	4 (3.5)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	1 (1.4)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	8 (6.3)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	8 (5.3)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	2 (1.7)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	7 (8.3)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	7 (4.8)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	2 (4.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	4 (8.2)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	5 (3.4)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: General disorders and administration site conditions - PT*: General physical health deterioration									
Age									
< 65	39	0 (0.0)	n.c.	28	2 (7.1)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	0 (0.0)	n.c.	169	6 (3.6)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	0 (0.0)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	46	0 (0.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	0 (0.0)	n.c.	94	8 (8.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	0 (0.0)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	0 (0.0)	n.c.	148	6 (4.1)	n.c.	n.c.	n.c.	n.c.
Female	56	0 (0.0)	n.c.	49	2 (4.1)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	87	0 (0.0)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	0 (0.0)	n.c.	112	8 (7.1)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	0 (0.0)	n.c.	143	8 (5.6)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	n.c.	49	2 (4.1)	n.c.	n.c.	n.c.	n.c.
Absent	151	0 (0.0)	n.c.	148	6 (4.1)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	0 (0.0)	n.c.	114	3 (2.6)	n.c.	n.c.	n.c.	n.c.
Low	84	0 (0.0)	n.c.	83	5 (6.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	0 (0.0)	n.c.	152	7 (4.6)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	0 (0.0)	n.c.	37	1 (2.7)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	1 (7.7)	n.c.	n.c.	n.c.	n.c.
Mild	49	0 (0.0)	n.c.	40	1 (2.5)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	0 (0.0)	n.c.	144	6 (4.2)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
SOC: Infections and infestations - PT^g: Conjunctivitis									
Age									
< 65	39	1 (2.6)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	8 (4.9)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	141	8 (5.7)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	1 (1.7)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	46	3 (6.5)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	4 (5.5)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	2 (2.4)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	7 (4.8)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	2 (3.6)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	87	5 (5.7)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	4 (3.5)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	3 (4.1)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	6 (4.7)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	9 (6.0)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	4 (3.4)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	5 (6.0)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	4 (2.7)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	5 (11.6)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	1 (16.7)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	2 (4.1)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	
Moderate/Severe	146	6 (4.1)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Investigations - PT^g: Neutrophil count decreased									
Age									
< 65	39	2 (5.1)	Not reached [-; -]	28	4 (14.3)	Not reached [-; -]	0.17 [0.02; 1.55]	0.116	0.951
≥ 65	162	7 (4.3)	Not reached [-; -]	169	20 (11.8)	Not reached [-; -]	0.34 [0.14; 0.80]	0.013	
Race									
White	141	7 (5.0)	Not reached [-; -]	138	13 (9.4)	Not reached [-; -]	0.50 [0.20; 1.25]	0.139	0.155
Non-white	60	2 (3.3)	Not reached [-; -]	59	11 (18.6)	Not reached [-; -]	0.08 [0.01; 0.61]	0.015	
Geographic Region									
North America	46	2 (4.3)	Not reached [-; -]	33	5 (15.2)	Not reached [-; -]	0.24 [0.05; 1.26]	0.093	0.645
Europe	73	2 (2.7)	Not reached [-; -]	94	11 (11.7)	Not reached [-; -]	0.22 [0.05; 1.00]	0.050 ^h	
Rest of World	82	5 (6.1)	Not reached [-; -]	70	8 (11.4)	Not reached [-; -]	0.40 [0.12; 1.34]	0.140	
Sex									
Male	145	7 (4.8)	Not reached [-; -]	148	20 (13.5)	Not reached [-; -]	0.29 [0.12; 0.71]	0.007	0.860
Female	56	2 (3.6)	Not reached [-; -]	49	4 (8.2)	Not reached [-; -]	0.38 [0.07; 2.05]	0.259	
Primary Disease Site of Origin									
Upper Tract	74	4 (5.4)	Not reached [-; -]	53	10 (18.9)	Not reached [-; -]	0.20 [0.05; 0.72]	0.014	0.608
Lower Tract	127	5 (3.9)	Not reached [-; -]	143	14 (9.8)	Not reached [-; -]	0.37 [0.13; 1.04]	0.060	
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	Not reached [-; -]	49	6 (12.2)	Not reached [-; -]	0.16 [0.02; 1.31]	0.088	0.407
Absent	151	8 (5.3)	Not reached [-; -]	148	18 (12.2)	Not reached [-; -]	0.35 [0.15; 0.83]	0.018	
Stratification Factor: PD-L1 Expression									
High	117	7 (6.0)	Not reached [-; -]	114	12 (10.5)	Not reached [-; -]	0.46 [0.17; 1.23]	0.122	0.129
Low	84	2 (2.4)	Not reached [-; -]	83	12 (14.5)	Not reached [-; -]	0.15 [0.03; 0.66]	0.012	
Metastatic Disease Site									
Visceral metastases	147	6 (4.1)	Not reached [-; -]	152	19 (12.5)	Not reached [-; -]	0.25 [0.09; 0.67]	0.006	0.463
Lymph node only	43	3 (7.0)	Not reached [-; -]	37	4 (10.8)	Not reached [-; -]	0.61 [0.14; 2.72]	0.515	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.710
Mild	49	4 (8.2)	Not reached [-; -]	40	6 (15.0)	Not reached [-; -]	0.51 [0.14; 1.79]	0.290	
Moderate/Severe	146	5 (3.4)	Not reached [-; -]	144	18 (12.5)	Not reached [-; -]	0.20 [0.07; 0.60]	0.004	
SOC: Investigations - PT^g: Platelet count decreased									
Age									
< 65	39	1 (2.6)	Not reached [-; -]	28	4 (14.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.995	0.755
≥ 65	162	2 (1.2)	Not reached [-; -]	169	30 (17.8)	Not reached [-; -]	0.03 [0.00; 0.22]	< 0.001	
Geographic Region									
North America	46	1 (2.2)	Not reached [-; -]	33	7 (21.2)	Not reached [-; -]	0.08 [0.01; 0.68]	0.020	0.933
Europe	73	1 (1.4)	Not reached [-; -]	94	14 (14.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.991	
Rest of World	82	1 (1.2)	Not reached [-; -]	70	13 (18.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.991	
Sex									
Male	145	2 (1.4)	Not reached [-; -]	148	25 (16.9)	Not reached [-; -]	0.04 [0.01; 0.27]	0.001	0.987
Female	56	1 (1.8)	Not reached [-; -]	49	9 (18.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.992	
Primary Disease Site of Origin									
Upper Tract	74	1 (1.4)	Not reached [-; -]	53	11 (20.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.992	0.731
Lower Tract	127	2 (1.6)	Not reached [-; -]	143	22 (15.4)	Not reached [-; -]	0.05 [0.01; 0.34]	0.003	
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	Not reached [-; -]	49	14 (28.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.119
Absent	151	3 (2.0)	Not reached [-; -]	148	20 (13.5)	Not reached [-; -]	0.04 [0.01; 0.32]	0.002	
Stratification Factor: PD-L1 Expression									
High	117	1 (0.9)	Not reached [-; -]	114	18 (15.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.989	0.316
Low	84	2 (2.4)	Not reached [-; -]	83	16 (19.3)	Not reached [-; -]	0.05 [0.01; 0.41]	0.005	
Metastatic Disease Site									
Visceral metastases	147	2 (1.4)	Not reached [-; -]	152	31 (20.4)	Not reached [-; -]	0.03 [0.00; 0.22]	< 0.001	0.562
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.092	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	1 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.497	0.489
Mild	49	2 (4.1)	Not reached [-; -]	40	8 (20.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.993	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Moderate/Severe	146	1 (0.7)	Not reached [-; -]	144	25 (17.4)	Not reached [-; -]	0.04 [0.00; 0.26]	0.001	
SOC: Investigations - PT^g: Weight decreased									
Age									
< 65	39	8 (20.5)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	2.24 [0.45; 11.07]	0.321	0.438
≥ 65	162	64 (39.5)	72.43 [34.29; -]	169	13 (7.7)	Not reached [-; -]	4.10 [2.23; 7.55]	< 0.001	
Race									
White	141	56 (39.7)	53.14 [32.14; -]	138	13 (9.4)	Not reached [-; -]	3.54 [1.91; 6.56]	< 0.001	0.605
Non-white	60	16 (26.7)	Not reached [81.43; -]	59	2 (3.4)	Not reached [-; -]	5.39 [1.19; 24.32]	0.028	
Geographic Region									
North America	46	20 (43.5)	34.29 [12.86; -]	33	1 (3.0)	Not reached [-; -]	13.32 [1.77; 100.07]	0.012	0.235
Europe	73	24 (32.9)	72.43 [50.86; -]	94	7 (7.4)	Not reached [-; -]	2.97 [1.23; 7.17]	0.016	
Rest of World	82	28 (34.1)	Not reached [37.00; -]	70	7 (10.0)	Not reached [-; -]	2.74 [1.17; 6.40]	0.020	
Sex									
Male	145	51 (35.2)	81.43 [42.14; -]	148	13 (8.8)	Not reached [-; -]	3.40 [1.82; 6.35]	< 0.001	0.376
Female	56	21 (37.5)	Not reached [31.14; -]	49	2 (4.1)	Not reached [-; -]	6.00 [1.38; 26.13]	0.017	
Primary Disease Site of Origin									
Upper Tract	74	21 (28.4)	Not reached [50.86; -]	53	1 (1.9)	Not reached [-; -]	10.83 [1.43; 81.89]	0.021	0.177
Lower Tract	127	51 (40.2)	72.43 [32.14; -]	143	14 (9.8)	Not reached [-; -]	3.44 [1.87; 6.31]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	44 (37.6)	81.43 [42.14; -]	114	8 (7.0)	Not reached [-; -]	4.12 [1.90; 8.92]	< 0.001	0.614
Low	84	28 (33.3)	Not reached [37.00; -]	83	7 (8.4)	Not reached [-; -]	3.28 [1.41; 7.65]	0.006	
Renal Function									
Normal	6	3 (50.0)	13.00 [6.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.014	0.163
Mild	49	24 (49.0)	37.00 [15.14; -]	40	3 (7.5)	Not reached [-; -]	5.42 [1.60; 18.42]	0.007	
Moderate/Severe	146	45 (30.8)	Not reached [72.43; -]	144	12 (8.3)	Not reached [-; -]	2.88 [1.49; 5.55]	0.002	
SOC: Investigations - PT^g: White blood cell count decreased									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	3 (10.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.038	0.097
≥ 65	162	4 (2.5)	Not reached [-; -]	169	8 (4.7)	Not reached [-; -]	0.38 [0.10; 1.42]	0.151	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	3 (2.1)	n.c.	138	6 (4.3)	n.c.	n.c.	n.c.	n.c.
Non-white	60	1 (1.7)	n.c.	59	5 (8.5)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	2 (4.3)	n.c.	33	2 (6.1)	n.c.	n.c.	n.c.	n.c.
Europe	73	0 (0.0)	n.c.	94	5 (5.3)	n.c.	n.c.	n.c.	
Rest of World	82	2 (2.4)	n.c.	70	4 (5.7)	n.c.	n.c.	n.c.	
Sex									
Male	145	4 (2.8)	Not reached [-; -]	148	11 (7.4)	Not reached [-; -]	0.28 [0.08; 0.97]	0.044	0.997
Female	56	0 (0.0)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
ECOG at Baseline									
0	87	2 (2.3)	Not reached [-; -]	85	9 (10.6)	Not reached [-; -]	0.13 [0.02; 0.74]	0.022	0.217
1-2	114	2 (1.8)	Not reached [-; -]	112	2 (1.8)	Not reached [-; -]	0.96 [0.13; 6.79]	0.964	
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	Not reached [-; -]	49	3 (6.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.083	0.153
Absent	151	4 (2.6)	Not reached [-; -]	148	8 (5.4)	Not reached [-; -]	0.36 [0.10; 1.31]	0.121	
Stratification Factor: PD-L1 Expression									
High	117	3 (2.6)	Not reached [-; -]	114	7 (6.1)	Not reached [-; -]	0.27 [0.06; 1.28]	0.100	0.663
Low	84	1 (1.2)	Not reached [-; -]	83	4 (4.8)	Not reached [-; -]	0.24 [0.03; 2.12]	0.198	
Metastatic Disease Site									
Visceral metastases	147	3 (2.0)	Not reached [-; -]	152	7 (4.6)	Not reached [-; -]	0.30 [0.07; 1.38]	0.122	0.141
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.048	
Renal Function									
Normal	6	1 (16.7)	Not reached [25.00; -]	13	1 (7.7)	Not reached [12.14; -]	0.53 [0.02; 11.82]	0.688	0.439
Mild	49	1 (2.0)	Not reached [-; -]	40	2 (5.0)	Not reached [-; -]	0.39 [0.04; 4.35]	0.447	
Moderate/Severe	146	2 (1.4)	Not reached [-; -]	144	8 (5.6)	Not reached [-; -]	0.24 [0.05; 1.12]	0.069	
SOC: Metabolism and nutrition disorders - PT ^g : Hyperglycaemia									
Age									
< 65	39	4 (10.3)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.080	0.307
≥ 65	162	24 (14.8)	Not reached [-; -]	169	5 (3.0)	Not reached [-; -]	4.65 [1.76; 12.28]	0.002	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	21 (14.9)	Not reached [-; -]	138	3 (2.2)	Not reached [-; -]	6.76 [2.01; 22.74]	0.002	0.476
Non-white	60	7 (11.7)	Not reached [-; -]	59	2 (3.4)	Not reached [-; -]	2.90 [0.59; 14.39]	0.192	
Geographic Region									
North America	46	8 (17.4)	Not reached [-; -]	33	1 (3.0)	Not reached [-; -]	5.60 [0.70; 44.77]	0.105	0.995
Europe	73	8 (11.0)	Not reached [-; -]	94	2 (2.1)	Not reached [-; -]	4.69 [0.98; 22.58]	0.054	
Rest of World	82	12 (14.6)	Not reached [-; -]	70	2 (2.9)	Not reached [-; -]	4.84 [1.07; 21.86]	0.040	
Sex									
Male	145	26 (17.9)	Not reached [-; -]	148	4 (2.7)	Not reached [-; -]	6.50 [2.26; 18.74]	< 0.001	0.306
Female	56	2 (3.6)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	1.70 [0.15; 18.71]	0.666	
ECOG at Baseline									
0	87	12 (13.8)	Not reached [-; -]	85	2 (2.4)	Not reached [-; -]	6.18 [1.38; 27.61]	0.017	0.890
1-2	114	16 (14.0)	Not reached [-; -]	112	3 (2.7)	Not reached [-; -]	4.58 [1.32; 15.94]	0.017	
Primary Disease Site of Origin									
Upper Tract	74	6 (8.1)	Not reached [-; -]	53	1 (1.9)	Not reached [-; -]	3.52 [0.41; 30.13]	0.251	0.737
Lower Tract	127	22 (17.3)	Not reached [-; -]	143	4 (2.8)	Not reached [-; -]	6.16 [2.11; 17.95]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	4.15 [0.46; 37.15]	0.203	0.918
Absent	151	23 (15.2)	Not reached [-; -]	148	4 (2.7)	Not reached [-; -]	5.49 [1.89; 15.94]	0.002	
Stratification Factor: PD-L1 Expression									
High	117	15 (12.8)	Not reached [-; -]	114	1 (0.9)	Not reached [-; -]	12.94 [1.69; 98.96]	0.014	0.159
Low	84	13 (15.5)	Not reached [-; -]	83	4 (4.8)	Not reached [-; -]	3.30 [1.08; 10.13]	0.037	
Metastatic Disease Site									
Visceral metastases	147	20 (13.6)	Not reached [-; -]	152	4 (2.6)	Not reached [-; -]	5.12 [1.74; 15.04]	0.003	0.984
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	5.12 [0.62; 42.59]	0.130	
Renal Function									
Normal	6	3 (50.0)	Not reached [1.00; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	0.123
Mild	49	13 (26.5)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	11.99 [1.57; 91.66]	0.017	
Moderate/Severe	146	12 (8.2)	Not reached [-; -]	144	4 (2.8)	Not reached [-; -]	2.40 [0.75; 7.66]	0.140	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	Participants with Event N ^b n (%)	Median Time ^c in weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}			
SOC: Metabolism and nutrition disorders - PT^g: Hyponatraemia									
Age									
< 65	39	1 (2.6)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	0.73 [0.05; 11.62]	0.821	0.363
≥ 65	162	27 (16.7)	Not reached [-; -]	169	10 (5.9)	Not reached [-; -]	2.43 [1.16; 5.07]	0.018	
Race									
White	141	20 (14.2)	Not reached [-; -]	138	5 (3.6)	Not reached [-; -]	3.53 [1.31; 9.52]	0.013	0.103
Non-white	60	8 (13.3)	Not reached [-; -]	59	6 (10.2)	Not reached [-; -]	1.03 [0.35; 3.04]	0.955	
Geographic Region									
North America	46	11 (23.9)	Not reached [60.86; -]	33	5 (15.2)	Not reached [-; -]	1.16 [0.39; 3.47]	0.788	0.371
Europe	73	8 (11.0)	Not reached [-; -]	94	2 (2.1)	Not reached [-; -]	5.16 [1.09; 24.30]	0.038	
Rest of World	82	9 (11.0)	Not reached [-; -]	70	4 (5.7)	Not reached [-; -]	1.63 [0.49; 5.37]	0.425	
ECOG at Baseline									
0	87	12 (13.8)	Not reached [-; -]	85	5 (5.9)	Not reached [-; -]	2.22 [0.78; 6.32]	0.134	0.882
1-2	114	16 (14.0)	Not reached [-; -]	112	6 (5.4)	Not reached [-; -]	2.12 [0.81; 5.54]	0.127	
Primary Disease Site of Origin									
Upper Tract	74	8 (10.8)	Not reached [-; -]	53	4 (7.5)	Not reached [-; -]	1.23 [0.37; 4.14]	0.736	0.274
Lower Tract	127	20 (15.7)	Not reached [-; -]	143	7 (4.9)	Not reached [-; -]	2.86 [1.19; 6.85]	0.018	
Stratification Factor: Liver Metastases									
Present	50	2 (4.0)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	0.89 [0.12; 6.41]	0.908	0.351
Absent	151	26 (17.2)	Not reached [-; -]	148	9 (6.1)	Not reached [-; -]	2.44 [1.13; 5.27]	0.023	
Stratification Factor: PD-L1 Expression									
High	117	18 (15.4)	Not reached [-; -]	114	8 (7.0)	Not reached [-; -]	2.04 [0.88; 4.74]	0.096	0.594
Low	84	10 (11.9)	Not reached [-; -]	83	3 (3.6)	Not reached [-; -]	2.55 [0.68; 9.49]	0.164	
Metastatic Disease Site									
Visceral metastases	147	20 (13.6)	Not reached [-; -]	152	10 (6.6)	Not reached [-; -]	1.89 [0.88; 4.06]	0.105	0.422
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	4.07 [0.48; 34.87]	0.200	
SOC: Nervous system disorders - PT^g: Dysgeusia									
Age									
< 65	39	10 (25.6)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	3.05 [0.65; 14.31]	0.156	0.648
≥ 65	162	36 (22.2)	Not reached [-; -]	169	7 (4.1)	Not reached [-; -]	5.35 [2.37; 12.08]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	33 (23.4)	Not reached [-; -]	138	7 (5.1)	Not reached [-; -]	4.63 [2.04; 10.50]	< 0.001	0.761
Non-white	60	13 (21.7)	Not reached [-; -]	59	2 (3.4)	Not reached [-; -]	5.57 [1.23; 25.11]	0.026	
Geographic Region									
North America	46	22 (47.8)	15.14 [8.14; -]	33	3 (9.1)	Not reached [-; -]	5.49 [1.63; 18.51]	0.006	0.495
Europe	73	12 (16.4)	Not reached [-; -]	94	5 (5.3)	Not reached [-; -]	3.21 [1.13; 9.13]	0.028	
Rest of World	82	12 (14.6)	Not reached [-; -]	70	1 (1.4)	Not reached [-; -]	8.97 [1.15; 70.06]	0.036	
Sex									
Male	145	35 (24.1)	Not reached [-; -]	148	7 (4.7)	Not reached [-; -]	5.14 [2.27; 11.64]	< 0.001	0.795
Female	56	11 (19.6)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	4.09 [0.90; 18.67]	0.069	
ECOG at Baseline									
0	87	25 (28.7)	Not reached [-; -]	85	5 (5.9)	Not reached [-; -]	4.94 [1.88; 12.98]	0.001	0.980
1-2	114	21 (18.4)	Not reached [-; -]	112	4 (3.6)	Not reached [-; -]	4.76 [1.62; 13.99]	0.005	
Primary Disease Site of Origin									
Upper Tract	74	14 (18.9)	Not reached [-; -]	53	2 (3.8)	Not reached [-; -]	5.27 [1.20; 23.20]	0.028	0.934
Lower Tract	127	32 (25.2)	Not reached [-; -]	143	7 (4.9)	Not reached [-; -]	4.81 [2.10; 11.00]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	9 (18.0)	Not reached [-; -]	49	3 (6.1)	Not reached [-; -]	2.68 [0.71; 10.11]	0.145	0.352
Absent	151	37 (24.5)	Not reached [-; -]	148	6 (4.1)	Not reached [-; -]	5.92 [2.49; 14.10]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	33 (22.4)	Not reached [-; -]	152	6 (3.9)	Not reached [-; -]	5.62 [2.35; 13.48]	< 0.001	0.955
Lymph node only	43	13 (30.2)	Not reached [31.43; -]	37	2 (5.4)	Not reached [-; -]	5.27 [1.17; 23.74]	0.030	
Renal Function									
Normal	6	2 (33.3)	Not reached [8.14; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.161	0.199
Mild	49	15 (30.6)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	11.91 [1.56; 91.05]	0.017	
Moderate/Severe	146	29 (19.9)	Not reached [-; -]	144	8 (5.6)	Not reached [-; -]	3.59 [1.64; 7.89]	0.001	
SOC: Nervous system disorders - PT ^g : Peripheral sensory neuropathy									
Age < 65	39	22 (56.4)	25.14 [16.29; 64.86]	28	3 (10.7)	Not reached [-; -]	4.27 [1.24; 14.68]	0.021	0.325

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
≥ 65	162	81 (50.0)	29.14 [22.29; 36.29]	169	7 (4.1)	Not reached [-; -]	8.68 [3.96; 19.04]	< 0.001	
Race									
White	141	66 (46.8)	30.14 [21.14; 45.14]	138	5 (3.6)	Not reached [-; -]	10.52 [4.20; 26.39]	< 0.001	0.277
Non-white	60	37 (61.7)	24.57 [19.29; 29.14]	59	5 (8.5)	Not reached [-; -]	4.29 [1.63; 11.31]	0.003	
Geographic Region									
North America	46	23 (50.0)	30.14 [16.43; 42.71]	33	3 (9.1)	Not reached [-; -]	3.39 [0.98; 11.65]	0.053	0.437
Europe	73	38 (52.1)	26.14 [16.00; 65.29]	94	5 (5.3)	Not reached [-; -]	8.78 [3.41; 22.63]	< 0.001	
Rest of World	82	42 (51.2)	28.43 [22.29; 64.86]	70	2 (2.9)	Not reached [-; -]	10.92 [2.59; 45.94]	0.001	
Sex									
Male	145	72 (49.7)	26.29 [19.86; 36.29]	148	7 (4.7)	Not reached [-; -]	8.69 [3.95; 19.11]	< 0.001	0.521
Female	56	31 (55.4)	29.29 [20.14; 42.14]	49	3 (6.1)	Not reached [-; -]	4.73 [1.40; 15.94]	0.012	
ECOG at Baseline									
0	87	49 (56.3)	22.29 [16.14; 30.14]	85	3 (3.5)	Not reached [-; -]	14.07 [4.35; 45.53]	< 0.001	0.173
1-2	114	54 (47.4)	30.14 [24.14; 48.86]	112	7 (6.3)	Not reached [-; -]	4.59 [2.03; 10.35]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	40 (54.1)	28.43 [20.14; 36.14]	53	2 (3.8)	Not reached [-; -]	9.22 [2.19; 38.92]	0.002	0.558
Lower Tract	127	63 (49.6)	29.14 [19.86; 52.43]	143	8 (5.6)	Not reached [-; -]	6.98 [3.30; 14.76]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	22 (44.0)	26.29 [16.14; -]	49	3 (6.1)	Not reached [-; -]	5.72 [1.68; 19.51]	0.005	0.548
Absent	151	81 (53.6)	28.43 [22.14; 36.14]	148	7 (4.7)	Not reached [-; -]	8.01 [3.65; 17.59]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	64 (54.7)	24.14 [19.57; 29.29]	114	7 (6.1)	Not reached [-; -]	6.78 [3.06; 15.00]	< 0.001	0.694
Low	84	39 (46.4)	31.00 [25.14; 65.29]	83	3 (3.6)	Not reached [-; -]	8.69 [2.63; 28.70]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	147	72 (49.0)	29.29 [24.14; 39.14]	152	5 (3.3)	Not reached [-; -]	10.16 [4.04; 25.52]	< 0.001	0.762
Lymph node only	43	24 (55.8)	21.14 [15.57; 27.71]	37	2 (5.4)	Not reached [-; -]	9.89 [2.31; 42.27]	0.002	
Renal Function									
Normal	6	5 (83.3)	10.86 [2.00; -]	13	1 (7.7)	Not reached [21.43; -]	10.32 [1.15; 92.95]	0.037	0.929
Mild	49	24 (49.0)	29.29 [18.00; -]	40	2 (5.0)	Not reached [-; -]	8.03 [1.86; 34.65]	0.005	
Moderate/Severe	146	74 (50.7)	26.29 [22.14; 36.29]	144	7 (4.9)	Not reached [-; -]	7.30 [3.31; 16.09]	< 0.001	
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Dysphonia									
Age									
< 65	39	1 (2.6)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	8 (4.9)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	
Race									
White	141	9 (6.4)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	5 (10.9)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	4 (5.5)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	8 (5.5)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	1 (1.8)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	
ECOG at Baseline									
0	87	6 (6.9)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	3 (2.6)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	74	2 (2.7)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	7 (5.5)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	6 (4.0)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	5 (4.3)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	4 (4.8)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	6 (4.1)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	3 (7.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	1 (16.7)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	3 (6.1)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	5 (3.4)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Pneumonitis									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.996
≥ 65	162	12 (7.4)	Not reached [-; -]	169	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	
Race									
White	141	6 (4.3)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	6 (10.0)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	46	3 (6.5)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	4 (5.5)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	5 (6.1)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	9 (6.2)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	3 (5.4)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
ECOG at Baseline									
0	87	7 (8.0)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	5 (4.4)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
Primary Disease Site of Origin									
Upper Tract	74	4 (5.4)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	8 (6.3)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	2 (4.0)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.300	0.997
Absent	151	10 (6.6)	Not reached [-; -]	148	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.012	
Stratification Factor: PD-L1 Expression									
High	117	7 (6.0)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	5 (6.0)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	9 (6.1)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	3 (7.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	3 (6.1)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	9 (6.2)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Respiratory, thoracic and mediastinal disorders - PT^g: Rhinorrhoea									
Age									
< 65	39	2 (5.1)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	5 (3.1)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Race									
White	141	5 (3.5)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	2 (3.3)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Geographic Region									
North America	46	2 (4.3)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	3 (4.1)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	82	2 (2.4)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Sex									
Male	145	6 (4.1)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	1 (1.8)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	3 (3.4)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	4 (3.5)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	3 (4.1)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	4 (3.1)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	6 (4.0)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	4 (3.4)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	3 (3.6)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	3 (2.0)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	4 (9.3)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	2 (4.1)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	5 (3.4)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
SOC: Skin and subcutaneous tissue disorders - PT^g: Alopecia									
Age									
< 65	39	11 (28.2)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	3.42 [0.74; 15.77]	0.115	0.696
≥ 65	162	50 (30.9)	Not reached [-; -]	169	10 (5.9)	Not reached [-; -]	5.26 [2.65; 10.43]	< 0.001	
Race									
White	141	35 (24.8)	Not reached [-; -]	138	7 (5.1)	Not reached [-; -]	4.56 [2.00; 10.37]	< 0.001	0.869
Non-white	60	26 (43.3)	Not reached [12.14; -]	59	5 (8.5)	Not reached [-; -]	5.43 [2.07; 14.20]	< 0.001	
Geographic Region									
North America	46	17 (37.0)	Not reached [11.00; -]	33	3 (9.1)	Not reached [-; -]	4.26 [1.24; 14.63]	0.021	0.906
Europe	73	14 (19.2)	Not reached [-; -]	94	4 (4.3)	Not reached [-; -]	3.76 [1.21; 11.69]	0.022	
Rest of World	82	30 (36.6)	Not reached [29.43; -]	70	5 (7.1)	Not reached [-; -]	5.35 [2.06; 13.91]	< 0.001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	31 (35.6)	Not reached [29.43; -]	85	3 (3.5)	Not reached [-; -]	10.11 [3.07; 33.32]	< 0.001	0.075
1-2	114	30 (26.3)	Not reached [-; -]	112	9 (8.0)	Not reached [-; -]	3.20 [1.51; 6.79]	0.002	
Primary Disease Site of Origin									
Upper Tract	74	22 (29.7)	Not reached [-; -]	53	4 (7.5)	Not reached [-; -]	4.29 [1.48; 12.49]	0.007	0.674
Lower Tract	127	39 (30.7)	Not reached [-; -]	143	8 (5.6)	Not reached [-; -]	5.13 [2.37; 11.09]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	34 (29.1)	Not reached [-; -]	114	10 (8.8)	Not reached [-; -]	3.40 [1.67; 6.92]	< 0.001	0.053
Low	84	27 (32.1)	Not reached [52.29; -]	83	2 (2.4)	Not reached [-; -]	12.40 [2.92; 52.62]	< 0.001	
Renal Function									
Normal	6	2 (33.3)	Not reached [2.86; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.024	0.348
Mild	49	12 (24.5)	Not reached [-; -]	40	3 (7.5)	Not reached [-; -]	2.56 [0.70; 9.38]	0.157	
Moderate/Severe	146	47 (32.2)	Not reached [-; -]	144	9 (6.3)	Not reached [-; -]	5.37 [2.62; 11.01]	< 0.001	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Dermatitis									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.998
≥ 65	162	10 (6.2)	Not reached [-; -]	169	1 (0.6)	Not reached [-; -]	10.01 [1.28; 78.27]	0.028	
Race									
White	141	6 (4.3)	n.c.	138	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Non-white	60	4 (6.7)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	1 (2.2)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	4 (5.5)	n.c.	94	1 (1.1)	n.c.	n.c.	n.c.	
Rest of World	82	5 (6.1)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	4 (2.8)	n.c.	148	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Female	56	6 (10.7)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	
ECOG at Baseline									
0	87	2 (2.3)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	8 (7.0)	n.c.	112	1 (0.9)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Primary Disease Site of Origin									
Upper Tract	74	4 (5.4)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	6 (4.7)	n.c.	143	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	2 (4.0)	n.c.	49	1 (2.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	8 (5.3)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	5 (4.3)	n.c.	114	1 (0.9)	n.c.	n.c.	n.c.	n.c.
Low	84	5 (6.0)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	5 (3.4)	n.c.	152	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	2 (4.7)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	2 (4.1)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	8 (5.5)	n.c.	144	1 (0.7)	n.c.	n.c.	n.c.	n.c.
SOC: Skin and subcutaneous tissue disorders - PT^g: Dry skin									
Age									
< 65	39	8 (20.5)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	0.389
≥ 65	162	29 (17.9)	Not reached [-; -]	169	2 (1.2)	Not reached [-; -]	11.45 [2.70; 48.58]	< 0.001	
Race									
White	141	31 (22.0)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	11.71 [2.77; 49.51]	< 0.001	0.437
Non-white	60	6 (10.0)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.020	
Geographic Region									
North America	46	13 (28.3)	Not reached [40.43; -]	33	1 (3.0)	Not reached [-; -]	6.99 [0.90; 54.65]	0.064	0.581
Europe	73	16 (21.9)	Not reached [-; -]	94	1 (1.1)	Not reached [-; -]	18.19 [2.40; 137.83]	0.005	
Rest of World	82	8 (9.8)	Not reached [-; -]	70	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.034	
Sex									
Male	145	28 (19.3)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	11.67 [2.75; 49.60]	< 0.001	0.370
Female	56	9 (16.1)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.019	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	22 (25.3)	Not reached [56.57; -]	85	1 (1.2)	Not reached [-; -]	18.26 [2.44; 136.59]	0.005	0.733
1-2	114	15 (13.2)	Not reached [-; -]	112	1 (0.9)	Not reached [-; -]	10.76 [1.40; 83.00]	0.023	
Primary Disease Site of Origin									
Upper Tract	74	9 (12.2)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.015	0.394
Lower Tract	127	28 (22.0)	Not reached [-; -]	143	2 (1.4)	Not reached [-; -]	12.00 [2.82; 51.02]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	1.92 [0.19; 19.10]	0.578	0.132
Absent	151	34 (22.5)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	26.97 [3.67; 198.36]	0.001	
Stratification Factor: PD-L1 Expression									
High	117	25 (21.4)	Not reached [-; -]	114	1 (0.9)	Not reached [-; -]	20.39 [2.74; 151.70]	0.003	0.597
Low	84	12 (14.3)	Not reached [-; -]	83	1 (1.2)	Not reached [-; -]	8.46 [1.08; 66.49]	0.042	
Metastatic Disease Site									
Visceral metastases	147	21 (14.3)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	17.83 [2.38; 133.73]	0.005	0.700
Lymph node only	43	14 (32.6)	Not reached [56.57; -]	37	1 (2.7)	Not reached [-; -]	9.71 [1.26; 75.00]	0.029	
Renal Function									
Normal	6	1 (16.7)	Not reached [12.86; -]	13	1 (7.7)	Not reached [-; -]	1.70 [0.10; 28.29]	0.713	0.151
Mild	49	15 (30.6)	Not reached [51.71; -]	40	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	
Moderate/Severe	146	21 (14.4)	Not reached [-; -]	144	1 (0.7)	Not reached [-; -]	15.59 [2.07; 117.27]	0.008	
SOC: Skin and subcutaneous tissue disorders - PT^g: Eczema									
Age									
< 65	39	5 (12.8)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.080	0.316
≥ 65	162	12 (7.4)	Not reached [-; -]	169	2 (1.2)	Not reached [-; -]	4.99 [1.09; 22.79]	0.038	
Race									
White	141	11 (7.8)	Not reached [-; -]	138	2 (1.4)	Not reached [-; -]	3.92 [0.84; 18.43]	0.083	0.213
Non-white	60	6 (10.0)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.016	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.494
Europe	73	10 (13.7)	Not reached [-; -]	94	2 (2.1)	Not reached [-; -]	5.23 [1.11; 24.63]	0.036	
Rest of World	82	7 (8.5)	Not reached [-; -]	70	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.023	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	145	12 (8.3)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	4.72 [1.02; 21.79]	0.047	0.298
Female	56	5 (8.9)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.048	
Primary Disease Site of Origin									
Upper Tract	74	8 (10.8)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.024	0.187
Lower Tract	127	9 (7.1)	Not reached [-; -]	143	2 (1.4)	Not reached [-; -]	3.87 [0.81; 18.58]	0.091	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	Not reached [62.00; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.159	0.386
Absent	151	14 (9.3)	Not reached [-; -]	148	2 (1.4)	Not reached [-; -]	5.81 [1.30; 25.92]	0.021	
Stratification Factor: PD-L1 Expression									
High	117	10 (8.5)	Not reached [-; -]	114	2 (1.8)	Not reached [-; -]	3.28 [0.68; 15.75]	0.139	0.151
Low	84	7 (8.3)	Not reached [-; -]	83	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.007	
Metastatic Disease Site									
Visceral metastases	147	11 (7.5)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	8.91 [1.13; 70.44]	0.038	0.597
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	4.52 [0.53; 38.59]	0.168	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.687
Mild	49	4 (8.2)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	3.40 [0.38; 30.41]	0.274	
Moderate/Severe	146	13 (8.9)	Not reached [-; -]	144	1 (0.7)	Not reached [-; -]	9.60 [1.23; 74.98]	0.031	
SOC: Skin and subcutaneous tissue disorders - PT^g: Pruritus									
Age									
< 65	39	14 (35.9)	Not reached [23.29; -]	28	2 (7.1)	Not reached [-; -]	5.12 [1.15; 22.80]	0.032	0.935
≥ 65	162	63 (38.9)	Not reached [48.57; -]	169	14 (8.3)	Not reached [-; -]	4.93 [2.75; 8.84]	< 0.001	
Race									
White	141	48 (34.0)	Not reached [81.14; -]	138	10 (7.2)	Not reached [-; -]	4.60 [2.31; 9.16]	< 0.001	0.857
Non-white	60	29 (48.3)	Not reached [2.14; -]	59	6 (10.2)	Not reached [-; -]	5.55 [2.30; 13.43]	< 0.001	
Geographic Region									
North America	46	23 (50.0)	22.14 [2.57; -]	33	3 (9.1)	Not reached [-; -]	6.39 [1.91; 21.40]	0.003	0.447
Europe	73	25 (34.2)	Not reached [48.57; -]	94	5 (5.3)	Not reached [-; -]	6.17 [2.34; 16.32]	< 0.001	
Rest of World	82	29 (35.4)	Not reached [81.14; -]	70	8 (11.4)	Not reached [-; -]	3.19 [1.45; 7.04]	0.004	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	145	55 (37.9)	Not reached [48.57; -]	148	10 (6.8)	Not reached [-; -]	5.73 [2.90; 11.32]	< 0.001	0.344
Female	56	22 (39.3)	Not reached [5.00; -]	49	6 (12.2)	Not reached [-; -]	3.62 [1.46; 8.96]	0.005	
ECOG at Baseline									
0	87	38 (43.7)	Not reached [17.71; -]	85	5 (5.9)	Not reached [-; -]	8.42 [3.30; 21.46]	< 0.001	0.116
1-2	114	39 (34.2)	Not reached [81.14; -]	112	11 (9.8)	Not reached [-; -]	3.37 [1.71; 6.65]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	26 (35.1)	Not reached [29.29; -]	53	3 (5.7)	Not reached [-; -]	6.54 [1.97; 21.71]	0.002	0.562
Lower Tract	127	51 (40.2)	Not reached [33.29; -]	143	13 (9.1)	Not reached [-; -]	4.56 [2.46; 8.44]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	15 (30.0)	Not reached [23.43; -]	49	4 (8.2)	Not reached [-; -]	3.16 [1.02; 9.76]	0.046	0.578
Absent	151	62 (41.1)	Not reached [33.29; -]	148	12 (8.1)	Not reached [-; -]	5.49 [2.95; 10.23]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	43 (36.8)	Not reached [48.57; -]	114	12 (10.5)	Not reached [-; -]	3.58 [1.88; 6.84]	< 0.001	0.110
Low	84	34 (40.5)	Not reached [22.14; -]	83	4 (4.8)	Not reached [-; -]	8.93 [3.15; 25.31]	< 0.001	
Renal Function									
Normal	6	3 (50.0)	Not reached [0.29; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.052
Mild	49	17 (34.7)	Not reached [52.29; -]	40	6 (15.0)	Not reached [-; -]	1.89 [0.72; 4.93]	0.194	
Moderate/Severe	146	57 (39.0)	Not reached [33.29; -]	144	10 (6.9)	Not reached [-; -]	6.19 [3.15; 12.16]	< 0.001	
SOC: Skin and subcutaneous tissue disorders - PT^g: Rash maculo-papular									
Age									
< 65	39	8 (20.5)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.031	0.340
≥ 65	162	62 (38.3)	Not reached [37.86; -]	169	6 (3.6)	Not reached [-; -]	11.12 [4.79; 25.80]	< 0.001	
Sex									
Male	145	54 (37.2)	Not reached [37.71; -]	148	4 (2.7)	Not reached [-; -]	14.67 [5.29; 40.64]	< 0.001	0.380
Female	56	16 (28.6)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	5.69 [1.28; 25.24]	0.022	
ECOG at Baseline									
0	87	35 (40.2)	Not reached [23.71; -]	85	3 (3.5)	Not reached [-; -]	10.90 [3.33; 35.68]	< 0.001	0.991
1-2	114	35 (30.7)	Not reached [-; -]	112	3 (2.7)	Not reached [-; -]	11.88 [3.64; 38.79]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Adverse Events	N ^b			N ^b					
Primary Disease Site of Origin									
Upper Tract	74	24 (32.4)	Not reached [-; -]	53	1 (1.9)	Not reached [-; -]	17.45 [2.35; 129.59]	0.005	0.630
Lower Tract	127	46 (36.2)	Not reached [37.86; -]	143	5 (3.5)	Not reached [-; -]	10.20 [4.03; 25.83]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	19 (38.0)	Not reached [9.14; -]	49	3 (6.1)	Not reached [-; -]	6.84 [2.01; 23.28]	0.002	0.290
Absent	151	51 (33.8)	Not reached [-; -]	148	3 (2.0)	Not reached [-; -]	15.99 [4.97; 51.45]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	43 (36.8)	Not reached [37.86; -]	114	2 (1.8)	Not reached [-; -]	20.45 [4.93; 84.86]	< 0.001	0.182
Low	84	27 (32.1)	Not reached [-; -]	83	4 (4.8)	Not reached [-; -]	6.86 [2.39; 19.70]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	53 (36.1)	Not reached [37.86; -]	152	6 (3.9)	Not reached [-; -]	8.81 [3.76; 20.62]	< 0.001	0.124
Lymph node only	43	14 (32.6)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Renal Function									
Normal	6	5 (83.3)	15.43 [1.86; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.008	0.346
Mild	49	18 (36.7)	Not reached [22.29; -]	40	1 (2.5)	Not reached [-; -]	15.68 [2.09; 117.91]	0.007	
Moderate/Severe	146	47 (32.2)	Not reached [-; -]	144	5 (3.5)	Not reached [-; -]	9.27 [3.67; 23.41]	< 0.001	
SOC: Skin and subcutaneous tissue disorders - PT^g: Skin hyperpigmentation									
Age									
< 65	39	2 (5.1)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	5 (3.1)	n.c.	169	0 (0.0)	n.c.	n.c.	n.c.	
Race									
White	141	3 (2.1)	n.c.	138	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-white	60	4 (6.7)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	1 (2.2)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	1 (1.4)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	82	5 (6.1)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	3 (2.1)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	56	4 (7.1)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
ECOG at Baseline									
0	87	4 (4.6)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1-2	114	3 (2.6)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Primary Disease Site of Origin									
Upper Tract	74	3 (4.1)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	4 (3.1)	n.c.	143	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: Liver Metastases									
Present	50	2 (4.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	5 (3.3)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Stratification Factor: PD-L1 Expression									
High	117	3 (2.6)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	4 (4.8)	n.c.	83	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Metastatic Disease Site									
Visceral metastases	147	6 (4.1)	n.c.	152	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	1 (2.3)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	1 (2.0)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Moderate/Severe	146	6 (4.1)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A specific adverse event appears on this report only if its incidence $\geq 10\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>h: Unrounded p-value < 0.050</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class</p>									

*Schwerwiegende unerwünschte Ereignisse*Tabelle 4G-99: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse (SOC) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									SOC^g: Blood and lymphatic system disorders	
Age										
< 65	39	2 (5.1)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.100	
≥ 65	162	4 (2.5)	Not reached [-; -]	169	25 (14.8)	Not reached [-; -]	0.10 [0.03; 0.34]	< 0.001		
Race										
White	141	6 (4.3)	Not reached [-; -]	138	20 (14.5)	Not reached [-; -]	0.12 [0.04; 0.41]	< 0.001	0.073	
Non-white	60	0 (0.0)	Not reached [-; -]	59	6 (10.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.011		
Geographic Region										
North America	46	1 (2.2)	Not reached [-; -]	33	3 (9.1)	Not reached [-; -]	0.19 [0.02; 1.82]	0.150	0.696	
Europe	73	4 (5.5)	Not reached [-; -]	94	16 (17.0)	Not reached [-; -]	0.06 [0.01; 0.48]	0.008		
Rest of World	82	1 (1.2)	Not reached [-; -]	70	7 (10.0)	Not reached [-; -]	0.12 [0.01; 0.94]	0.043		
Sex										
Male	145	5 (3.4)	Not reached [-; -]	148	21 (14.2)	Not reached [-; -]	0.12 [0.04; 0.42]	< 0.001	0.674	
Female	56	1 (1.8)	Not reached [-; -]	49	5 (10.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994		
ECOG at Baseline										
0	87	2 (2.3)	Not reached [-; -]	85	9 (10.6)	Not reached [-; -]	0.09 [0.01; 0.73]	0.024	0.988	
1-2	114	4 (3.5)	Not reached [-; -]	112	17 (15.2)	Not reached [-; -]	0.09 [0.02; 0.41]	0.002		
Primary Disease Site of Origin										
Upper Tract	74	0 (0.0)	Not reached [-; -]	53	4 (7.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.015	0.100	
Lower Tract	127	6 (4.7)	Not reached [-; -]	143	21 (14.7)	Not reached [-; -]	0.13 [0.04; 0.44]	0.001		
Stratification Factor: Liver Metastases										
Present	50	2 (4.0)	Not reached [-; -]	49	10 (20.4)	Not reached [-; -]	0.17 [0.04; 0.76]	0.021	0.894	
Absent	151	4 (2.6)	Not reached [-; -]	148	16 (10.8)	Not reached [-; -]	0.05 [0.01; 0.39]	0.004		
Stratification Factor: PD-L1 Expression										
High	117	2 (1.7)	Not reached [-; -]	114	12 (10.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.991	0.555	
Low	84	4 (4.8)	Not reached [-; -]	83	14 (16.9)	Not reached [-; -]	0.19 [0.05; 0.65]	0.008		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Metastatic Disease Site	
Visceral metastases	147	3 (2.0)	Not reached [-; -]	152	23 (15.1)	Not reached [-; -]	0.11 [0.03; 0.38]	< 0.001	0.212	
Lymph node only	43	2 (4.7)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996		
Renal Function										
Normal	6	0 (0.0)	Not reached [-; -]	13	1 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.497	0.874	
Mild	49	1 (2.0)	Not reached [-; -]	40	4 (10.0)	Not reached [-; -]	0.20 [0.02; 1.75]	0.145		
Moderate/Severe	146	5 (3.4)	Not reached [-; -]	144	21 (14.6)	Not reached [-; -]	0.08 [0.02; 0.32]	< 0.001		
SOC ^g : Skin and subcutaneous tissue disorders										
Age										
< 65	39	1 (2.6)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.402	0.716	
≥ 65	162	10 (6.2)	Not reached [-; -]	169	1 (0.6)	Not reached [-; -]	9.59 [1.22; 75.21]	0.031		
Race										
White	141	8 (5.7)	n.c.	138	1 (0.7)	n.c.	n.c.	n.c.	n.c.	
Non-white	60	3 (5.0)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.		
Geographic Region										
North America	46	1 (2.2)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	73	6 (8.2)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.		
Rest of World	82	4 (4.9)	n.c.	70	1 (1.4)	n.c.	n.c.	n.c.		
Sex										
Male	145	9 (6.2)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	8.53 [1.08; 67.56]	0.042	0.574	
Female	56	2 (3.6)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.199		
ECOG at Baseline										
0	87	5 (5.7)	n.c.	85	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
1-2	114	6 (5.3)	n.c.	112	1 (0.9)	n.c.	n.c.	n.c.		
Primary Disease Site of Origin										
Upper Tract	74	3 (4.1)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	127	8 (6.3)	n.c.	143	1 (0.7)	n.c.	n.c.	n.c.		
Stratification Factor: Liver Metastases										
Present	50	4 (8.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Absent	151	7 (4.6)	n.c.	148	1 (0.7)	n.c.	n.c.	n.c.		

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: PD-L1 Expression	
High	117	6 (5.1)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Low	84	5 (6.0)	n.c.	83	1 (1.2)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	147	9 (6.1)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	8.43 [1.06; 66.87]	0.044	0.567	
Lymph node only	43	2 (4.7)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.187		
Renal Function										
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	49	3 (6.1)	n.c.	40	1 (2.5)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	146	8 (5.5)	n.c.	144	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
a: Database Cutoff Date: 08AUG2023										
b: Number of participants: all-participants-as-treated population, cisplatin ineligible										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
g: A system organ class appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class										

Tabelle 4G-100: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse (PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									SOC: Blood and lymphatic system disorders - PT ^g : Febrile neutropenia	
Age										
< 65	39	0 (0.0)	n.c.	28	1 (3.6)	n.c.	n.c.	n.c.	n.c.	
≥ 65	162	1 (0.6)	n.c.	169	8 (4.7)	n.c.	n.c.	n.c.	n.c.	
Race										
White	141	1 (0.7)	n.c.	138	7 (5.1)	n.c.	n.c.	n.c.	n.c.	
Non-white	60	0 (0.0)	n.c.	59	2 (3.4)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Geographic Region	
North America	46	0 (0.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Europe	73	1 (1.4)	n.c.	94	7 (7.4)	n.c.	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	2 (2.9)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	145	1 (0.7)	n.c.	148	6 (4.1)	n.c.	n.c.	n.c.	n.c.	
Female	56	0 (0.0)	n.c.	49	3 (6.1)	n.c.	n.c.	n.c.	n.c.	
ECOG at Baseline										
0	87	0 (0.0)	n.c.	85	3 (3.5)	n.c.	n.c.	n.c.	n.c.	
1-2	114	1 (0.9)	n.c.	112	6 (5.4)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	74	0 (0.0)	n.c.	53	1 (1.9)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	127	1 (0.8)	n.c.	143	8 (5.6)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases										
Present	50	1 (2.0)	n.c.	49	6 (12.2)	n.c.	n.c.	n.c.	n.c.	
Absent	151	0 (0.0)	n.c.	148	3 (2.0)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression										
High	117	0 (0.0)	n.c.	114	4 (3.5)	n.c.	n.c.	n.c.	n.c.	
Low	84	1 (1.2)	n.c.	83	5 (6.0)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	147	1 (0.7)	n.c.	152	8 (5.3)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	43	0 (0.0)	n.c.	37	1 (2.7)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Mild	49	1 (2.0)	n.c.	40	3 (7.5)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	146	0 (0.0)	n.c.	144	6 (4.2)	n.c.	n.c.	n.c.	n.c.	
SOC: Blood and lymphatic system disorders - PT ^g : Thrombocytopenia										
Age										
< 65	39	0 (0.0)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
≥ 65	162	0 (0.0)	n.c.	169	8 (4.7)	n.c.	n.c.	n.c.	n.c.	

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Race	
White	141	0 (0.0)	n.c.	138	6 (4.3)	n.c.	n.c.	n.c.	n.c.	
Non-white	60	0 (0.0)	n.c.	59	2 (3.4)	n.c.	n.c.	n.c.	n.c.	
Geographic Region										
North America	46	0 (0.0)	n.c.	33	2 (6.1)	n.c.	n.c.	n.c.	n.c.	
Europe	73	0 (0.0)	n.c.	94	5 (5.3)	n.c.	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	1 (1.4)	n.c.	n.c.	n.c.	n.c.	
Sex										
Male	145	0 (0.0)	n.c.	148	6 (4.1)	n.c.	n.c.	n.c.	n.c.	
Female	56	0 (0.0)	n.c.	49	2 (4.1)	n.c.	n.c.	n.c.	n.c.	
ECOG at Baseline										
0	87	0 (0.0)	n.c.	85	2 (2.4)	n.c.	n.c.	n.c.	n.c.	
1-2	114	0 (0.0)	n.c.	112	6 (5.4)	n.c.	n.c.	n.c.	n.c.	
Primary Disease Site of Origin										
Upper Tract	74	0 (0.0)	n.c.	53	1 (1.9)	n.c.	n.c.	n.c.	n.c.	
Lower Tract	127	0 (0.0)	n.c.	143	6 (4.2)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases										
Present	50	0 (0.0)	n.c.	49	4 (8.2)	n.c.	n.c.	n.c.	n.c.	
Absent	151	0 (0.0)	n.c.	148	4 (2.7)	n.c.	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression										
High	117	0 (0.0)	n.c.	114	4 (3.5)	n.c.	n.c.	n.c.	n.c.	
Low	84	0 (0.0)	n.c.	83	4 (4.8)	n.c.	n.c.	n.c.	n.c.	
Metastatic Disease Site										
Visceral metastases	147	0 (0.0)	n.c.	152	8 (5.3)	n.c.	n.c.	n.c.	n.c.	
Lymph node only	43	0 (0.0)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.	
Renal Function										
Normal	6	0 (0.0)	n.c.	13	1 (7.7)	n.c.	n.c.	n.c.	n.c.	
Mild	49	0 (0.0)	n.c.	40	1 (2.5)	n.c.	n.c.	n.c.	n.c.	
Moderate/Severe	146	0 (0.0)	n.c.	144	6 (4.2)	n.c.	n.c.	n.c.	n.c.	
a: Database Cutoff Date: 08AUG2023										
b: Number of participants: all-participants-as-treated population, cisplatin ineligible										

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									<p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A specific adverse event appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class</p>	

Tabelle 4G-101: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									SOC^g: Blood and lymphatic system disorders	
Age										
< 65	39	8 (20.5)	Not reached [-; -]	28	15 (53.6)	13.00 [5.14; -]	0.14 [0.05; 0.43]	< 0.001	0.407	
≥ 65	162	35 (21.6)	Not reached [-; -]	169	120 (71.0)	5.14 [4.14; 6.43]	0.14 [0.09; 0.21]	< 0.001		
Race										
White	141	33 (23.4)	Not reached [-; -]	138	95 (68.8)	5.86 [4.14; 7.86]	0.16 [0.10; 0.24]	< 0.001	0.251	
Non-white	60	10 (16.7)	Not reached [-; -]	59	40 (67.8)	5.14 [3.00; 12.00]	0.09 [0.04; 0.21]	< 0.001		
Geographic Region										
North America	46	8 (17.4)	Not reached [-; -]	33	19 (57.6)	9.00 [3.14; -]	0.19 [0.08; 0.43]	< 0.001	0.778	
Europe	73	19 (26.0)	Not reached [-; -]	94	65 (69.1)	5.00 [3.71; 7.00]	0.15 [0.09; 0.28]	< 0.001		
Rest of World	82	16 (19.5)	Not reached [-; -]	70	51 (72.9)	6.00 [4.14; 8.14]	0.11 [0.06; 0.21]	< 0.001		
Primary Disease Site of Origin										
Upper Tract	74	16 (21.6)	Not reached [76.14; -]	53	33 (62.3)	6.00 [4.00; 16.14]	0.15 [0.08; 0.30]	< 0.001	0.582	
Lower Tract	127	27 (21.3)	Not reached [-; -]	143	101 (70.6)	5.14 [4.29; 7.14]	0.14 [0.08; 0.22]	< 0.001		
Stratification Factor: PD-L1 Expression										
High	117	23 (19.7)	Not reached [-; -]	114	79 (69.3)	5.14 [4.29; 7.14]	0.12 [0.07; 0.20]	< 0.001	0.493	
Low	84	20 (23.8)	Not reached [-; -]	83	56 (67.5)	6.14 [3.00; 10.29]	0.17 [0.10; 0.29]	< 0.001		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Metastatic Disease Site									
Visceral metastases	147	35 (23.8)	Not reached [-; -]	152	101 (66.4)	5.57 [4.00; 7.71]	0.17 [0.11; 0.26]	< 0.001	0.102
Lymph node only	43	5 (11.6)	Not reached [-; -]	37	27 (73.0)	6.71 [4.14; 12.14]	0.06 [0.02; 0.19]	< 0.001	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	9 (69.2)	4.14 [1.57; -]	n.a. [n.a.; n.a.]	0.011	0.151
Mild	49	11 (22.4)	Not reached [-; -]	40	27 (67.5)	6.71 [4.00; 12.00]	0.19 [0.09; 0.40]	< 0.001	
Moderate/Severe	146	32 (21.9)	Not reached [-; -]	144	99 (68.8)	5.71 [4.29; 7.14]	0.13 [0.08; 0.20]	< 0.001	
SOC^g: Investigations									
Age									
< 65	39	7 (17.9)	Not reached [-; -]	28	5 (17.9)	Not reached [-; -]	0.65 [0.19; 2.22]	0.494	0.652
≥ 65	162	22 (13.6)	Not reached [-; -]	169	31 (18.3)	Not reached [-; -]	0.49 [0.27; 0.88]	0.018	
Race									
White	141	21 (14.9)	Not reached [-; -]	138	20 (14.5)	Not reached [-; -]	0.73 [0.38; 1.40]	0.348	0.074
Non-white	60	8 (13.3)	Not reached [-; -]	59	16 (27.1)	Not reached [-; -]	0.25 [0.09; 0.69]	0.007	
Geographic Region									
North America	46	5 (10.9)	Not reached [-; -]	33	6 (18.2)	Not reached [-; -]	0.48 [0.14; 1.61]	0.234	0.826
Europe	73	11 (15.1)	Not reached [-; -]	94	16 (17.0)	Not reached [-; -]	0.52 [0.22; 1.26]	0.148	
Rest of World	82	13 (15.9)	Not reached [-; -]	70	14 (20.0)	Not reached [-; -]	0.50 [0.22; 1.13]	0.097	
Sex									
Male	145	22 (15.2)	Not reached [-; -]	148	32 (21.6)	Not reached [-; -]	0.49 [0.28; 0.89]	0.019	0.266
Female	56	7 (12.5)	Not reached [-; -]	49	4 (8.2)	Not reached [-; -]	0.74 [0.19; 2.86]	0.657	
Primary Disease Site of Origin									
Upper Tract	74	6 (8.1)	Not reached [-; -]	53	10 (18.9)	Not reached [-; -]	0.34 [0.12; 0.97]	0.044	0.134
Lower Tract	127	23 (18.1)	Not reached [-; -]	143	26 (18.2)	Not reached [-; -]	0.62 [0.34; 1.15]	0.131	
Stratification Factor: Liver Metastases									
Present	50	8 (16.0)	Not reached [62.86; -]	49	12 (24.5)	Not reached [-; -]	0.29 [0.09; 0.91]	0.033	0.653
Absent	151	21 (13.9)	Not reached [-; -]	148	24 (16.2)	Not reached [-; -]	0.63 [0.34; 1.16]	0.135	
Stratification Factor: PD-L1 Expression									
High	117	20 (17.1)	Not reached [-; -]	114	17 (14.9)	Not reached [-; -]	0.76 [0.38; 1.53]	0.441	0.071

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Low	84	9 (10.7)	Not reached [-; -]	83	19 (22.9)	Not reached [-; -]	0.30 [0.13; 0.72]	0.007	
Metastatic Disease Site									
Visceral metastases	147	21 (14.3)	Not reached [-; -]	152	31 (20.4)	Not reached [-; -]	0.43 [0.23; 0.80]	0.007	0.078
Lymph node only	43	8 (18.6)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	1.76 [0.45; 6.89]	0.417	
Renal Function									
Normal	6	2 (33.3)	Not reached [2.00; -]	13	1 (7.7)	Not reached [12.14; -]	3.93 [0.36; 43.48]	0.264	0.285
Mild	49	9 (18.4)	Not reached [-; -]	40	8 (20.0)	Not reached [-; -]	0.64 [0.23; 1.76]	0.386	
Moderate/Severe	146	18 (12.3)	Not reached [-; -]	144	27 (18.8)	Not reached [-; -]	0.39 [0.20; 0.77]	0.006	
SOC ^g : Metabolism and nutrition disorders									
Age									
< 65	39	6 (15.4)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	1.88 [0.37; 9.63]	0.449	0.984
≥ 65	162	39 (24.1)	Not reached [-; -]	169	19 (11.2)	Not reached [-; -]	1.82 [1.03; 3.20]	0.038	
Race									
White	141	30 (21.3)	Not reached [-; -]	138	13 (9.4)	Not reached [-; -]	2.01 [1.03; 3.92]	0.039	0.598
Non-white	60	15 (25.0)	Not reached [-; -]	59	8 (13.6)	Not reached [-; -]	1.42 [0.58; 3.48]	0.443	
Geographic Region									
North America	46	12 (26.1)	Not reached [-; -]	33	8 (24.2)	Not reached [20.14; -]	0.82 [0.32; 2.08]	0.675	0.240
Europe	73	13 (17.8)	Not reached [-; -]	94	7 (7.4)	Not reached [-; -]	1.99 [0.77; 5.12]	0.156	
Rest of World	82	20 (24.4)	Not reached [-; -]	70	6 (8.6)	Not reached [-; -]	2.55 [1.01; 6.47]	0.049	
ECOG at Baseline									
0	87	18 (20.7)	Not reached [-; -]	85	9 (10.6)	Not reached [-; -]	1.94 [0.86; 4.35]	0.109	0.880
1-2	114	27 (23.7)	Not reached [-; -]	112	12 (10.7)	Not reached [-; -]	1.68 [0.83; 3.42]	0.150	
Primary Disease Site of Origin									
Upper Tract	74	17 (23.0)	Not reached [-; -]	53	7 (13.2)	Not reached [-; -]	1.51 [0.62; 3.71]	0.367	0.565
Lower Tract	127	28 (22.0)	Not reached [-; -]	143	14 (9.8)	Not reached [-; -]	1.89 [0.97; 3.68]	0.060	
Stratification Factor: Liver Metastases									
Present	50	10 (20.0)	Not reached [62.29; -]	49	4 (8.2)	Not reached [-; -]	1.97 [0.59; 6.54]	0.270	0.674
Absent	151	35 (23.2)	Not reached [-; -]	148	17 (11.5)	Not reached [-; -]	1.74 [0.96; 3.15]	0.069	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Stratification Factor: PD-L1 Expression										
High	117	23 (19.7)	Not reached [-; -]	114	13 (11.4)	Not reached [-; -]	1.56 [0.78; 3.12]	0.208	0.353	
Low	84	22 (26.2)	Not reached [62.29; -]	83	8 (9.6)	Not reached [-; -]	2.20 [0.95; 5.09]	0.066		
Metastatic Disease Site										
Visceral metastases	147	35 (23.8)	Not reached [-; -]	152	17 (11.2)	Not reached [-; -]	1.80 [0.99; 3.28]	0.054	0.906	
Lymph node only	43	7 (16.3)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	1.98 [0.51; 7.66]	0.323		
SOC ^g : Skin and subcutaneous tissue disorders										
Age										
< 65	39	6 (15.4)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.217	0.515	
≥ 65	162	33 (20.4)	Not reached [-; -]	169	2 (1.2)	Not reached [-; -]	15.18 [3.62; 63.67]	< 0.001		
Race										
White	141	25 (17.7)	Not reached [-; -]	138	1 (0.7)	Not reached [-; -]	20.73 [2.79; 154.28]	0.003	0.652	
Non-white	60	14 (23.3)	Not reached [-; -]	59	1 (1.7)	Not reached [-; -]	9.64 [1.23; 75.20]	0.031		
Geographic Region										
North America	46	10 (21.7)	Not reached [74.71; -]	33	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.014	0.650	
Europe	73	12 (16.4)	Not reached [-; -]	94	1 (1.1)	Not reached [-; -]	13.57 [1.74; 106.00]	0.013		
Rest of World	82	17 (20.7)	Not reached [-; -]	70	1 (1.4)	Not reached [-; -]	10.15 [1.32; 78.00]	0.026		
Sex										
Male	145	28 (19.3)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	23.13 [3.12; 171.67]	0.002	0.440	
Female	56	11 (19.6)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	7.10 [0.90; 56.22]	0.063		
ECOG at Baseline										
0	87	17 (19.5)	Not reached [-; -]	85	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.136	
1-2	114	22 (19.3)	Not reached [-; -]	112	2 (1.8)	Not reached [-; -]	9.45 [2.20; 40.57]	0.003		
Primary Disease Site of Origin										
Upper Tract	74	13 (17.6)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.290	
Lower Tract	127	26 (20.5)	Not reached [-; -]	143	2 (1.4)	Not reached [-; -]	11.54 [2.70; 49.28]	< 0.001		
Stratification Factor: Liver Metastases										
Present	50	10 (20.0)	Not reached [-; -]	49	1 (2.0)	Not reached [-; -]	9.64 [1.23; 75.82]	0.031	0.506	
Absent	151	29 (19.2)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	20.86 [2.81; 155.02]	0.003		

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									Stratification Factor: PD-L1 Expression	
High	117	24 (20.5)	Not reached [-; -]	114	1 (0.9)	Not reached [-; -]	17.13 [2.28; 128.61]	0.006	0.748	
Low	84	15 (17.9)	Not reached [-; -]	83	1 (1.2)	Not reached [-; -]	13.32 [1.75; 101.54]	0.012		
Metastatic Disease Site										
Visceral metastases	147	31 (21.1)	Not reached [-; -]	152	2 (1.3)	Not reached [-; -]	13.20 [3.12; 55.77]	< 0.001	0.462	
Lymph node only	43	6 (14.0)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.044		
Renal Function										
Normal	6	1 (16.7)	Not reached [9.29; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.157	0.687	
Mild	49	11 (22.4)	Not reached [-; -]	40	1 (2.5)	Not reached [-; -]	6.93 [0.87; 55.40]	0.068		
Moderate/Severe	146	27 (18.5)	Not reached [-; -]	144	1 (0.7)	Not reached [-; -]	21.29 [2.87; 158.06]	0.003		
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A system organ class appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); PD-L1: Programmed Cell Death - Ligand 1; SOC: System Organ Class</p>										

Tabelle 4G-102: Subgruppenanalysen mit statistisch nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (PT) der Studie KEYNOTE A39

Study: KEYNOTE-A39 ^a		EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
									SOC: Blood and lymphatic system disorders - PT ^g : Anaemia	
Age										
< 65	39	4 (10.3)	Not reached [-; -]	28	9 (32.1)	28.43 [14.14; -]	0.17 [0.04; 0.69]	0.013	0.899	
≥ 65	162	22 (13.6)	Not reached [-; -]	169	71 (42.0)	Not reached [12.29; -]	0.19 [0.11; 0.32]	< 0.001		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Race									
White	141	19 (13.5)	Not reached [-; -]	138	56 (40.6)	28.43 [13.00; -]	0.21 [0.12; 0.37]	< 0.001	0.508
Non-white	60	7 (11.7)	Not reached [-; -]	59	24 (40.7)	Not reached [13.00; -]	0.12 [0.05; 0.34]	< 0.001	
Geographic Region									
North America	46	7 (15.2)	Not reached [-; -]	33	11 (33.3)	Not reached [9.14; -]	0.35 [0.13; 0.91]	0.030	0.586
Europe	73	12 (16.4)	Not reached [-; -]	94	44 (46.8)	14.86 [11.29; -]	0.17 [0.08; 0.36]	< 0.001	
Rest of World	82	7 (8.5)	Not reached [-; -]	70	25 (35.7)	Not reached [15.14; -]	0.14 [0.06; 0.36]	< 0.001	
Sex									
Male	145	19 (13.1)	Not reached [-; -]	148	58 (39.2)	28.43 [14.14; -]	0.20 [0.11; 0.36]	< 0.001	0.420
Female	56	7 (12.5)	Not reached [-; -]	49	22 (44.9)	15.14 [8.29; -]	0.14 [0.05; 0.35]	< 0.001	
ECOG at Baseline									
0	87	13 (14.9)	Not reached [-; -]	85	27 (31.8)	Not reached [-; -]	0.30 [0.15; 0.61]	< 0.001	0.067
1-2	114	13 (11.4)	Not reached [-; -]	112	53 (47.3)	13.29 [11.14; -]	0.13 [0.06; 0.26]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	10 (13.5)	Not reached [-; -]	53	18 (34.0)	Not reached [13.14; -]	0.27 [0.12; 0.61]	0.002	0.428
Lower Tract	127	16 (12.6)	Not reached [-; -]	143	62 (43.4)	28.43 [12.29; -]	0.15 [0.08; 0.29]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	12 (24.0)	Not reached [-; -]	49	22 (44.9)	Not reached [8.29; -]	0.38 [0.18; 0.80]	0.011	0.053
Absent	151	14 (9.3)	Not reached [-; -]	148	58 (39.2)	28.43 [14.86; -]	0.12 [0.06; 0.23]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	13 (11.1)	Not reached [-; -]	114	50 (43.9)	Not reached [13.00; -]	0.12 [0.06; 0.25]	< 0.001	0.211
Low	84	13 (15.5)	Not reached [-; -]	83	30 (36.1)	28.43 [13.00; -]	0.30 [0.15; 0.58]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	21 (14.3)	Not reached [-; -]	152	64 (42.1)	Not reached [12.14; -]	0.21 [0.12; 0.36]	< 0.001	0.589
Lymph node only	43	3 (7.0)	Not reached [-; -]	37	12 (32.4)	28.43 [14.14; -]	0.08 [0.02; 0.43]	0.003	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	4 (30.8)	28.43 [4.14; -]	n.a. [n.a.; n.a.]	0.037	0.488
Mild	49	4 (8.2)	Not reached [-; -]	40	9 (22.5)	Not reached [-; -]	0.31 [0.10; 1.02]	0.054	
Moderate/Severe	146	22 (15.1)	Not reached [-; -]	144	67 (46.5)	15.14 [11.29; -]	0.17 [0.10; 0.30]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Blood and lymphatic system disorders - PT^g: Febrile neutropenia									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.238	0.601
≥ 65	162	1 (0.6)	Not reached [-; -]	169	9 (5.3)	Not reached [-; -]	0.10 [0.01; 0.83]	0.032	
Race									
White	141	1 (0.7)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	2 (3.4)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	0 (0.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	1 (1.4)	n.c.	94	8 (8.5)	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	2 (2.9)	n.c.	n.c.	n.c.	
Sex									
Male	145	1 (0.7)	n.c.	148	7 (4.7)	n.c.	n.c.	n.c.	n.c.
Female	56	0 (0.0)	n.c.	49	3 (6.1)	n.c.	n.c.	n.c.	
ECOG at Baseline									
0	87	0 (0.0)	n.c.	85	3 (3.5)	n.c.	n.c.	n.c.	n.c.
1-2	114	1 (0.9)	n.c.	112	7 (6.3)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	n.c.	53	2 (3.8)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	1 (0.8)	n.c.	143	8 (5.6)	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	n.c.	49	6 (12.2)	n.c.	n.c.	n.c.	n.c.
Absent	151	0 (0.0)	n.c.	148	4 (2.7)	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression									
High	117	0 (0.0)	n.c.	114	4 (3.5)	n.c.	n.c.	n.c.	n.c.
Low	84	1 (1.2)	n.c.	83	6 (7.2)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	1 (0.7)	Not reached [-; -]	152	9 (5.9)	Not reached [-; -]	0.10 [0.01; 0.83]	0.032	0.622
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.281	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	0 (0.0)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	1 (2.0)	n.c.	40	3 (7.5)	n.c.	n.c.	n.c.	
Moderate/Severe	146	0 (0.0)	n.c.	144	7 (4.9)	n.c.	n.c.	n.c.	
SOC: Blood and lymphatic system disorders - PT^g: Leukopenia									
Age									
< 65	39	1 (2.6)	Not reached [-; -]	28	1 (3.6)	Not reached [-; -]	0.73 [0.05; 11.73]	0.827	0.220
≥ 65	162	1 (0.6)	Not reached [-; -]	169	12 (7.1)	Not reached [-; -]	0.08 [0.01; 0.63]	0.016	
Race									
White	141	2 (1.4)	Not reached [-; -]	138	10 (7.2)	Not reached [-; -]	0.19 [0.04; 0.85]	0.030	0.321
Non-white	60	0 (0.0)	Not reached [-; -]	59	3 (5.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.077	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.722
Europe	73	0 (0.0)	Not reached [-; -]	94	3 (3.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.108	
Rest of World	82	2 (2.4)	Not reached [-; -]	70	10 (14.3)	Not reached [-; -]	0.16 [0.04; 0.75]	0.019	
Sex									
Male	145	2 (1.4)	Not reached [-; -]	148	11 (7.4)	Not reached [-; -]	0.18 [0.04; 0.82]	0.027	0.379
Female	56	0 (0.0)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.126	
ECOG at Baseline									
0	87	1 (1.1)	Not reached [-; -]	85	9 (10.6)	Not reached [-; -]	0.10 [0.01; 0.81]	0.031	0.584
1-2	114	1 (0.9)	Not reached [-; -]	112	4 (3.6)	Not reached [-; -]	0.24 [0.03; 2.11]	0.197	
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	Not reached [-; -]	53	2 (3.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.082	0.349
Lower Tract	127	2 (1.6)	Not reached [-; -]	143	11 (7.7)	Not reached [-; -]	0.20 [0.04; 0.88]	0.034	
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	Not reached [-; -]	49	3 (6.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.081	0.341
Absent	151	2 (1.3)	Not reached [-; -]	148	10 (6.8)	Not reached [-; -]	0.18 [0.04; 0.84]	0.029	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
Metastatic Disease Site									
Visceral metastases	147	2 (1.4)	Not reached [-; -]	152	11 (7.2)	Not reached [-; -]	0.18 [0.04; 0.81]	0.026	0.537
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.266	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.638
Mild	49	1 (2.0)	Not reached [-; -]	40	2 (5.0)	Not reached [-; -]	0.40 [0.04; 4.41]	0.455	
Moderate/Severe	146	1 (0.7)	Not reached [-; -]	144	11 (7.6)	Not reached [-; -]	0.09 [0.01; 0.66]	0.019	
SOC: Blood and lymphatic system disorders - PT ^g : Neutropenia									
Age									
< 65	39	3 (7.7)	Not reached [-; -]	28	11 (39.3)	Not reached [8.29; -]	0.04 [0.00; 0.32]	0.002	0.839
≥ 65	162	11 (6.8)	Not reached [-; -]	169	67 (39.6)	Not reached [14.86; -]	0.12 [0.06; 0.23]	< 0.001	
Race									
White	141	11 (7.8)	Not reached [-; -]	138	55 (39.9)	Not reached [13.86; -]	0.11 [0.06; 0.23]	< 0.001	0.374
Non-white	60	3 (5.0)	Not reached [-; -]	59	23 (39.0)	Not reached [10.29; -]	0.07 [0.02; 0.28]	< 0.001	
Geographic Region									
North America	46	1 (2.2)	Not reached [-; -]	33	9 (27.3)	Not reached [13.14; -]	0.06 [0.01; 0.50]	0.009	0.640
Europe	73	4 (5.5)	Not reached [-; -]	94	35 (37.2)	Not reached [14.00; -]	0.11 [0.04; 0.31]	< 0.001	
Rest of World	82	9 (11.0)	Not reached [-; -]	70	34 (48.6)	16.14 [7.71; -]	0.10 [0.04; 0.25]	< 0.001	
ECOG at Baseline									
0	87	9 (10.3)	Not reached [-; -]	85	31 (36.5)	Not reached [-; -]	0.18 [0.08; 0.41]	< 0.001	0.062
1-2	114	5 (4.4)	Not reached [-; -]	112	47 (42.0)	Not reached [13.29; -]	0.05 [0.02; 0.15]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	5 (6.8)	Not reached [-; -]	53	20 (37.7)	Not reached [13.14; -]	0.08 [0.02; 0.27]	< 0.001	0.952
Lower Tract	127	9 (7.1)	Not reached [-; -]	143	57 (39.9)	Not reached [13.86; -]	0.11 [0.05; 0.24]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	4 (8.0)	Not reached [-; -]	49	19 (38.8)	Not reached [13.29; -]	0.11 [0.03; 0.39]	< 0.001	0.619
Absent	151	10 (6.6)	Not reached [-; -]	148	59 (39.9)	Not reached [14.00; -]	0.10 [0.05; 0.20]	< 0.001	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b			N ^b					
Stratification Factor: PD-L1 Expression									
High	117	8 (6.8)	Not reached [-; -]	114	44 (38.6)	Not reached [14.86; -]	0.11 [0.05; 0.25]	< 0.001	0.900
Low	84	6 (7.1)	Not reached [-; -]	83	34 (41.0)	Not reached [10.29; -]	0.09 [0.03; 0.25]	< 0.001	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	6 (46.2)	Not reached [2.14; -]	n.a. [n.a.; n.a.]	0.066	0.197
Mild	49	6 (12.2)	Not reached [-; -]	40	16 (40.0)	Not reached [8.29; -]	0.18 [0.06; 0.51]	0.001	
Moderate/Severe	146	8 (5.5)	Not reached [-; -]	144	56 (38.9)	Not reached [13.86; -]	0.08 [0.03; 0.18]	< 0.001	
SOC: Blood and lymphatic system disorders - PT ^g : Thrombocytopenia									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	6 (21.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.464
≥ 65	162	2 (1.2)	Not reached [-; -]	169	53 (31.4)	Not reached [-; -]	0.03 [0.01; 0.13]	< 0.001	
Race									
White	141	2 (1.4)	Not reached [-; -]	138	44 (31.9)	Not reached [-; -]	0.03 [0.01; 0.14]	< 0.001	0.293
Non-white	60	0 (0.0)	Not reached [-; -]	59	15 (25.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	9 (27.3)	Not reached [17.00; -]	n.a. [n.a.; n.a.]	< 0.001	0.238
Europe	73	2 (2.7)	Not reached [-; -]	94	34 (36.2)	Not reached [19.29; -]	0.06 [0.01; 0.24]	< 0.001	
Rest of World	82	0 (0.0)	Not reached [-; -]	70	16 (22.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Sex									
Male	145	2 (1.4)	Not reached [-; -]	148	46 (31.1)	Not reached [-; -]	0.04 [0.01; 0.15]	< 0.001	0.276
Female	56	0 (0.0)	Not reached [-; -]	49	13 (26.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
ECOG at Baseline									
0	87	2 (2.3)	Not reached [-; -]	85	26 (30.6)	Not reached [-; -]	0.06 [0.01; 0.25]	< 0.001	0.072
1-2	114	0 (0.0)	Not reached [-; -]	112	33 (29.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Primary Disease Site of Origin									
Upper Tract	74	1 (1.4)	Not reached [-; -]	53	14 (26.4)	Not reached [-; -]	0.04 [0.01; 0.32]	0.002	0.615
Lower Tract	127	1 (0.8)	Not reached [-; -]	143	44 (30.8)	Not reached [-; -]	0.02 [0.00; 0.15]	< 0.001	

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]	N ^b	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)									
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	Not reached [-; -]	49	16 (32.7)	Not reached [19.29; -]	0.05 [0.01; 0.37]	0.003	0.504
Absent	151	1 (0.7)	Not reached [-; -]	148	43 (29.1)	Not reached [-; -]	0.02 [0.00; 0.13]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	2 (1.7)	Not reached [-; -]	114	32 (28.1)	Not reached [-; -]	0.05 [0.01; 0.21]	< 0.001	0.121
Low	84	0 (0.0)	Not reached [-; -]	83	27 (32.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Metastatic Disease Site									
Visceral metastases	147	1 (0.7)	Not reached [-; -]	152	45 (29.6)	Not reached [-; -]	0.02 [0.00; 0.13]	< 0.001	0.440
Lymph node only	43	1 (2.3)	Not reached [-; -]	37	12 (32.4)	Not reached [16.14; -]	0.06 [0.01; 0.44]	0.006	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	4 (30.8)	Not reached [2.14; -]	n.a. [n.a.; n.a.]	0.117	0.630
Mild	49	1 (2.0)	Not reached [-; -]	40	10 (25.0)	Not reached [-; -]	0.07 [0.01; 0.56]	0.012	
Moderate/Severe	146	1 (0.7)	Not reached [-; -]	144	45 (31.3)	Not reached [-; -]	0.02 [0.00; 0.12]	< 0.001	
SOC: Investigations - PT*: Neutrophil count decreased									
Age									
< 65	39	2 (5.1)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	0.36 [0.03; 3.92]	0.398	0.451
≥ 65	162	5 (3.1)	Not reached [-; -]	169	17 (10.1)	Not reached [-; -]	0.28 [0.10; 0.76]	0.012	
Race									
White	141	5 (3.5)	Not reached [-; -]	138	11 (8.0)	Not reached [-; -]	0.42 [0.15; 1.22]	0.111	0.441
Non-white	60	2 (3.3)	Not reached [-; -]	59	8 (13.6)	Not reached [-; -]	0.11 [0.01; 0.87]	0.036	
Geographic Region									
North America	46	0 (0.0)	Not reached [-; -]	33	5 (15.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.065
Europe	73	2 (2.7)	Not reached [-; -]	94	8 (8.5)	Not reached [-; -]	0.30 [0.06; 1.40]	0.125	
Rest of World	82	5 (6.1)	Not reached [-; -]	70	6 (8.6)	Not reached [-; -]	0.55 [0.15; 1.94]	0.351	
Sex									
Male	145	5 (3.4)	Not reached [-; -]	148	16 (10.8)	Not reached [-; -]	0.24 [0.08; 0.72]	0.011	0.614
Female	56	2 (3.6)	Not reached [-; -]	49	3 (6.1)	Not reached [-; -]	0.51 [0.08; 3.03]	0.456	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Participants with Event n (%)	Median Time ^e in weeks [95 %-CI]		Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b			N ^b					
ECOG at Baseline									
0	87	2 (2.3)	Not reached [-; -]	85	12 (14.1)	Not reached [-; -]	0.15 [0.03; 0.66]	0.012	0.104
1-2	114	5 (4.4)	Not reached [-; -]	112	7 (6.3)	Not reached [-; -]	0.54 [0.16; 1.83]	0.321	
Primary Disease Site of Origin									
Upper Tract	74	4 (5.4)	Not reached [-; -]	53	7 (13.2)	Not reached [-; -]	0.29 [0.07; 1.12]	0.073	0.679
Lower Tract	127	3 (2.4)	Not reached [-; -]	143	12 (8.4)	Not reached [-; -]	0.26 [0.07; 0.92]	0.037	
Stratification Factor: Liver Metastases									
Present	50	1 (2.0)	Not reached [-; -]	49	5 (10.2)	Not reached [-; -]	0.18 [0.02; 1.56]	0.120	0.550
Absent	151	6 (4.0)	Not reached [-; -]	148	14 (9.5)	Not reached [-; -]	0.32 [0.12; 0.90]	0.030	
Stratification Factor: PD-L1 Expression									
High	117	6 (5.1)	Not reached [-; -]	114	10 (8.8)	Not reached [-; -]	0.47 [0.16; 1.37]	0.164	0.105
Low	84	1 (1.2)	Not reached [-; -]	83	9 (10.8)	Not reached [-; -]	0.10 [0.01; 0.77]	0.027	
Metastatic Disease Site									
Visceral metastases	147	4 (2.7)	Not reached [-; -]	152	16 (10.5)	Not reached [-; -]	0.18 [0.05; 0.61]	0.006	0.126
Lymph node only	43	3 (7.0)	Not reached [-; -]	37	2 (5.4)	Not reached [-; -]	1.24 [0.21; 7.40]	0.816	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.953
Mild	49	3 (6.1)	Not reached [-; -]	40	6 (15.0)	Not reached [-; -]	0.37 [0.09; 1.48]	0.161	
Moderate/Severe	146	4 (2.7)	Not reached [-; -]	144	13 (9.0)	Not reached [-; -]	0.21 [0.06; 0.75]	0.016	
SOC: Investigations - PT^g: Platelet count decreased									
Age									
< 65	39	0 (0.0)	Not reached [-; -]	28	2 (7.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.096	0.998
≥ 65	162	0 (0.0)	Not reached [-; -]	169	15 (8.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Race									
White	141	0 (0.0)	n.c.	138	8 (5.8)	n.c.	n.c.	n.c.	n.c.
Non-white	60	0 (0.0)	n.c.	59	9 (15.3)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	0 (0.0)	n.c.	33	3 (9.1)	n.c.	n.c.	n.c.	n.c.
Europe	73	0 (0.0)	n.c.	94	6 (6.4)	n.c.	n.c.	n.c.	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of World	82	0 (0.0)	n.c.	70	8 (11.4)	n.c.	n.c.	n.c.	
Sex									
Male	145	0 (0.0)	Not reached [-; -]	148	15 (10.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Female	56	0 (0.0)	Not reached [-; -]	49	2 (4.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.128	
ECOG at Baseline									
0	87	0 (0.0)	Not reached [-; -]	85	12 (14.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
1-2	114	0 (0.0)	Not reached [-; -]	112	5 (4.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022	
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	Not reached [-; -]	53	6 (11.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	0.998
Lower Tract	127	0 (0.0)	Not reached [-; -]	143	11 (7.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.001	
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	Not reached [-; -]	49	6 (12.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.013	0.998
Absent	151	0 (0.0)	Not reached [-; -]	148	11 (7.4)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	0 (0.0)	n.c.	114	9 (7.9)	n.c.	n.c.	n.c.	n.c.
Low	84	0 (0.0)	n.c.	83	8 (9.6)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	0 (0.0)	Not reached [-; -]	152	15 (9.9)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Lymph node only	43	0 (0.0)	Not reached [-; -]	37	1 (2.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.190	
Renal Function									
Normal	6	0 (0.0)	Not reached [-; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	> 0.999
Mild	49	0 (0.0)	Not reached [-; -]	40	4 (10.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.017	
Moderate/Severe	146	0 (0.0)	Not reached [-; -]	144	13 (9.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
SOC: Investigations - PT*: White blood cell count decreased									
Age									
< 65	39	0 (0.0)	n.c.	28	1 (3.6)	n.c.	n.c.	n.c.	n.c.
≥ 65	162	0 (0.0)	n.c.	169	6 (3.6)	n.c.	n.c.	n.c.	
Race									
White	141	0 (0.0)	n.c.	138	3 (2.2)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Non-white	60	0 (0.0)	n.c.	59	4 (6.8)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	0 (0.0)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	0 (0.0)	n.c.	94	4 (4.3)	n.c.	n.c.	n.c.	
Rest of World	82	0 (0.0)	n.c.	70	3 (4.3)	n.c.	n.c.	n.c.	
Sex									
Male	145	0 (0.0)	n.c.	148	7 (4.7)	n.c.	n.c.	n.c.	n.c.
Female	56	0 (0.0)	n.c.	49	0 (0.0)	n.c.	n.c.	n.c.	
ECOG at Baseline									
0	87	0 (0.0)	n.c.	85	5 (5.9)	n.c.	n.c.	n.c.	n.c.
1-2	114	0 (0.0)	n.c.	112	2 (1.8)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	74	0 (0.0)	n.c.	53	2 (3.8)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	0 (0.0)	n.c.	143	5 (3.5)	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases									
Present	50	0 (0.0)	n.c.	49	3 (6.1)	n.c.	n.c.	n.c.	n.c.
Absent	151	0 (0.0)	n.c.	148	4 (2.7)	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression									
High	117	0 (0.0)	n.c.	114	6 (5.3)	n.c.	n.c.	n.c.	n.c.
Low	84	0 (0.0)	n.c.	83	1 (1.2)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	0 (0.0)	n.c.	152	5 (3.3)	n.c.	n.c.	n.c.	n.c.
Lymph node only	43	0 (0.0)	n.c.	37	1 (2.7)	n.c.	n.c.	n.c.	
Renal Function									
Normal	6	0 (0.0)	n.c.	13	1 (7.7)	n.c.	n.c.	n.c.	n.c.
Mild	49	0 (0.0)	n.c.	40	2 (5.0)	n.c.	n.c.	n.c.	
Moderate/Severe	146	0 (0.0)	n.c.	144	4 (2.8)	n.c.	n.c.	n.c.	

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Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
SOC: Metabolism and nutrition disorders - PT^g: Hyperglycaemia									
Age									
< 65	39	1 (2.6)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.397	0.731
≥ 65	162	11 (6.8)	Not reached [-; -]	169	1 (0.6)	Not reached [-; -]	10.31 [1.32; 80.52]	0.026	
Race									
White	141	7 (5.0)	n.c.	138	1 (0.7)	n.c.	n.c.	n.c.	n.c.
Non-white	60	5 (8.3)	n.c.	59	0 (0.0)	n.c.	n.c.	n.c.	
Geographic Region									
North America	46	3 (6.5)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	4 (5.5)	n.c.	94	1 (1.1)	n.c.	n.c.	n.c.	
Rest of World	82	5 (6.1)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	11 (7.6)	Not reached [-; -]	148	1 (0.7)	Not reached [-; -]	10.36 [1.33; 80.94]	0.026	0.713
Female	56	1 (1.8)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.412	
ECOG at Baseline									
0	87	5 (5.7)	n.c.	85	1 (1.2)	n.c.	n.c.	n.c.	n.c.
1-2	114	7 (6.1)	n.c.	112	0 (0.0)	n.c.	n.c.	n.c.	
Primary Disease Site of Origin									
Upper Tract	74	5 (6.8)	n.c.	53	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Lower Tract	127	7 (5.5)	n.c.	143	1 (0.7)	n.c.	n.c.	n.c.	
Stratification Factor: Liver Metastases									
Present	50	3 (6.0)	n.c.	49	1 (2.0)	n.c.	n.c.	n.c.	n.c.
Absent	151	9 (6.0)	n.c.	148	0 (0.0)	n.c.	n.c.	n.c.	
Stratification Factor: PD-L1 Expression									
High	117	6 (5.1)	n.c.	114	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Low	84	6 (7.1)	n.c.	83	1 (1.2)	n.c.	n.c.	n.c.	
Metastatic Disease Site									
Visceral metastases	147	10 (6.8)	Not reached [-; -]	152	1 (0.7)	Not reached [-; -]	9.33 [1.18; 73.68]	0.034	0.698
Lymph node only	43	1 (2.3)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.354	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Renal Function									
Normal	6	2 (33.3)	n.c.	13	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Mild	49	5 (10.2)	n.c.	40	0 (0.0)	n.c.	n.c.	n.c.	
Moderate/Severe	146	5 (3.4)	n.c.	144	1 (0.7)	n.c.	n.c.	n.c.	
SOC: Skin and subcutaneous tissue disorders - PT^g: Rash maculo-papular									
Age									
< 65	39	3 (7.7)	Not reached [-; -]	28	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.220	0.998
≥ 65	162	17 (10.5)	Not reached [-; -]	169	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Race									
White	141	15 (10.6)	Not reached [-; -]	138	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Non-white	60	5 (8.3)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.058	
Geographic Region									
North America	46	8 (17.4)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Europe	73	6 (8.2)	n.c.	94	0 (0.0)	n.c.	n.c.	n.c.	
Rest of World	82	6 (7.3)	n.c.	70	0 (0.0)	n.c.	n.c.	n.c.	
Sex									
Male	145	14 (9.7)	Not reached [-; -]	148	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Female	56	6 (10.7)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.046	
ECOG at Baseline									
0	87	10 (11.5)	Not reached [-; -]	85	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.998
1-2	114	10 (8.8)	Not reached [-; -]	112	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Primary Disease Site of Origin									
Upper Tract	74	8 (10.8)	Not reached [-; -]	53	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.033	0.998
Lower Tract	127	12 (9.4)	Not reached [-; -]	143	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Stratification Factor: Liver Metastases									
Present	50	5 (10.0)	Not reached [-; -]	49	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.027	0.998
Absent	151	15 (9.9)	Not reached [-; -]	148	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Stratification Factor: PD-L1 Expression									
High	117	11 (9.4)	Not reached [-; -]	114	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.998

Study: KEYNOTE-A39 ^a	EV+Pembro			Plat+Gem			EV+Pembro vs. Plat+Gem		p-Value for Interaction Test ^f
	Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	
Low	84	9 (10.7)	Not reached [-; -]	83	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Metastatic Disease Site									
Visceral metastases	147	17 (11.6)	Not reached [-; -]	152	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Lymph node only	43	2 (4.7)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.348	
Renal Function									
Normal	6	1 (16.7)	Not reached [9.29; -]	13	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.157	> 0.999
Mild	49	8 (16.3)	Not reached [-; -]	40	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.023	
Moderate/Severe	146	11 (7.5)	Not reached [-; -]	144	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	
<p>a: Database Cutoff Date: 08AUG2023</p> <p>b: Number of participants: all-participants-as-treated population, cisplatin ineligible</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> <p>g: A specific adverse event appears on this report only if its incidence $\geq 5\%$ or (incidence $\geq 1\%$ and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated</p> <p>CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-L1: Programmed Cell Death - Ligand 1; PT: Preferred Term; SOC: System Organ Class</p>									

Anhang 4-G8: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI Pembrolizumab) und Unerwünschten Ereignisse von besonderem Interesse (AESI EV) anhand der zugeordneten PT

Tabelle 4G-103: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI Pembrolizumab) anhand der zugeordneten PT in der Studie KEYNOTE A39

AEOSI	Preferred Terms
Pneumonitis	Acute interstitial pneumonitis, Autoimmune lung disease, Interstitial lung disease, Pneumonitis, Idiopathic pneumonia syndrome, Organising pneumonia, Immune-mediated lung disease
Colitis	Colitis, Colitis microscopic, Enterocolitis, Enterocolitis haemorrhagic, Necrotising colitis, Colitis erosive, Autoimmune colitis, Immune-mediated enterocolitis
Hepatitis	Hepatitis, Immune-mediated hepatitis, Autoimmune hepatitis, Hepatitis acute, Hepatitis fulminant, Drug-induced liver injury
Nephritis	Nephritis, Autoimmune nephritis, Chronic autoimmune glomerulonephritis, Fibrillary glomerulonephritis, Focal segmental glomerulosclerosis, Glomerulonephritis, Glomerulonephritis acute, Glomerulonephritis membranoproliferative, Glomerulonephritis membranous, Glomerulonephritis minimal lesion, Glomerulonephritis proliferative, Glomerulonephritis rapidly progressive, Mesangioproliferative glomerulonephritis, Nephritis haemorrhagic, Tubulointerstitial nephritis, Nephrotic syndrome, Immune-mediated nephritis
Adrenal Insufficiency	Adrenal insufficiency, Adrenocortical insufficiency acute, Secondary adrenocortical insufficiency, Primary adrenal insufficiency, Addison's disease, Immune-mediated adrenal insufficiency
Hypophysitis	Hypophysitis, Hypopituitarism, Lymphocytic hypophysitis, Immune-mediated hypophysitis
Hyperthyroidism	Hyperthyroidism, Thyrotoxic crisis, Immune-mediated hyperthyroidism, Graves' disease
Hypothyroidism	Hypothyroidism, Hypothyroidic goitre, Myxoedema, Myxoedema coma, Primary hypothyroidism, Autoimmune hypothyroidism, Immune-mediated hypothyroidism

AEOSI	Preferred Terms
Thyroiditis	Thyroid disorder, Thyroiditis, Autoimmune thyroiditis, Thyroiditis acute, Silent thyroiditis, Autoimmune thyroid disorder, Immune-mediated thyroiditis
Type 1 Diabetes Mellitus	Diabetic ketoacidosis, Diabetic ketoacidotic hyperglycaemic coma, Fulminant type 1 diabetes mellitus, Latent autoimmune diabetes in adults, Type 1 diabetes mellitus, Euglycaemic diabetic ketoacidosis, Diabetic ketosis, Ketosis-prone diabetes mellitus
Severe Skin Reactions Including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN): or Severe Skin (continued): If grade 3 or higher:	Dermatitis bullous, Dermatitis exfoliative, Dermatitis exfoliative generalised, Epidermal necrosis, Erythema multiforme, Exfoliative rash, Pemphigoid, Mucous membrane pemphigoid, Pemphigus, Skin necrosis, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Toxic skin eruption, SJS-TEN overlap, Lichen planus pemphigoides Rash, Rash erythematous, Rash maculo-papular, Rash pruritic, Rash pustular, Pruritus, Pruritus genital, Lichen planus, Oral lichen planus, Cutaneous vasculitis, Vasculitic rash
Uveitis	Iritis, Uveitis, Cyclitis, Autoimmune uveitis, Iridocyclitis, Vogt-Koyanagi-Harada disease, Chorioretinitis, Choroiditis, Immune-mediated uveitis, Choroidal effusion, Choroidal detachment, Serous retinal detachment
Pancreatitis	Pancreatitis, Autoimmune pancreatitis, Pancreatitis acute, Pancreatitis haemorrhagic, Pancreatitis necrotising, Immune-mediated pancreatitis
Myositis	Myositis, Necrotising myositis, Polymyositis, Immune-mediated myositis, Rhabdomyolysis, Myopathy, Dermatomyositis, Autoimmune myositis
Guillain-Barre Syndrome	Demyelinating polyneuropathy, Guillain-Barre syndrome, Axonal neuropathy, Multifocal motor neuropathy, Polyneuropathy idiopathic progressive, Miller Fisher syndrome, Subacute inflammatory demyelinating polyneuropathy
Myocarditis	Myocarditis, Autoimmune myocarditis, Hypersensitivity myocarditis, Immune-mediated myocarditis

AEOSI	Preferred Terms
Encephalitis	Encephalitis, Encephalitis autoimmune, Limbic encephalitis, Noninfective encephalitis, Immune-mediated encephalitis
Sarcoidosis	Sarcoidosis, Cutaneous sarcoidosis, Ocular sarcoidosis, Pulmonary sarcoidosis, Sarcoidosis of lymph node
Infusion Reactions	Hypersensitivity, Drug hypersensitivity, Anaphylactic reaction, Anaphylactoid reaction, Cytokine release syndrome, Serum sickness, Serum sickness-like reaction, Infusion related reaction, Infusion related hypersensitivity reaction
Myasthenic Syndrome	Myasthenic syndrome, Myasthenia gravis, Myasthenia gravis crisis, Ocular myasthenia, Immune-mediated myasthenia gravis
Myelitis	Myelitis, Myelitis transverse, Acute necrotising myelitis, Immune-mediated myelitis
Vasculitis	Anti-neutrophil cytoplasmic antibody positive vasculitis, Aortitis, Arteritis, Arteritis coronary, Behcet's syndrome, Central nervous system vasculitis, Cerebral arteritis, Diffuse vasculitis, Eosinophilic granulomatosis with polyangiitis, Granulomatosis with polyangiitis, Haemorrhagic vasculitis, Hypersensitivity vasculitis, Microscopic polyangiitis, Ocular vasculitis, Polyarteritis nodosa, Pulmonary vasculitis, Renal arteritis, Renal vasculitis, Retinal vasculitis, Takayasu's arteritis, Giant cell arteritis, Vasculitis, Vasculitis gastrointestinal, Vasculitis necrotising
Cholangitis Sclerosing	Cholangitis sclerosing, Autoimmune cholangitis, Immune-mediated cholangitis
Hypoparathyroidism	Hypoparathyroidism, Primary hypoparathyroidism
Arthritis	Autoimmune arthritis, Immune-mediated arthritis
HLH	Haemophagocytic lymphohistiocytosis
Optic Neuritis	Optic neuritis, Immune-mediated optic neuritis
Gastritis	Gastritis, Gastritis erosive, Gastritis haemorrhagic, Haemorrhagic erosive gastritis, Immune-mediated gastritis, Ulcerative gastritis
Database Cutoff Date: 08AUG2023 AEOSI: Adverse Events Of Special Interest SJS-TEN: Stevens-Johnson syndrome-toxic epidermal necrolysis	

Tabelle 4G-104: Definition der Unerwünschten Ereignisse von besonderem Interesse (AESI EV) anhand der zugeordneten PT in der Studie KEYNOTE A39

AESI	Preferred Term
Hyperglycemia	Blood glucose increased, Diabetes mellitus, Diabetic

	hyperglycaemic coma, Glucose tolerance impaired, Glycosylated haemoglobin increased, Hyperglycaemia, Impaired fasting glucose, Type 1 diabetes mellitus, Type 2 diabetes mellitus
Infusion-related reactions	Administration site extravasation, Bronchospasm, Hypersensitivity, Infusion related reaction, Infusion site extravasation, Infusion site pain, Infusion site reaction
Ocular disorders	Blepharitis, Conjunctivitis, Conjunctivitis allergic, Corneal abrasion, Corneal degeneration, Corneal erosion, Corneal toxicity, Dry eye, Exposure keratitis, Eye irritation, Keratitis, Keratoconus, Lacrimation increased, Meibomian gland dysfunction, Ocular discomfort, Punctate keratitis, Vision blurred, Visual acuity reduced, Visual impairment
Peripheral neuropathy	Burning sensation, Dysaesthesia, Gait disturbance, Hypoaesthesia, Immune-mediated neuropathy, Muscular weakness, Neuralgia, Neuropathy peripheral, Neurotoxicity, Paraesthesia, Peripheral motor neuropathy, Peripheral sensorimotor neuropathy, Peripheral sensory neuropathy, Peroneal nerve palsy, Skin burning sensation
Skin reactions	Acute generalised exanthematous pustulosis, Blister, Conjunctivitis, Cutaneous vasculitis, Dermatitis, Dermatitis bullous, Dermatitis contact, Dermatitis exfoliative, Dermatitis exfoliative generalised, Drug eruption, Dyshidrotic eczema, Eczema, Erythema, Erythema multiforme, Hand dermatitis, Intertrigo, Mouth ulceration, Palmar-plantar erythrodysesthesia syndrome, Pemphigoid, Plantar erythema, Pseudocellulitis, Rash, Rash erythematous, Rash macular, Rash maculo-papular, Rash morbilliform, Rash papular, Rash pruritic, Rash vesicular, SJS-TEN overlap, Seborrhoeic dermatitis, Skin erosion, Skin exfoliation, Skin irritation, Skin toxicity, Stasis dermatitis, Stomatitis, Symmetrical drug-related intertriginous and flexural exanthema, Toxic epidermal necrolysis, Toxic erythema of chemotherapy, Toxic skin eruption
Database Cutoff Date: 08AUG2023 AESI: Adverse Events of Special Interest SJS-TEN: Stevens-Johnson syndrome-toxic epidermal necrolysis	