Dokumentvorlage, Version vom 26.12.2021

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4 A

KEYTRUDA® in Kombination mit Trastuzumab sowie einer Fluoropyrimidin- und Platin-basierten Chemotherapie zur Erstlinienbehandlung des lokal fortgeschrittenen nicht resezierbaren oder metastasierenden HER2-positiven Adenokarzinoms des Magens oder des gastroösophagealen Übergangs bei Erwachsenen mit PD-L1-exprimierenden Tumoren (CPS ≥ 1)

Medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen

Stand: 29.12.2023

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Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Rücklaufquoten des EORTC QLQ-C30, die Rücklaufquoten des EORTC QLQ-STO22 und die Rücklaufquoten des EQ-5D VAS dargestellt.

Alle Ergebnisse beziehen sich auf den dritten Datenschnitt (29. März 2023).

Anhang 4-G1.1: Rücklaufquoten des EORTC QLQ-C30

Tabelle 4G-1: Gründe für das Fehlen von Werten im EORTC QLQ-C30

		Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
Treatment Visit	Category	n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**291**	**(100.0)**	**286**	**(100.0)**
	Completed	272	(93.5)	274	(95.8)
	Compliance (% in those expected to complete questionnaires)	272	(93.5)	274	(95.8)
	Not completed	19	(6.5)	12	(4.2)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	5	(1.7)	5	(1.7)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	0	(0.0)
	Other	6	(2.1)	3	(1.0)
	With visit, no record	4	(1.4)	4	(1.4)
	Missing by Design	**0**	**(0.0)**	**0**	**(0.0)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 3	**Expected to Complete Questionnaires**	**273**	**(93.8)**	**266**	**(93.0)**
	Completed	261	(89.7)	245	(85.7)
	Compliance (% in those expected to complete questionnaires)	261	(95.6)	245	(92.1)
	Not completed	12	(4.1)	21	(7.3)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	1	(0.3)	7	(2.4)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	4	(1.4)
	Other	6	(2.1)	6	(2.1)
	With visit, no record	1	(0.3)	2	(0.7)
	Missing by Design	**18**	**(6.2)**	**20**	**(7.0)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	3	(1.0)	4	(1.4)
	Visit not scheduled	15	(5.2)	16	(5.6)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
WEEK 6	**Expected to Complete Questionnaires**	**261**	**(89.7)**	**255**	**(89.2)**
	Completed	249	(85.6)	233	(81.5)
	Compliance (% in those expected to complete questionnaires)	249	(95.4)	233	(91.4)
	Not completed	12	(4.1)	22	(7.7)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	6	(2.1)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	4	(1.4)	11	(3.8)
	With visit, no record	0	(0.0)	4	(1.4)
	Missing by Design	**30**	**(10.3)**	**31**	**(10.8)**
	Discontinued due to adverse event	4	(1.4)	7	(2.4)
	Discontinued due to clinical progression	0	(0.0)	1	(0.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	2	(0.7)	2	(0.7)
	Visit not scheduled	24	(8.2)	21	(7.3)
WEEK 9	**Expected to Complete Questionnaires**	**259**	**(89.0)**	**240**	**(83.9)**
	Completed	243	(83.5)	216	(75.5)
	Compliance (% in those expected to complete questionnaires)	243	(93.8)	216	(90.0)
	Not completed	16	(5.5)	24	(8.4)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Not completed due to site staff error	5	(1.7)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	2	(0.7)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	5	(1.7)
	Other	3	(1.0)	7	(2.4)
	With visit, no record	5	(1.7)	6	(2.1)
	Missing by Design	**32**	**(11.0)**	**46**	**(16.1)**
	Discontinued due to adverse event	6	(2.1)	10	(3.5)
	Discontinued due to clinical progression	0	(0.0)	2	(0.7)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	2	(0.7)	2	(0.7)
	Discontinued due to withdrawal by participant	1	(0.3)	1	(0.3)
	Participant died	0	(0.0)	1	(0.3)
	Visit not scheduled	23	(7.9)	30	(10.5)
WEEK 12	**Expected to Complete Questionnaires**	**263**	**(90.4)**	**243**	**(85.0)**
	Completed	250	(85.9)	225	(78.7)
	Compliance (% in those expected to complete questionnaires)	250	(95.1)	225	(92.6)
	Not completed	13	(4.5)	18	(6.3)
	Participant did not complete due to disease under study	0	(0.0)	2	(0.7)
	Not completed due to site staff error	4	(1.4)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	3	(1.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Other	2	(0.7)	5	(1.7)
	With visit, no record	2	(0.7)	1	(0.3)
	Missing by Design	**28**	**(9.6)**	**43**	**(15.0)**
	Discontinued due to adverse event	8	(2.7)	12	(4.2)
	Discontinued due to clinical progression	0	(0.0)	3	(1.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	7	(2.4)	9	(3.1)
	Discontinued due to withdrawal by participant	2	(0.7)	1	(0.3)
	Participant died	0	(0.0)	3	(1.0)
	Visit not scheduled	11	(3.8)	15	(5.2)
WEEK 18	**Expected to Complete Questionnaires**	**249**	**(85.6)**	**231**	**(80.8)**
	Completed	212	(72.9)	189	(66.1)
	Compliance (% in those expected to complete questionnaires)	212	(85.1)	189	(81.8)
	Not completed	37	(12.7)	42	(14.7)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)
	Not completed due to site staff error	6	(2.1)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	3	(1.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	5	(1.7)
	Other	4	(1.4)	12	(4.2)
	With visit, no record	23	(7.9)	17	(5.9)
	Missing by Design	**42**	**(14.4)**	**55**	**(19.2)**
	Discontinued due to adverse event	10	(3.4)	19	(6.6)
	Discontinued due to clinical progression	3	(1.0)	5	(1.7)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to non-study anti-cancer therapy	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	1	(0.3)
	Discontinued due to progressive disease	17	(5.8)	18	(6.3)
	Discontinued due to withdrawal by participant	3	(1.0)	3	(1.0)
	Participant died	3	(1.0)	2	(0.7)
	Visit not scheduled	4	(1.4)	7	(2.4)
WEEK 24	**Expected to Complete Questionnaires**	**223**	**(76.6)**	**192**	**(67.1)**
	Completed	195	(67.0)	151	(52.8)
	Compliance (% in those expected to complete questionnaires)	195	(87.4)	151	(78.6)
	Not completed	28	(9.6)	41	(14.3)
	Participant did not complete due to disease under study	1	(0.3)	2	(0.7)
	Not completed due to site staff error	6	(2.1)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	4	(1.4)	3	(1.0)
	Other	2	(0.7)	10	(3.5)
	With visit, no record	14	(4.8)	20	(7.0)
	Missing by Design	**68**	**(23.4)**	**94**	**(32.9)**
	Discontinued due to adverse event	14	(4.8)	21	(7.3)
	Discontinued due to clinical progression	6	(2.1)	11	(3.8)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	29	(10.0)	40	(14.0)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Participant died	3	(1.0)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Visit not scheduled	7	(2.4)	10	(3.5)
WEEK 30	**Expected to Complete Questionnaires**	**208**	**(71.5)**	**175**	**(61.2)**
	Completed	178	(61.2)	134	(46.9)
	Compliance (% in those expected to complete questionnaires)	178	(85.6)	134	(76.6)
	Not completed	30	(10.3)	41	(14.3)
	Participant did not complete due to disease under study	2	(0.7)	3	(1.0)
	Not completed due to site staff error	6	(2.1)	1	(0.3)
	Participant in hospital or hospice	1	(0.3)	1	(0.3)
	Participant was physically unable to complete	0	(0.0)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	1	(0.3)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	3	(1.0)	8	(2.8)
	With visit, no record	17	(5.8)	23	(8.0)
	Missing by Design	**83**	**(28.5)**	**111**	**(38.8)**
	Discontinued due to adverse event	16	(5.5)	21	(7.3)
	Discontinued due to clinical progression	8	(2.7)	13	(4.5)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	40	(13.7)	63	(22.0)
	Discontinued due to withdrawal by participant	5	(1.7)	4	(1.4)
	Participant died	5	(1.7)	2	(0.7)
	Visit not scheduled	5	(1.7)	4	(1.4)
WEEK 36	**Expected to Complete Questionnaires**	**179**	**(61.5)**	**143**	**(50.0)**
	Completed	152	(52.2)	115	(40.2)
	Compliance (% in those expected to complete questionnaires)	152	(84.9)	115	(80.4)
	Not completed	27	(9.3)	28	(9.8)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant did not complete due to disease under study	1	(0.3)	0	(0.0)
	Not completed due to site staff error	4	(1.4)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	3	(1.0)
	Other	9	(3.1)	6	(2.1)
	With visit, no record	11	(3.8)	14	(4.9)
	Missing by Design	**112**	**(38.5)**	**143**	**(50.0)**
	Discontinued due to adverse event	19	(6.5)	22	(7.7)
	Discontinued due to clinical progression	9	(3.1)	14	(4.9)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	2	(0.7)
	Discontinued due to progressive disease	68	(23.4)	89	(31.1)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Participant died	0	(0.0)	2	(0.7)
	Visit not scheduled	5	(1.7)	6	(2.1)
WEEK 42	**Expected to Complete Questionnaires**	**172**	**(59.1)**	**124**	**(43.4)**
	Completed	151	(51.9)	101	(35.3)
	Compliance (% in those expected to complete questionnaires)	151	(87.8)	101	(81.5)
	Not completed	21	(7.2)	23	(8.0)
	Participant did not complete due to disease under study	2	(0.7)	1	(0.3)
	Not completed due to site staff error	3	(1.0)	3	(1.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	3	(1.0)	8	(2.8)
	With visit, no record	10	(3.4)	8	(2.8)
	Missing by Design	**119**	**(40.9)**	**162**	**(56.6)**
	Discontinued due to adverse event	19	(6.5)	24	(8.4)
	Discontinued due to clinical progression	9	(3.1)	15	(5.2)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	74	(25.4)	111	(38.8)
	Discontinued due to withdrawal by participant	6	(2.1)	5	(1.7)
	Participant died	2	(0.7)	0	(0.0)
	Visit not scheduled	3	(1.0)	1	(0.3)
WEEK 48	**Expected to Complete Questionnaires**	**157**	**(54.0)**	**109**	**(38.1)**
	Completed	150	(51.5)	106	(37.1)
	Compliance (% in those expected to complete questionnaires)	150	(95.5)	106	(97.2)
	Not completed	7	(2.4)	3	(1.0)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	3	(1.0)	0	(0.0)
	Other	3	(1.0)	1	(0.3)
	With visit, no record	0	(0.0)	1	(0.3)
	Missing by Design	**134**	**(46.0)**	**177**	**(61.9)**
	Discontinued due to adverse event	20	(6.9)	24	(8.4)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291 n	(%)	Placebo + Trastuzumab + FP or CAPOX N=286 n	(%)
	Discontinued due to clinical progression	10	(3.4)	15	(5.2)
	Discontinued due to non-study anti-cancer therapy	5	(1.7)	4	(1.4)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	91	(31.3)	125	(43.7)
	Discontinued due to withdrawal by participant	6	(2.1)	6	(2.1)
	Participant died	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)

Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason.

Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N).

Missing by design includes: adverse event, death, discontinuation, translations not available, and no visit scheduled.

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CPS: Combined Positive Score ; FP: Cisplatin plus 5-FU Database Cutoff Date: 29MAR2023

Anhang 4-G1.2: Rücklaufquoten des EORTC QLQ-STO22

Tabelle 4G-2: Gründe für das Fehlen von Werten im EORTC QLQ-STO22

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291 n	(%)	Placebo + Trastuzumab + FP or CAPOX N=286 n	(%)
BASELINE	**Expected to Complete Questionnaires**	**291**	**(100.0)**	**285**	**(99.7)**
	Completed	271	(93.1)	273	(95.5)
	Compliance (% in those expected to complete questionnaires)	271	(93.1)	273	(95.8)
	Not completed	20	(6.9)	12	(4.2)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	6	(2.1)	5	(1.7)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	0	(0.0)
	Other	6	(2.1)	3	(1.0)
	With visit, no record	4	(1.4)	4	(1.4)
	Missing by Design	**0**	**(0.0)**	**1**	**(0.3)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Translation not available in participants language	0	(0.0)	1	(0.3)
	Participant died	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 3	**Expected to Complete Questionnaires**	**273**	**(93.8)**	**266**	**(93.0)**
	Completed	260	(89.3)	245	(85.7)
	Compliance (% in those expected to complete questionnaires)	260	(95.2)	245	(92.1)
	Not completed	13	(4.5)	21	(7.3)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	1	(0.3)	7	(2.4)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	4	(1.4)
	Other	7	(2.4)	6	(2.1)
	With visit, no record	1	(0.3)	2	(0.7)
	Missing by Design	**18**	**(6.2)**	**20**	**(7.0)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	3	(1.0)	4	(1.4)
	Visit not scheduled	15	(5.2)	16	(5.6)
WEEK 6	**Expected to Complete Questionnaires**	**261**	**(89.7)**	**255**	**(89.2)**
	Completed	249	(85.6)	231	(80.8)
	Compliance (% in those expected to complete questionnaires)	249	(95.4)	231	(90.6)
	Not completed	12	(4.1)	24	(8.4)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	6	(2.1)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	4	(1.4)	13	(4.5)
	With visit, no record	0	(0.0)	4	(1.4)
	Missing by Design	**30**	**(10.3)**	**31**	**(10.8)**
	Discontinued due to adverse event	4	(1.4)	7	(2.4)
	Discontinued due to clinical progression	0	(0.0)	1	(0.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	2	(0.7)	2	(0.7)
	Visit not scheduled	24	(8.2)	21	(7.3)
WEEK 9	**Expected to Complete Questionnaires**	**259**	**(89.0)**	**240**	**(83.9)**
	Completed	243	(83.5)	213	(74.5)
	Compliance (% in those expected to complete questionnaires)	243	(93.8)	213	(88.8)
	Not completed	16	(5.5)	27	(9.4)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)
	Not completed due to site staff error	5	(1.7)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	2	(0.7)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	5	(1.7)
	Other	3	(1.0)	10	(3.5)
	With visit, no record	5	(1.7)	6	(2.1)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Missing by Design	**32**	**(11.0)**	**46**	**(16.1)**
	Discontinued due to adverse event	6	(2.1)	10	(3.5)
	Discontinued due to clinical progression	0	(0.0)	2	(0.7)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	2	(0.7)	2	(0.7)
	Discontinued due to withdrawal by participant	1	(0.3)	1	(0.3)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	1	(0.3)
	Visit not scheduled	23	(7.9)	30	(10.5)
WEEK 12	**Expected to Complete Questionnaires**	**263**	**(90.4)**	**243**	**(85.0)**
	Completed	249	(85.6)	225	(78.7)
	Compliance (% in those expected to complete questionnaires)	249	(94.7)	225	(92.6)
	Not completed	14	(4.8)	18	(6.3)
	Participant did not complete due to disease under study	0	(0.0)	2	(0.7)
	Not completed due to site staff error	4	(1.4)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	3	(1.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	3	(1.0)	3	(1.0)
	Other	2	(0.7)	5	(1.7)
	With visit, no record	2	(0.7)	1	(0.3)
	Missing by Design	**28**	**(9.6)**	**43**	**(15.0)**
	Discontinued due to adverse event	8	(2.7)	12	(4.2)
	Discontinued due to clinical progression	0	(0.0)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	7	(2.4)	9	(3.1)
	Discontinued due to withdrawal by participant	2	(0.7)	1	(0.3)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	3	(1.0)
	Visit not scheduled	11	(3.8)	15	(5.2)
WEEK 18	**Expected to Complete Questionnaires**	**249**	**(85.6)**	**231**	**(80.8)**
	Completed	212	(72.9)	188	(65.7)
	Compliance (% in those expected to complete questionnaires)	212	(85.1)	188	(81.4)
	Not completed	37	(12.7)	43	(15.0)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)
	Not completed due to site staff error	6	(2.1)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	3	(1.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	1	(0.3)
	Participant refused for other reasons	2	(0.7)	5	(1.7)
	Other	4	(1.4)	12	(4.2)
	With visit, no record	23	(7.9)	17	(5.9)
	Missing by Design	**42**	**(14.4)**	**55**	**(19.2)**
	Discontinued due to adverse event	10	(3.4)	19	(6.6)
	Discontinued due to clinical progression	3	(1.0)	5	(1.7)
	Discontinued due to non-study anti-cancer therapy	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	1	(0.3)
	Discontinued due to progressive disease	17	(5.8)	18	(6.3)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to withdrawal by participant	3	(1.0)	3	(1.0)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	3	(1.0)	2	(0.7)
	Visit not scheduled	4	(1.4)	7	(2.4)
WEEK 24	**Expected to Complete Questionnaires**	**223**	**(76.6)**	**192**	**(67.1)**
	Completed	193	(66.3)	152	(53.1)
	Compliance (% in those expected to complete questionnaires)	193	(86.5)	152	(79.2)
	Not completed	30	(10.3)	40	(14.0)
	Participant did not complete due to disease under study	1	(0.3)	2	(0.7)
	Not completed due to site staff error	7	(2.4)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	4	(1.4)	3	(1.0)
	Other	3	(1.0)	9	(3.1)
	With visit, no record	14	(4.8)	20	(7.0)
	Missing by Design	**68**	**(23.4)**	**94**	**(32.9)**
	Discontinued due to adverse event	14	(4.8)	21	(7.3)
	Discontinued due to clinical progression	6	(2.1)	11	(3.8)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	29	(10.0)	40	(14.0)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	3	(1.0)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Visit not scheduled	7	(2.4)	10	(3.5)
WEEK 30	**Expected to Complete Questionnaires**	**208**	**(71.5)**	**175**	**(61.2)**
	Completed	178	(61.2)	135	(47.2)
	Compliance (% in those expected to complete questionnaires)	178	(85.6)	135	(77.1)
	Not completed	30	(10.3)	40	(14.0)
	Participant did not complete due to disease under study	2	(0.7)	3	(1.0)
	Not completed due to site staff error	6	(2.1)	1	(0.3)
	Participant in hospital or hospice	1	(0.3)	1	(0.3)
	Participant was physically unable to complete	0	(0.0)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	1	(0.3)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	3	(1.0)	7	(2.4)
	With visit, no record	17	(5.8)	23	(8.0)
	Missing by Design	**83**	**(28.5)**	**111**	**(38.8)**
	Discontinued due to adverse event	16	(5.5)	21	(7.3)
	Discontinued due to clinical progression	8	(2.7)	13	(4.5)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	40	(13.7)	63	(22.0)
	Discontinued due to withdrawal by participant	5	(1.7)	4	(1.4)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	5	(1.7)	2	(0.7)
	Visit not scheduled	5	(1.7)	4	(1.4)
WEEK 36	**Expected to Complete Questionnaires**	**179**	**(61.5)**	**143**	**(50.0)**
	Completed	151	(51.9)	115	(40.2)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Compliance (% in those expected to complete questionnaires)	151	(84.4)	115	(80.4)
	Not completed	28	(9.6)	28	(9.8)
	Participant did not complete due to disease under study	1	(0.3)	0	(0.0)
	Not completed due to site staff error	5	(1.7)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	3	(1.0)
	Other	9	(3.1)	6	(2.1)
	With visit, no record	11	(3.8)	14	(4.9)
	Missing by Design	**112**	**(38.5)**	**143**	**(50.0)**
	Discontinued due to adverse event	19	(6.5)	22	(7.7)
	Discontinued due to clinical progression	9	(3.1)	14	(4.9)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	2	(0.7)
	Discontinued due to progressive disease	68	(23.4)	89	(31.1)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	2	(0.7)
	Visit not scheduled	5	(1.7)	6	(2.1)
WEEK 42	**Expected to Complete Questionnaires**	**172**	**(59.1)**	**124**	**(43.4)**
	Completed	151	(51.9)	101	(35.3)
	Compliance (% in those expected to complete questionnaires)	151	(87.8)	101	(81.5)
	Not completed	21	(7.2)	23	(8.0)
	Participant did not complete due to disease under study	2	(0.7)	1	(0.3)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Not completed due to site staff error	3	(1.0)	3	(1.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	3	(1.0)	8	(2.8)
	With visit, no record	10	(3.4)	8	(2.8)
	Missing by Design	**119**	**(40.9)**	**162**	**(56.6)**
	Discontinued due to adverse event	19	(6.5)	24	(8.4)
	Discontinued due to clinical progression	9	(3.1)	15	(5.2)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	74	(25.4)	111	(38.8)
	Discontinued due to withdrawal by participant	6	(2.1)	5	(1.7)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	2	(0.7)	0	(0.0)
	Visit not scheduled	3	(1.0)	1	(0.3)
WEEK 48	**Expected to Complete Questionnaires**	**157**	**(54.0)**	**109**	**(38.1)**
	Completed	150	(51.5)	106	(37.1)
	Compliance (% in those expected to complete questionnaires)	150	(95.5)	106	(97.2)
	Not completed	7	(2.4)	3	(1.0)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Participant refused for other reasons	3	(1.0)	0	(0.0)
	Other	3	(1.0)	1	(0.3)
	With visit, no record	0	(0.0)	1	(0.3)
	Missing by Design	**134**	**(46.0)**	**177**	**(61.9)**
	Discontinued due to adverse event	20	(6.9)	24	(8.4)
	Discontinued due to clinical progression	10	(3.4)	15	(5.2)
	Discontinued due to non-study anti-cancer therapy	5	(1.7)	4	(1.4)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	91	(31.3)	125	(43.7)
	Discontinued due to withdrawal by participant	6	(2.1)	6	(2.1)
	Translation not available in participants language	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)

Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason.

Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N).

Missing by design includes: adverse event, death, discontinuation, translations not available, and no visit scheduled.

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CPS: Combined Positive Score; FP: Cisplatin plus 5-FU

Database Cutoff Date: 29MAR2023

Anhang 4-G1.3: Rücklaufquoten des EQ-5D VAS

Tabelle 4G-3: Gründe für das Fehlen von Werten im EQ-5D VAS

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**291**	**(100.0)**	**286**	**(100.0)**
	Completed	275	(94.5)	275	(96.2)
	Compliance (% in those expected to complete questionnaires)	275	(94.5)	275	(96.2)
	Not completed	16	(5.5)	11	(3.8)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(0.7)	5	(1.7)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	0	(0.0)
	Other	6	(2.1)	2	(0.7)
	With visit, no record	4	(1.4)	4	(1.4)
	Missing by Design	**0**	**(0.0)**	**0**	**(0.0)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
WEEK 3	**Expected to Complete Questionnaires**	**273**	**(93.8)**	**266**	**(93.0)**
	Completed	261	(89.7)	248	(86.7)
	Compliance (% in those expected to complete questionnaires)	261	(95.6)	248	(93.2)
	Not completed	12	(4.1)	18	(6.3)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	1	(0.3)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	4	(1.4)
	Other	6	(2.1)	5	(1.7)
	With visit, no record	1	(0.3)	2	(0.7)
	Missing by Design	**18**	**(6.2)**	**20**	**(7.0)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	3	(1.0)	4	(1.4)
	Visit not scheduled	15	(5.2)	16	(5.6)
WEEK 6	**Expected to Complete Questionnaires**	**261**	**(89.7)**	**255**	**(89.2)**
	Completed	249	(85.6)	234	(81.8)
	Compliance (% in those expected to complete questionnaires)	249	(95.4)	234	(91.8)
	Not completed	12	(4.1)	21	(7.3)
	Participant did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	4	(1.4)	10	(3.5)
	With visit, no record	0	(0.0)	4	(1.4)
	Missing by Design	**30**	**(10.3)**	**31**	**(10.8)**
	Discontinued due to adverse event	4	(1.4)	7	(2.4)
	Discontinued due to clinical progression	0	(0.0)	1	(0.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by participant	0	(0.0)	0	(0.0)
	Participant died	2	(0.7)	2	(0.7)
	Visit not scheduled	24	(8.2)	21	(7.3)
WEEK 9	**Expected to Complete Questionnaires**	**259**	**(89.0)**	**240**	**(83.9)**
	Completed	245	(84.2)	216	(75.5)
	Compliance (% in those expected to complete questionnaires)	245	(94.6)	216	(90.0)
	Not completed	14	(4.8)	24	(8.4)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)
	Not completed due to site staff error	4	(1.4)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	1	(0.3)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	5	(1.7)
	Other	3	(1.0)	7	(2.4)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	With visit, no record	5	(1.7)	6	(2.1)
	Missing by Design	**32**	**(11.0)**	**46**	**(16.1)**
	Discontinued due to adverse event	6	(2.1)	10	(3.5)
	Discontinued due to clinical progression	0	(0.0)	2	(0.7)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	2	(0.7)	2	(0.7)
	Discontinued due to withdrawal by participant	1	(0.3)	1	(0.3)
	Participant died	0	(0.0)	1	(0.3)
	Visit not scheduled	23	(7.9)	30	(10.5)
WEEK 12	**Expected to Complete Questionnaires**	**263**	**(90.4)**	**243**	**(85.0)**
	Completed	250	(85.9)	225	(78.7)
	Compliance (% in those expected to complete questionnaires)	250	(95.1)	225	(92.6)
	Not completed	13	(4.5)	18	(6.3)
	Participant did not complete due to disease under study	0	(0.0)	2	(0.7)
	Not completed due to site staff error	4	(1.4)	5	(1.7)
	Participant in hospital or hospice	0	(0.0)	1	(0.3)
	Participant was physically unable to complete	3	(1.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	3	(1.0)
	Other	2	(0.7)	5	(1.7)
	With visit, no record	2	(0.7)	1	(0.3)
	Missing by Design	**28**	**(9.6)**	**43**	**(15.0)**
	Discontinued due to adverse event	8	(2.7)	12	(4.2)
	Discontinued due to clinical progression	0	(0.0)	3	(1.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	7	(2.4)	9	(3.1)
	Discontinued due to withdrawal by participant	2	(0.7)	1	(0.3)
	Participant died	0	(0.0)	3	(1.0)
	Visit not scheduled	11	(3.8)	15	(5.2)
WEEK 18	**Expected to Complete Questionnaires**	**249**	**(85.6)**	**231**	**(80.8)**
	Completed	212	(72.9)	190	(66.4)
	Compliance (% in those expected to complete questionnaires)	212	(85.1)	190	(82.3)
	Not completed	37	(12.7)	41	(14.3)
	Participant did not complete due to disease under study	0	(0.0)	1	(0.3)
	Not completed due to site staff error	6	(2.1)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	3	(1.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	2	(0.7)	5	(1.7)
	Other	4	(1.4)	11	(3.8)
	With visit, no record	23	(7.9)	17	(5.9)
	Missing by Design	**42**	**(14.4)**	**55**	**(19.2)**
	Discontinued due to adverse event	10	(3.4)	19	(6.6)
	Discontinued due to clinical progression	3	(1.0)	5	(1.7)
	Discontinued due to non-study anti-cancer therapy	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	1	(0.3)
	Discontinued due to progressive disease	17	(5.8)	18	(6.3)
	Discontinued due to withdrawal by participant	3	(1.0)	3	(1.0)
	Participant died	3	(1.0)	2	(0.7)
	Visit not scheduled	4	(1.4)	7	(2.4)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
WEEK 24	**Expected to Complete Questionnaires**	**223**	**(76.6)**	**192**	**(67.1)**
	Completed	196	(67.4)	152	(53.1)
	Compliance (% in those expected to complete questionnaires)	196	(87.9)	152	(79.2)
	Not completed	27	(9.3)	40	(14.0)
	Participant did not complete due to disease under study	1	(0.3)	2	(0.7)
	Not completed due to site staff error	5	(1.7)	4	(1.4)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	1	(0.3)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	4	(1.4)	3	(1.0)
	Other	2	(0.7)	9	(3.1)
	With visit, no record	14	(4.8)	20	(7.0)
	Missing by Design	**68**	**(23.4)**	**94**	**(32.9)**
	Discontinued due to adverse event	14	(4.8)	21	(7.3)
	Discontinued due to clinical progression	6	(2.1)	11	(3.8)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	29	(10.0)	40	(14.0)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Participant died	3	(1.0)	3	(1.0)
	Visit not scheduled	7	(2.4)	10	(3.5)
WEEK 30	**Expected to Complete Questionnaires**	**208**	**(71.5)**	**175**	**(61.2)**
	Completed	178	(61.2)	136	(47.6)
	Compliance (% in those expected to complete questionnaires)	178	(85.6)	136	(77.7)
	Not completed	30	(10.3)	39	(13.6)
	Participant did not complete due to disease under study	2	(0.7)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Not completed due to site staff error	5	(1.7)	1	(0.3)
	Participant in hospital or hospice	1	(0.3)	1	(0.3)
	Participant was physically unable to complete	0	(0.0)	2	(0.7)
	Participant lost to follow-up/unable to contact	0	(0.0)	1	(0.3)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	4	(1.4)	6	(2.1)
	With visit, no record	17	(5.8)	23	(8.0)
	Missing by Design	**83**	**(28.5)**	**111**	**(38.8)**
	Discontinued due to adverse event	16	(5.5)	21	(7.3)
	Discontinued due to clinical progression	8	(2.7)	13	(4.5)
	Discontinued due to non-study anti-cancer therapy	3	(1.0)	3	(1.0)
	Discontinued due to physician decision	1	(0.3)	1	(0.3)
	Discontinued due to progressive disease	40	(13.7)	63	(22.0)
	Discontinued due to withdrawal by participant	5	(1.7)	4	(1.4)
	Participant died	5	(1.7)	2	(0.7)
	Visit not scheduled	5	(1.7)	4	(1.4)
WEEK 36	**Expected to Complete Questionnaires**	**179**	**(61.5)**	**143**	**(50.0)**
	Completed	153	(52.6)	115	(40.2)
	Compliance (% in those expected to complete questionnaires)	153	(85.5)	115	(80.4)
	Not completed	26	(8.9)	28	(9.8)
	Participant did not complete due to disease under study	1	(0.3)	0	(0.0)
	Not completed due to site staff error	4	(1.4)	4	(1.4)
	Participant in hospital or hospice	1	(0.3)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	3	(1.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Other	8	(2.7)	6	(2.1)
	With visit, no record	11	(3.8)	14	(4.9)
	Missing by Design	**112**	**(38.5)**	**143**	**(50.0)**
	Discontinued due to adverse event	19	(6.5)	22	(7.7)
	Discontinued due to clinical progression	9	(3.1)	14	(4.9)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	2	(0.7)
	Discontinued due to progressive disease	68	(23.4)	89	(31.1)
	Discontinued due to withdrawal by participant	5	(1.7)	5	(1.7)
	Participant died	0	(0.0)	2	(0.7)
	Visit not scheduled	5	(1.7)	6	(2.1)
WEEK 42	**Expected to Complete Questionnaires**	**172**	**(59.1)**	**124**	**(43.4)**
	Completed	151	(51.9)	102	(35.7)
	Compliance (% in those expected to complete questionnaires)	151	(87.8)	102	(82.3)
	Not completed	21	(7.2)	22	(7.7)
	Participant did not complete due to disease under study	2	(0.7)	1	(0.3)
	Not completed due to site staff error	3	(1.0)	3	(1.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	2	(0.7)	1	(0.3)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	1	(0.3)	2	(0.7)
	Other	3	(1.0)	7	(2.4)
	With visit, no record	10	(3.4)	8	(2.8)
	Missing by Design	**119**	**(40.9)**	**162**	**(56.6)**
	Discontinued due to adverse event	19	(6.5)	24	(8.4)
	Discontinued due to clinical progression	9	(3.1)	15	(5.2)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Discontinued due to non-study anti-cancer therapy	4	(1.4)	3	(1.0)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	74	(25.4)	111	(38.8)
	Discontinued due to withdrawal by participant	6	(2.1)	5	(1.7)
	Participant died	2	(0.7)	0	(0.0)
	Visit not scheduled	3	(1.0)	1	(0.3)
WEEK 48	**Expected to Complete Questionnaires**	**157**	**(54.0)**	**109**	**(38.1)**
	Completed	150	(51.5)	106	(37.1)
	Compliance (% in those expected to complete questionnaires)	150	(95.5)	106	(97.2)
	Not completed	7	(2.4)	3	(1.0)
	Participant did not complete due to disease under study	1	(0.3)	1	(0.3)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Participant in hospital or hospice	0	(0.0)	0	(0.0)
	Participant was physically unable to complete	0	(0.0)	0	(0.0)
	Participant lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Participant refused for other reasons	3	(1.0)	0	(0.0)
	Other	3	(1.0)	1	(0.3)
	With visit, no record	0	(0.0)	1	(0.3)
	Missing by Design	**134**	**(46.0)**	**177**	**(61.9)**
	Discontinued due to adverse event	20	(6.9)	24	(8.4)
	Discontinued due to clinical progression	10	(3.4)	15	(5.2)
	Discontinued due to non-study anti-cancer therapy	5	(1.7)	4	(1.4)
	Discontinued due to physician decision	2	(0.7)	3	(1.0)
	Discontinued due to progressive disease	91	(31.3)	125	(43.7)
	Discontinued due to withdrawal by participant	6	(2.1)	6	(2.1)
	Participant died	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + Trastuzumab + FP or CAPOX N=291		Placebo + Trastuzumab + FP or CAPOX N=286	
		n	(%)	n	(%)
	Visit not scheduled	0	(0.0)	0	(0.0)

Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason.

Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N).

Missing by design includes: adverse event, death, discontinuation, translations not available, and no visit scheduled.

5-FU: 5-Fluorouracil ; CAPOX: Oxaliplatin plus Capecitabine; CPS: Combined Positive Score ; FP: Cisplatin plus 5-FU;

Database Cutoff Date: 29MAR2023

Anhang 4-G2: Auswertungen über den Studienverlauf für die Endpunkte Krankheitssymptomatik und Gesundheitszustand anhand von EORTC QLQ-C30, EORTC QLQ-STO22 und EQ-5D VAS (KEYNOTE 811)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Auswertungen über den Studienverlauf des EORTC QLQ-C30, des EORTC QLQ-STO22 und des EQ-5D VAS dargestellt.

Alle Ergebnisse beziehen sich auf den dritten Datenschnitt (29. März 2023).

Anhang 4-G2.1: Auswertungen über den Studienverlauf des EORTC QLQ-C30

Auswertung über den Studienverlauf

EORTC QLQ-C30

EORTC QLQ-C30: Symptomskala Erschöpfung

Tabelle 4G-4: Auswertung über den Studienverlauf der Symptomskala Erschöpfung des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Erschöpfung	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	26,4 (24,3)	29,2 (24,7)
Median (Q1; Q3)	22,2 (11,1; 33,3)	27,8 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	27,8 (22,3)	27,7 (22,5)
Median (Q1; Q3)	33,3 (11,1; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	27,4 (21,7)	27,9 (23,5)
Median (Q1; Q3)	33,3 (11,1; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	28,2 (22,2)	26,8 (22,6)
Median (Q1; Q3)	33,3 (11,1; 33,3)	22,2 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	25,8 (21,7)	27,1 (23,9)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189

EORTC QLQ-C30 Erschöpfung	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Mittelwert (SD)	28,8 (24,4)	27,7 (23,0)
Median (Q1; Q3)	33,3 (11,1; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	25,2 (21,1)	24,3 (22,6)
Median (Q1; Q3)	22,2 (11,1; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 30		
N[c]	178	134
Mittelwert (SD)	24,6 (23,2)	23,5 (22,7)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	22,3 (20,4)	20,7 (20,2)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 42		
N[c]	151	101
Mittelwert (SD)	21,4 (20,0)	22,7 (22,5)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 88,9	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	22,4 (21,5)	22,5 (22,4)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

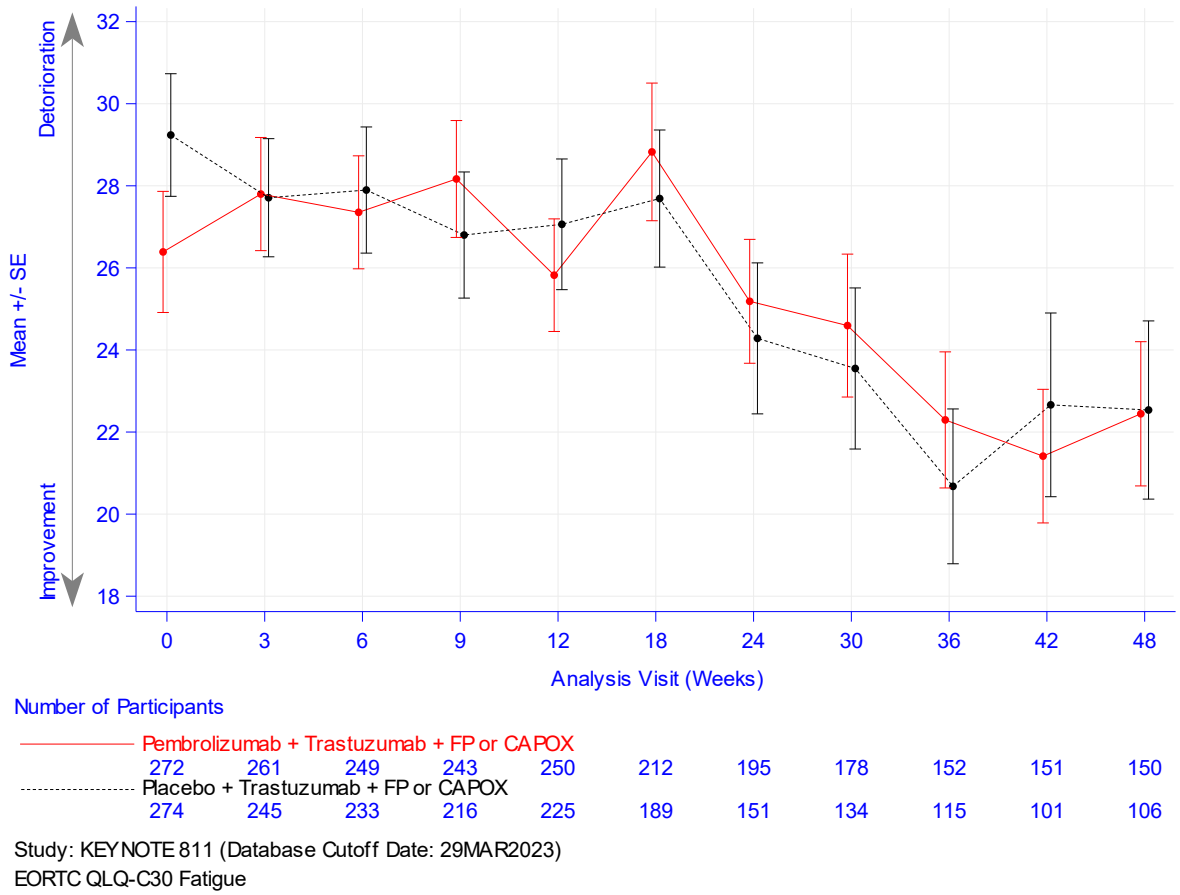

Abbildung 4G-1: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Erschöpfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Übelkeit und Erbrechen

Tabelle 4G-5: Auswertung über den Studienverlauf der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Übelkeit und Erbrechen	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	11,3 (20,3)	10,9 (20,5)
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 3		
N[c]	261	245
Mittelwert (SD)	12,4 (18,5)	14,1 (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; 66,7

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
Woche 6		
N[c]	249	233
Mittelwert (SD)	14,6 (20,2)	12,0 (18,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	13,4 (20,4)	10,6 (17,3)
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 12		
N[c]	250	225
Mittelwert (SD)	12,6 (18,7)	10,7 (20,3)
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 18		
N[c]	212	189
Mittelwert (SD)	13,7 (22,2)	10,2 (17,8)
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 24		
N[c]	195	151
Mittelwert (SD)	8,9 (18,0)	7,3 (15,0)
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 30		
N[c]	178	134
Mittelwert (SD)	8,1 (16,7)	6,3 (15,5)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	5,5 (13,3)	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; 83,3
Woche 42		
N[c]	151	101
Mittelwert (SD)	4,6 (10,0)	7,1 (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; 83,3
Woche 48		
N[c]	150	106
Mittelwert (SD)	5,6 (13,2)	8,3 (21,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 100,0
a: Datenschnitt: 29. März 2023		

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

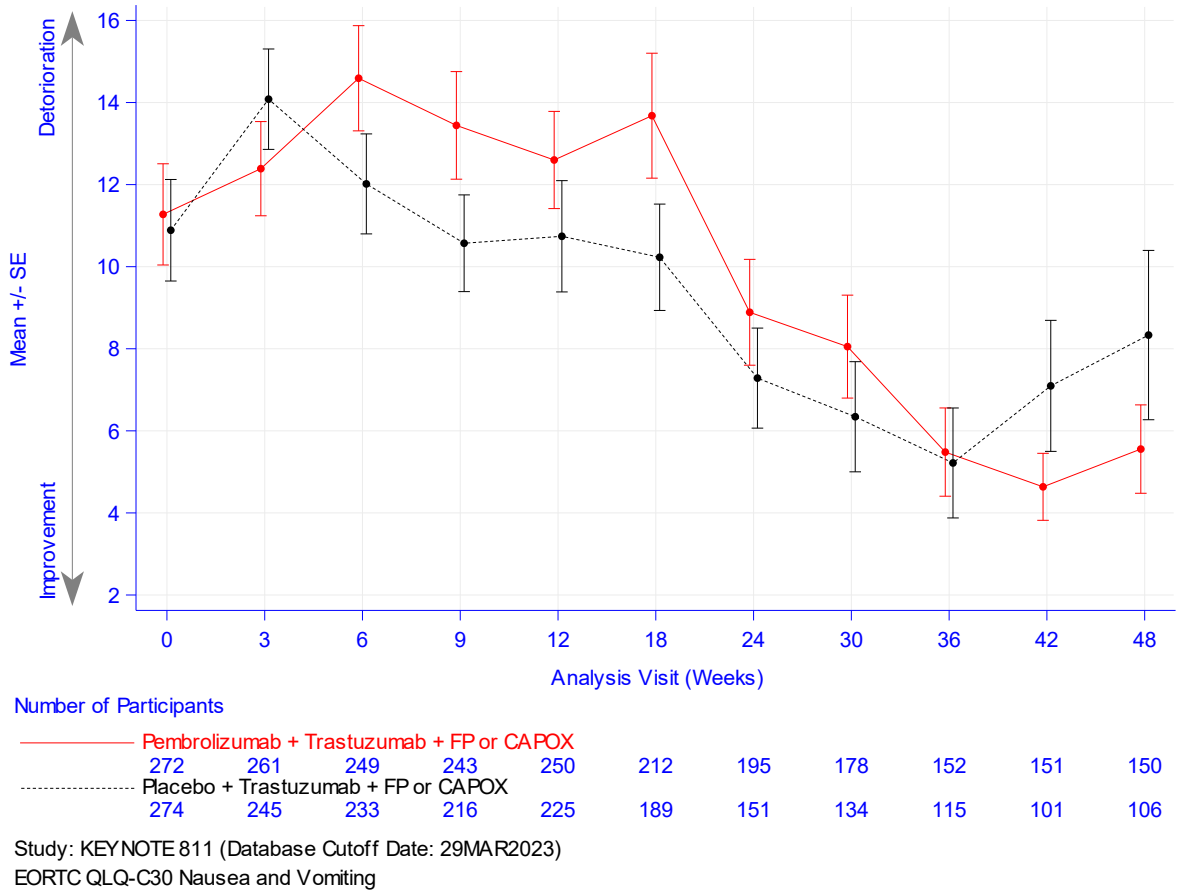

Abbildung 4G-2: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Übelkeit und Erbrechen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Schmerz

Tabelle 4G-6: Auswertung über den Studienverlauf der Symptomskala Schmerz des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Schmerzen	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	23,0 (26,0)	22,2 (25,5)
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 3		
N[c]	261	245
Mittelwert (SD)	16,2 (22,1)	16,3 (20,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	13,2 (19,1)	16,2 (22,2)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	13,2 (20,6)	13,3 (19,8)
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 12		
N[c]	250	225
Mittelwert (SD)	11,5 (18,8)	14,1 (22,1)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	12,7 (19,3)	16,4 (22,8)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	13,0 (19,7)	14,7 (20,0)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 30		
N[c]	178	134
Mittelwert (SD)	15,3 (20,8)	12,9 (20,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Schmerzen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	152	115
Mittelwert (SD)	9,8 (16,1)	10,9 (17,0)
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 42		
N[c]	151	101
Mittelwert (SD)	9,7 (16,1)	14,0 (20,8)
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 48		
N[c]	150	106
Mittelwert (SD)	11,9 (19,3)	11,3 (18,6)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

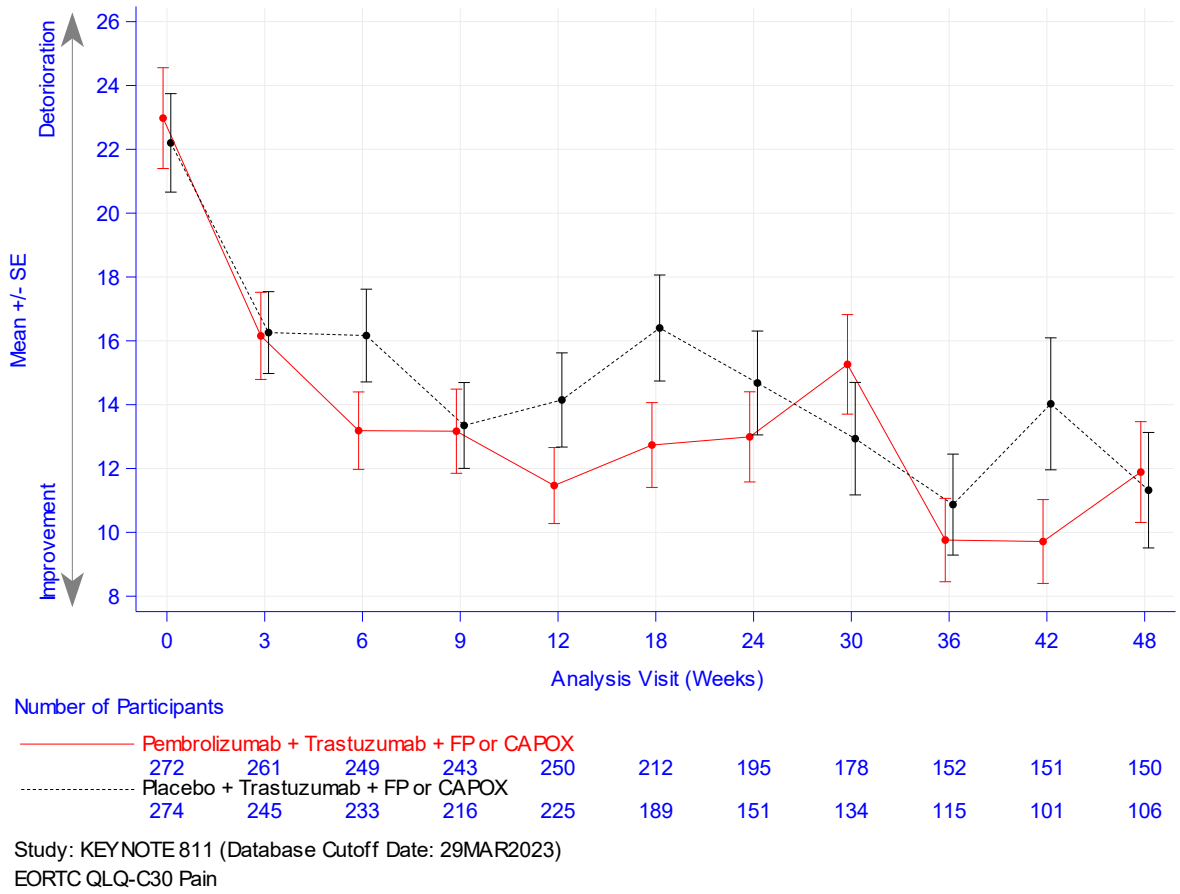

Abbildung 4G-3: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerz zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Dyspnoe

Tabelle 4G-7: Auswertung über den Studienverlauf der Symptomskala Dyspnoe des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Dyspnoe	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	10,9 (19,0)	10,3 (21,0)
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]	261	245
Mittelwert (SD)	8,7 (17,6)	9,4 (18,3)
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 Dyspnoe	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
Woche 6		
N[c]	249	233
Mittelwert (SD)	9,8 (17,1)	9,3 (18,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	11,7 (19,1)	9,3 (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 12		
N[c]	250	225
Mittelwert (SD)	10,5 (19,4)	10,2 (21,3)
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 18		
N[c]	212	189
Mittelwert (SD)	9,4 (18,2)	11,1 (20,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	12,6 (22,9)	9,7 (17,9)
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 30		
N[c]	178	134
Mittelwert (SD)	10,7 (20,2)	9,5 (19,4)
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 36		
N[c]	152	115
Mittelwert (SD)	9,2 (15,9)	7,5 (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; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	7,9 (15,3)	6,9 (15,1)
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 48		
N[c]	150	106
Mittelwert (SD)	10,0 (16,7)	9,7 (18,4)
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: 29. März 2023
b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

EORTC QLQ-C30 Dyspnoe	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

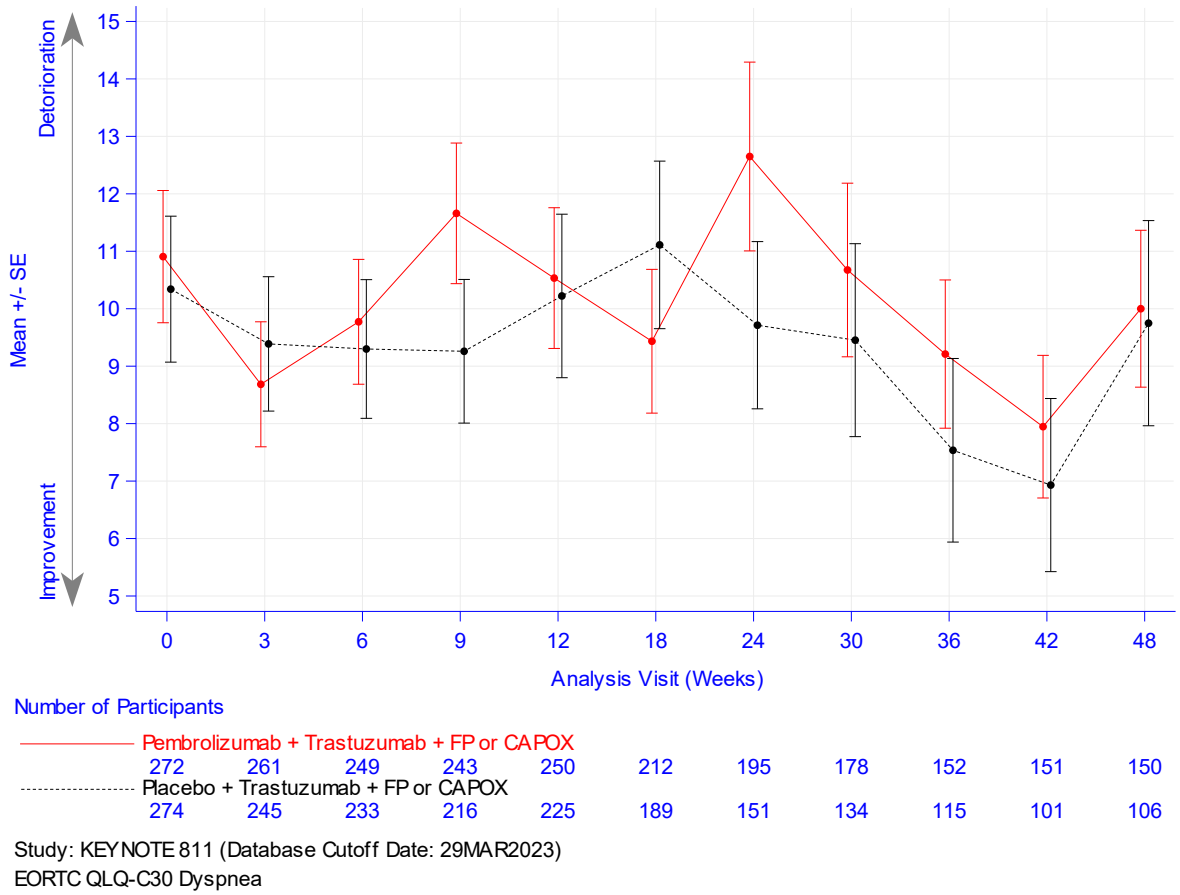

Abbildung 4G-4: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Dyspnoe zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Schlaflosigkeit

Tabelle 4G-8: Auswertung über den Studienverlauf der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Schlaflosigkeit	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	23,5 (29,1)	22,1 (30,1)
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 3		
N[c]	261	245
Mittelwert (SD)	18,4 (25,0)	20,7 (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 6		
N[c]	249	233
Mittelwert (SD)	17,9 (23,6)	17,6 (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 9		
N[c]	243	216
Mittelwert (SD)	17,6 (23,5)	17,9 (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 12		
N[c]	250	225
Mittelwert (SD)	15,5 (22,2)	18,4 (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 18		
N[c]	212	189
Mittelwert (SD)	16,5 (25,7)	14,6 (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
Woche 24		
N[c]	195	151
Mittelwert (SD)	15,2 (24,9)	16,1 (25,5)
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 30		
N[c]	178	134
Mittelwert (SD)	17,6 (25,8)	15,7 (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

EORTC QLQ-C30 Schlaflosigkeit	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	152	115
Mittelwert (SD)	14,0 (21,5)	14,8 (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 42		
N[c]	151	101
Mittelwert (SD)	15,2 (24,3)	13,5 (24,1)
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 48		
N[c]	150	106
Mittelwert (SD)	13,1 (20,8)	13,5 (23,4)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

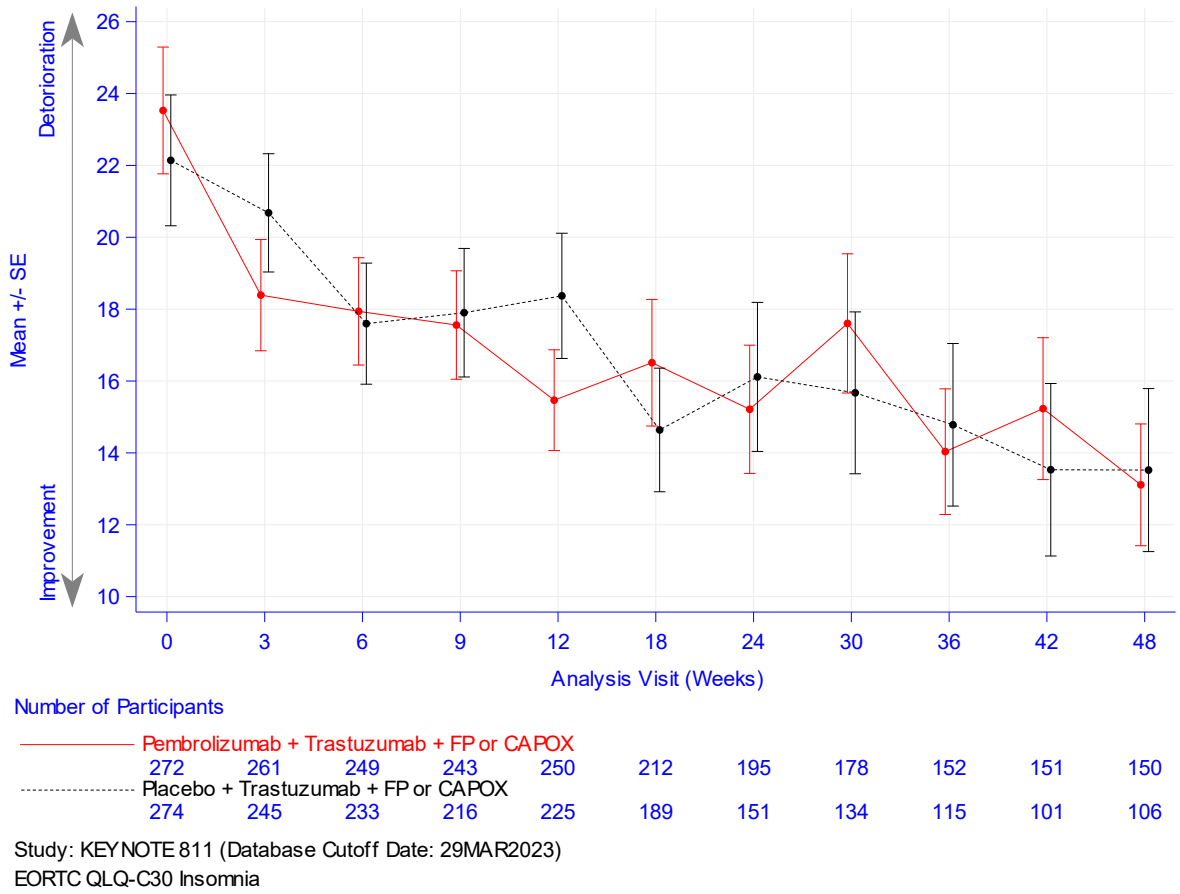

Abbildung 4G-5: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schlaflosigkeit zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Appetitverlust

Tabelle 4G-9: Auswertung über den Studienverlauf der Symptomskala Appetitverlust des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Appetitverlust	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	25,2 (31,2)	26,4 (31,3)
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 3		
N[c]	261	245
Mittelwert (SD)	22,5 (27,7)	26,9 (29,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	22,2 (25,9)	22,2 (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 9		
N[c]	243	216
Mittelwert (SD)	23,5 (27,8)	20,8 (28,3)
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 12		
N[c]	250	225
Mittelwert (SD)	20,0 (25,2)	20,1 (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 18		
N[c]	212	189
Mittelwert (SD)	21,9 (27,3)	22,6 (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 24		
N[c]	195	151
Mittelwert (SD)	18,3 (24,9)	16,1 (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 30		
N[c]	178	134
Mittelwert (SD)	16,1 (23,8)	14,4 (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
Woche 36		
N[c]	152	115
Mittelwert (SD)	13,2 (21,1)	11,3 (20,7)
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 42		
N[c]	151	101
Mittelwert (SD)	11,9 (22,2)	14,2 (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 48		
N[c]	150	106
Mittelwert (SD)	13,1 (22,8)	11,9 (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

EORTC QLQ-C30 Appetitverlust	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

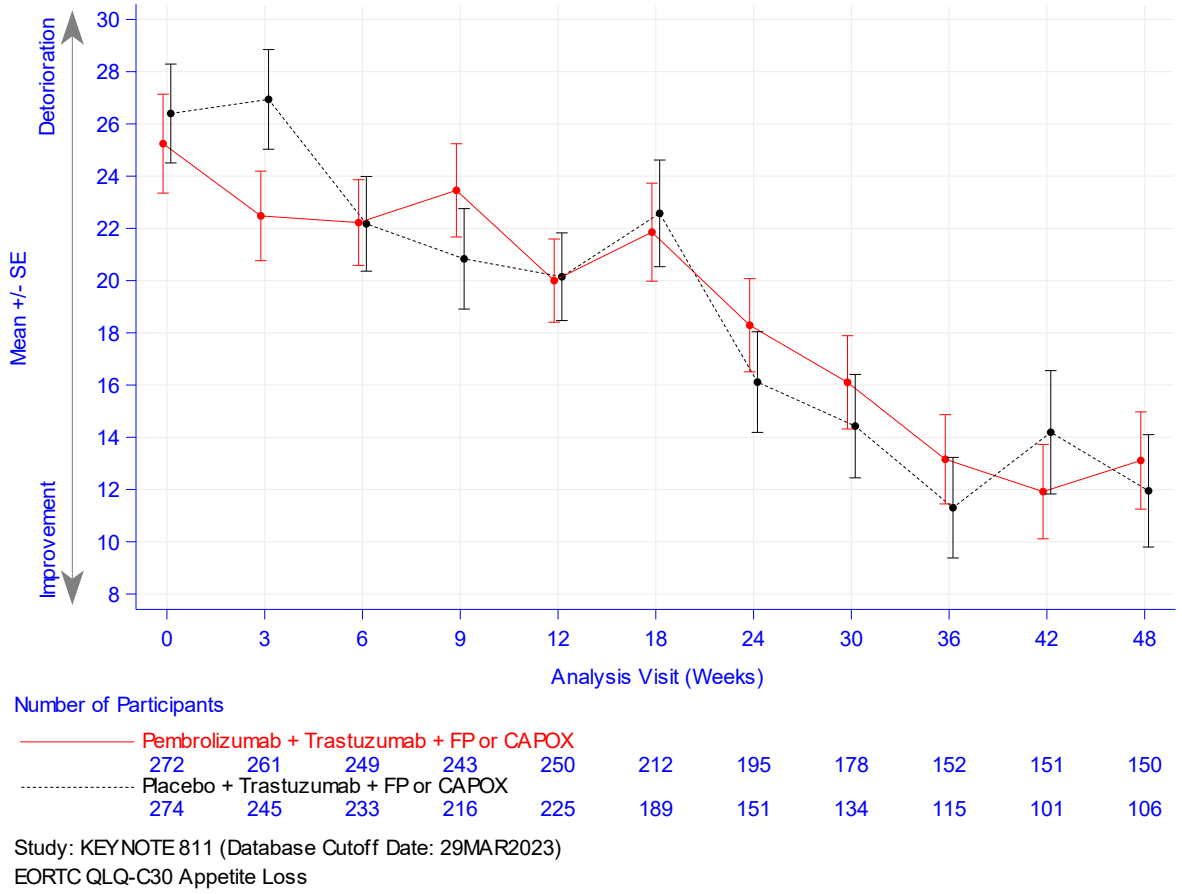

Abbildung 4G-6: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Appetitverlust zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Verstopfung

Tabelle 4G-10: Auswertung über den Studienverlauf der Symptomskala Verstopfung des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Verstopfung	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	18,0 (27,0)	15,2 (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 3		
N[c]	261	245
Mittelwert (SD)	13,5 (23,3)	11,4 (19,5)
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 6		
N[c]	249	233
Mittelwert (SD)	9,9 (19,6)	10,9 (20,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	12,5 (22,6)	11,4 (21,2)
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 12		
N[c]	250	225
Mittelwert (SD)	11,5 (20,3)	10,1 (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; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	12,9 (21,6)	11,1 (21,2)
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 24		
N[c]	195	151
Mittelwert (SD)	12,3 (23,9)	9,5 (18,6)
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 30		
N[c]	178	134
Mittelwert (SD)	10,7 (21,9)	7,5 (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

EORTC QLQ-C30 Verstopfung	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	152	115
Mittelwert (SD)	9,2 (18,1)	8,1 (16,9)
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 42		
N[c]	151	101
Mittelwert (SD)	7,7 (16,5)	9,6 (19,1)
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 48		
N[c]	150	106
Mittelwert (SD)	8,7 (17,5)	8,2 (18,3)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

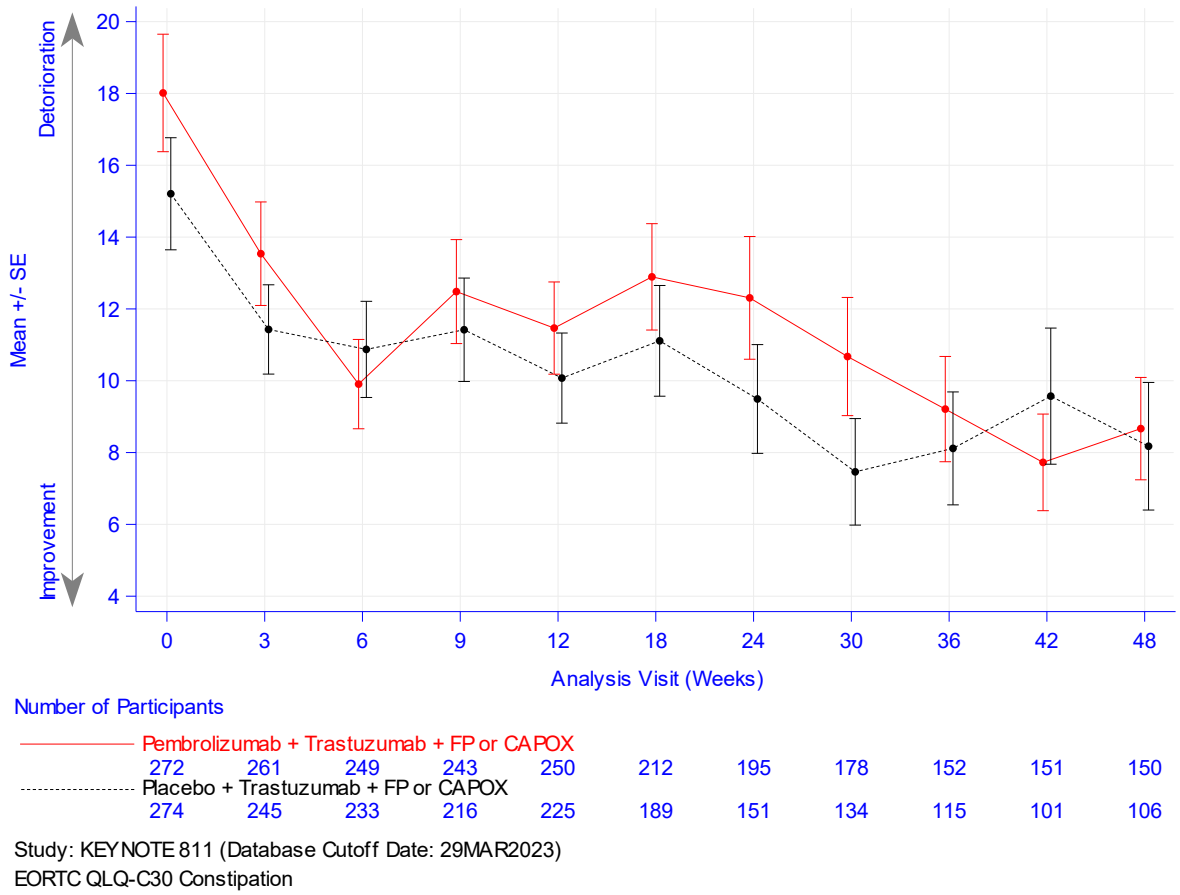

Abbildung 4G-7: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Verstopfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Diarrhö

Tabelle 4G-11: Auswertung über den Studienverlauf der Symptomskala Diarrhö des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Diarrhoe	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	4,9 (12,5)	6,1 (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; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	17,5 (26,1)	17,7 (25,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)

EORTC QLQ-C30 Diarrhoe	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	17,0 (25,9)	14,3 (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 9		
N[c]	243	216
Mittelwert (SD)	16,3 (26,1)	12,3 (22,3)
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 12		
N[c]	250	225
Mittelwert (SD)	11,2 (20,5)	11,3 (22,3)
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 18		
N[c]	212	189
Mittelwert (SD)	11,6 (22,7)	11,1 (21,7)
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 24		
N[c]	195	151
Mittelwert (SD)	8,4 (18,6)	7,1 (14,7)
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 30		
N[c]	178	134
Mittelwert (SD)	9,4 (19,4)	4,5 (13,4)
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 36		
N[c]	152	115
Mittelwert (SD)	9,4 (19,0)	5,8 (13,4)
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 42		
N[c]	151	101
Mittelwert (SD)	7,3 (15,8)	7,9 (15,7)
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 48		
N[c]	150	106
Mittelwert (SD)	6,7 (17,3)	6,6 (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; 66,7

EORTC QLQ-C30 Diarrhoe	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

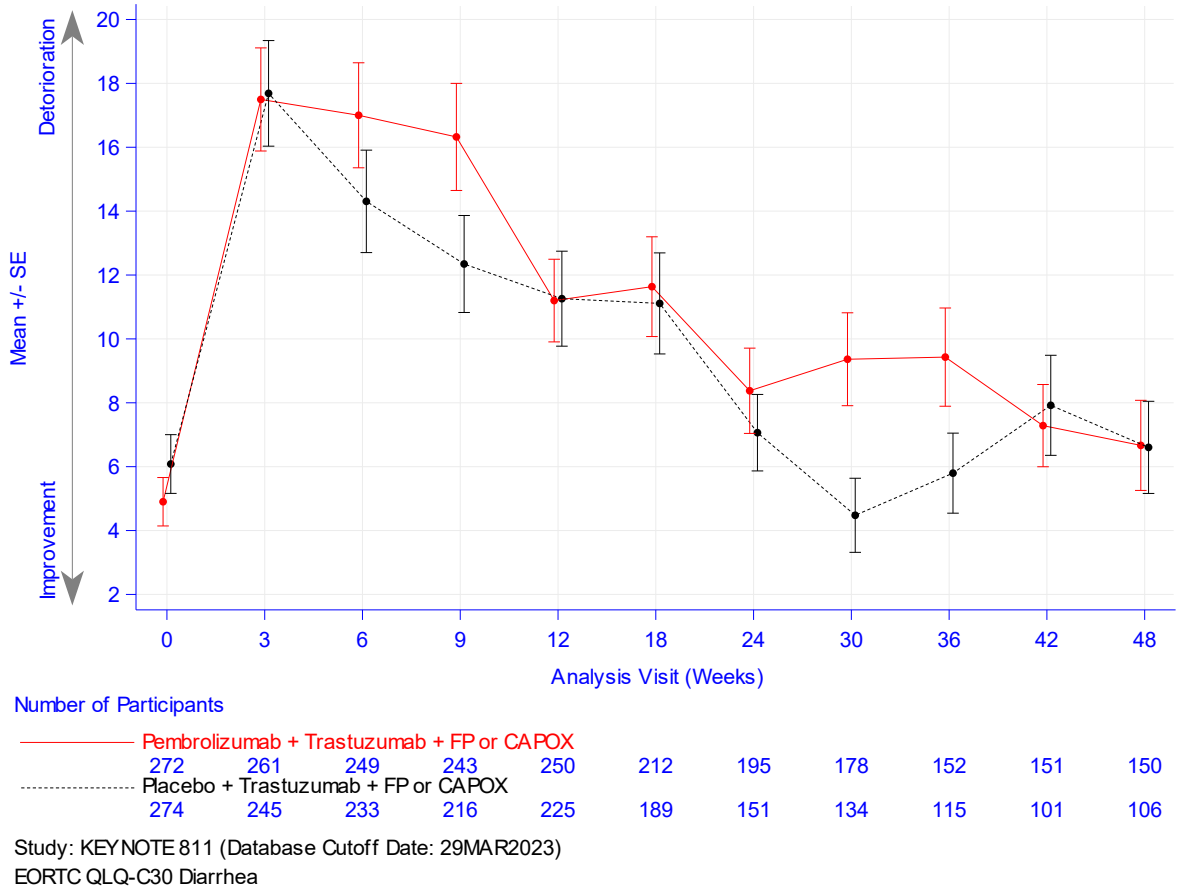

Abbildung 4G-8: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Diarrhö zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22

EORTC QLQ-STO22: Symptomskala Angst

Tabelle 4G-12: Auswertung über den Studienverlauf der Symptomskala Angst des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Angst	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	37,9 (25,5)	37,4 (28,2)
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 3		
N[c]	260	245
Mittelwert (SD)	32,8 (26,2)	33,6 (26,7)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	31,8 (25,5)	32,6 (27,3)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	213
Mittelwert (SD)	30,2 (24,5)	29,0 (25,1)
Median (Q1; Q3)	33,3 (11,1; 44,4)	22,2 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	249	225
Mittelwert (SD)	28,2 (24,6)	30,7 (27,6)
Median (Q1; Q3)	22,2 (11,1; 44,4)	22,2 (0,0; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	188
Mittelwert (SD)	30,1 (25,2)	29,3 (26,2)
Median (Q1; Q3)	22,2 (11,1; 44,4)	22,2 (0,0; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 24		
N[c]	193	152
Mittelwert (SD)	28,2 (25,0)	29,7 (26,0)
Median (Q1; Q3)	22,2 (11,1; 44,4)	22,2 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 30		
N[c]	178	135
Mittelwert (SD)	26,1 (25,9)	28,2 (26,4)
Median (Q1; Q3)	22,2 (0,0; 44,4)	22,2 (0,0; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-STO22 Angst	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	151	115
Mittelwert (SD)	25,9 (23,6)	26,5 (24,0)
Median (Q1; Q3)	22,2 (0,0; 44,4)	22,2 (0,0; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	24,0 (21,7)	26,2 (25,5)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	24,4 (23,1)	24,1 (24,7)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

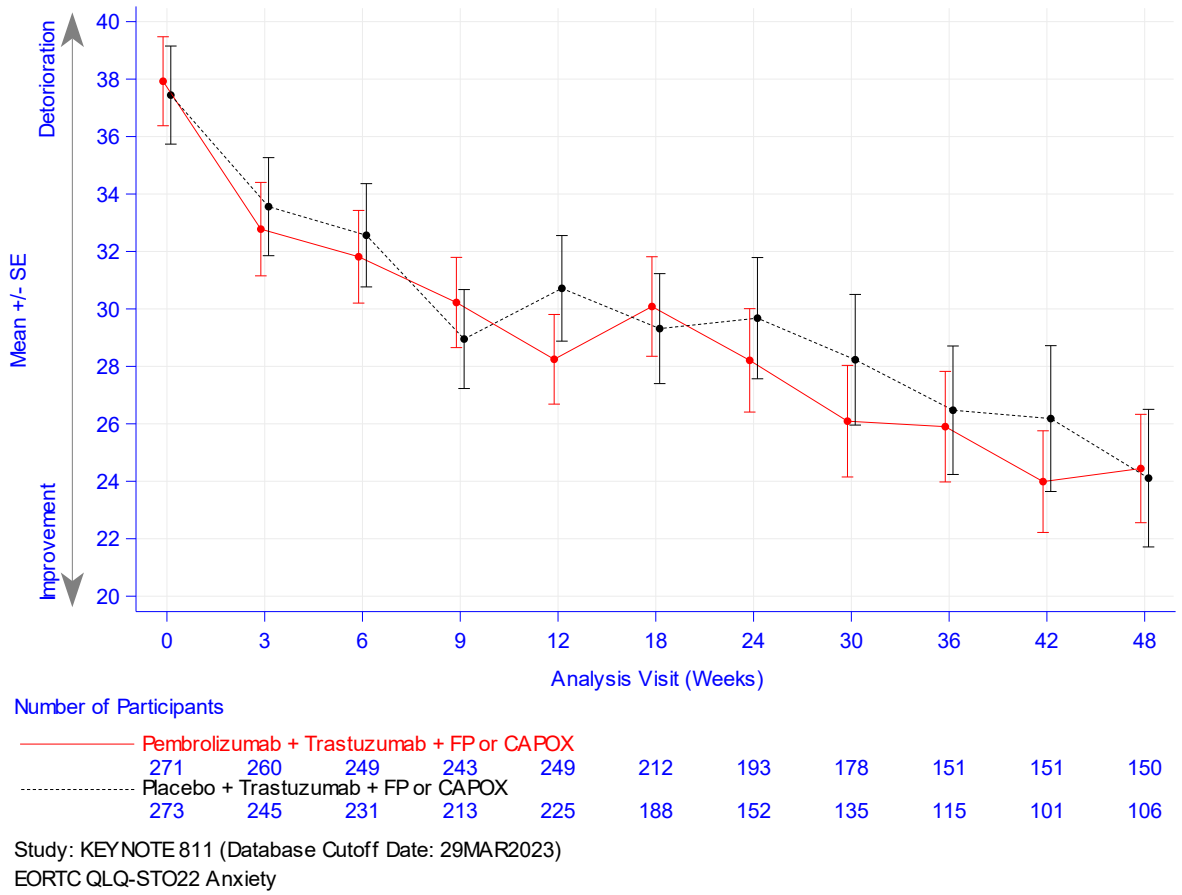

Abbildung 4G-9: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Angst zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Körperbild

Tabelle 4G-13: Auswertung über den Studienverlauf der Symptomskala Körperbild des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Körperbild	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	14,5 (24,2)	19,3 (28,6)
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 3		
N[c]	260	245
Mittelwert (SD)	16,3 (25,6)	17,1 (25,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)

EORTC QLQ-STO22 Körperbild	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	16,2 (26,3)	17,6 (26,7)
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 9		
N[c]	243	213
Mittelwert (SD)	17,0 (26,0)	14,7 (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 12		
N[c]	249	225
Mittelwert (SD)	16,7 (25,8)	17,2 (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 18		
N[c]	212	188
Mittelwert (SD)	18,4 (27,2)	17,6 (27,2)
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 24		
N[c]	193	152
Mittelwert (SD)	18,5 (27,8)	16,0 (24,9)
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 30		
N[c]	178	135
Mittelwert (SD)	16,1 (25,4)	15,6 (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 36		
N[c]	151	115
Mittelwert (SD)	14,3 (22,6)	12,2 (19,9)
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 42		
N[c]	151	101
Mittelwert (SD)	12,8 (21,0)	11,2 (22,2)
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 48		
N[c]	150	106
Mittelwert (SD)	13,8 (23,6)	11,3 (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

EORTC QLQ-STO22 Körperbild	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

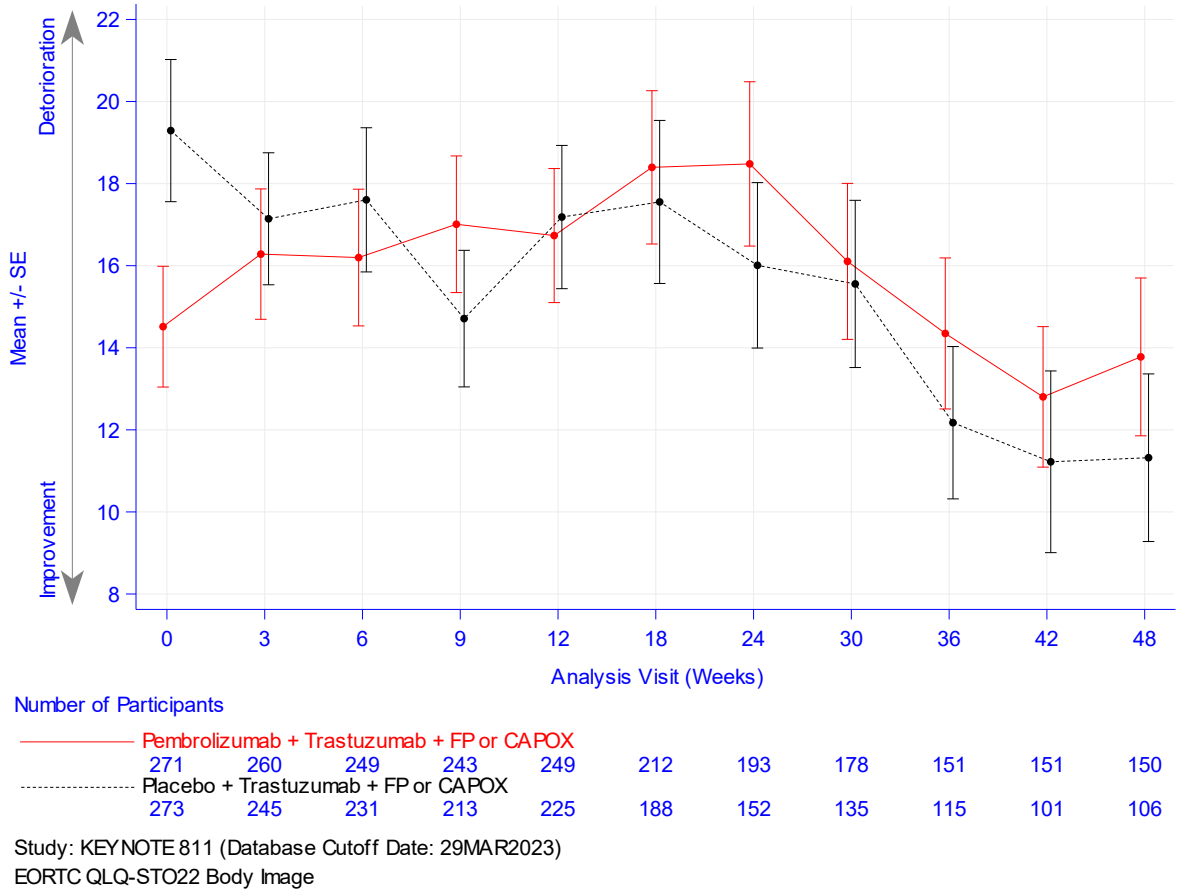

Abbildung 4G-10: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Körperbild zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Mundtrockenheit

Tabelle 4G-14: Auswertung über den Studienverlauf der Symptomskala Mundtrockenheit des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Mundtrockenheit	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	17,0 (24,3)	19,2 (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 3		
N[c]	260	245
Mittelwert (SD)	18,2 (24,9)	21,0 (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 6		
N[c]	249	231
Mittelwert (SD)	20,6 (24,6)	20,3 (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 9		
N[c]	243	213
Mittelwert (SD)	23,3 (26,3)	20,7 (25,5)
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 12		
N[c]	249	225
Mittelwert (SD)	19,9 (25,0)	20,0 (24,4)
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 18		
N[c]	212	188
Mittelwert (SD)	24,1 (26,4)	16,5 (22,5)
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 24		
N[c]	193	152
Mittelwert (SD)	19,7 (23,9)	13,6 (20,8)
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 30		
N[c]	178	135
Mittelwert (SD)	17,2 (22,2)	14,6 (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

EORTC QLQ-STO22 Mundtrockenheit	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	151	115
Mittelwert (SD)	16,1 (22,4)	11,0 (20,1)
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 42		
N[c]	151	101
Mittelwert (SD)	14,3 (20,2)	11,6 (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 48		
N[c]	150	106
Mittelwert (SD)	15,8 (21,7)	10,1 (20,1)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

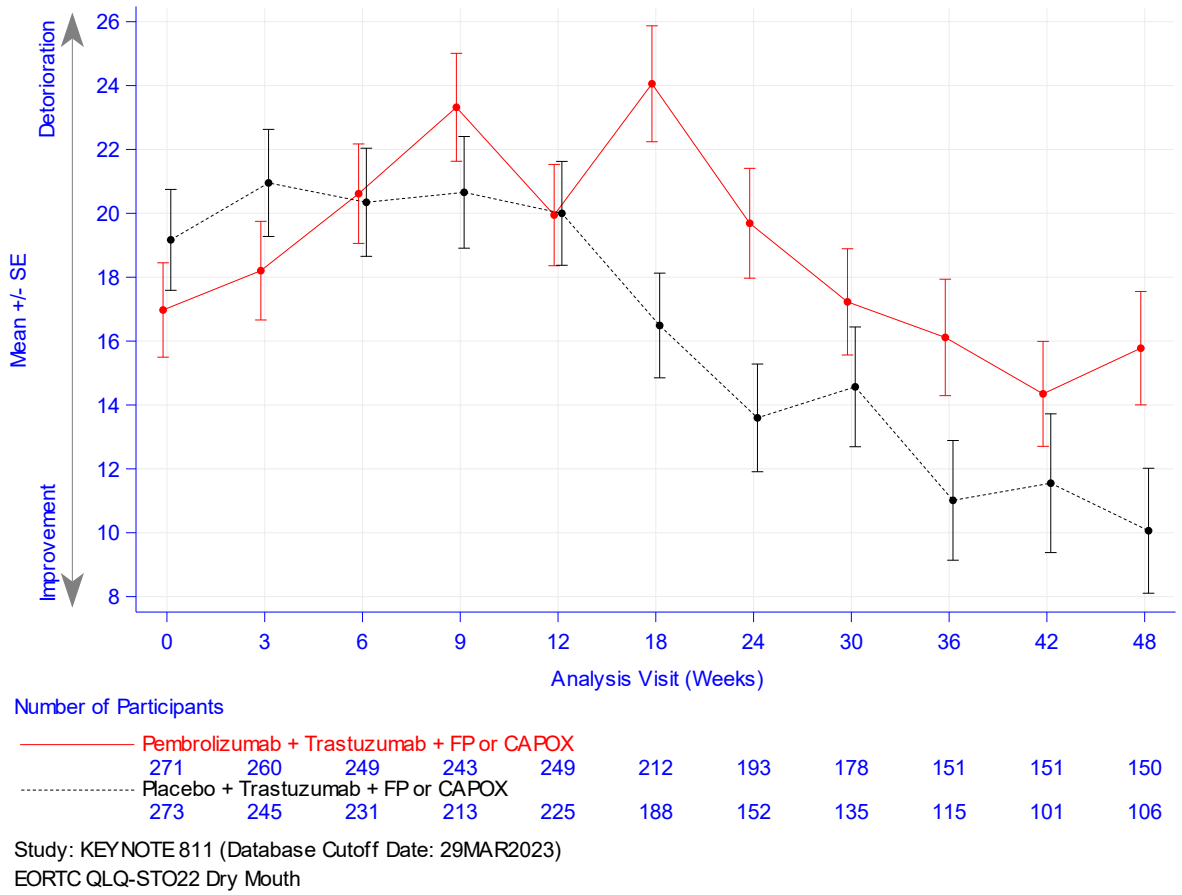

Abbildung 4G-11: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Mundtrockenheit zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Dysphagie

Tabelle 4G-15: Auswertung über den Studienverlauf der Symptomskala Angst des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Dysphagie	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	15,6 (23,0)	13,7 (19,9)
Median (Q1; Q3)	11,1 (0,0; 22,2)	0,0 (0,0; 22,2)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 3		
N[c]	260	245
Mittelwert (SD)	10,8 (19,5)	9,7 (16,5)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)

EORTC QLQ-STO22 Dysphagie	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	8,0 (14,1)	7,6 (15,7)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	213
Mittelwert (SD)	9,3 (16,5)	7,6 (14,7)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	249	225
Mittelwert (SD)	8,4 (16,1)	8,8 (18,3)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	188
Mittelwert (SD)	8,8 (14,5)	7,8 (14,5)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 77,8
Woche 24		
N[c]	193	152
Mittelwert (SD)	7,6 (15,2)	6,1 (12,5)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 30		
N[c]	178	135
Mittelwert (SD)	8,3 (16,0)	8,2 (16,8)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	151	115
Mittelwert (SD)	5,8 (9,9)	5,9 (12,8)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 44,4	0,0; 66,7
Woche 42		
N[c]	151	101
Mittelwert (SD)	5,2 (10,9)	5,0 (9,7)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 77,8	0,0; 55,6
Woche 48		
N[c]	150	106
Mittelwert (SD)	5,1 (9,9)	5,7 (14,2)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 0,0)
Min, Max	0,0; 55,6	0,0; 66,7

EORTC QLQ-STO22 Dysphagie	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

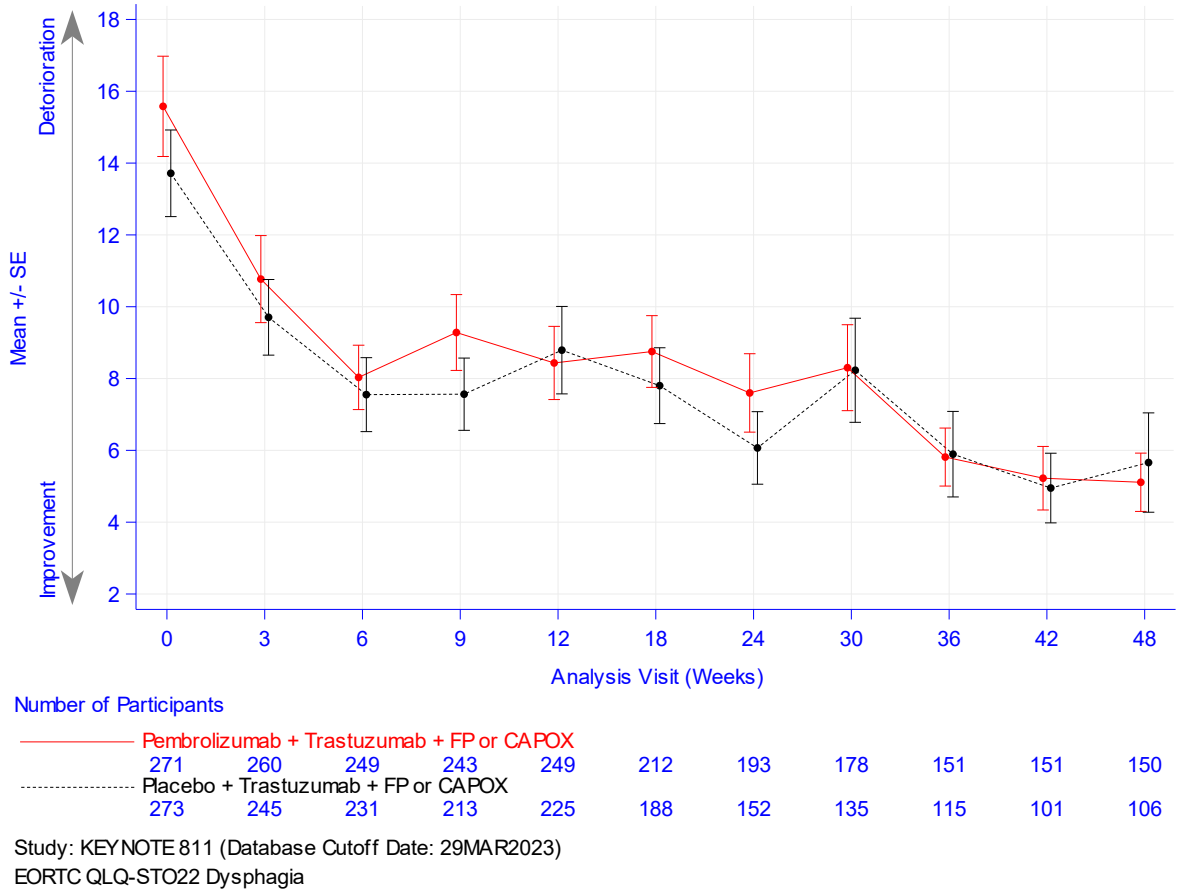

Abbildung 4G-12: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Dysphagie zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Einschränkungen beim Essen

Tabelle 4G-16: Auswertung über den Studienverlauf der Symptomskala Einschränkungen beim Essen des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Einschränkungen beim Essen	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	22,1 (24,4)	20,7 (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; 100,0
Woche 3		
N[c]	260	245
Mittelwert (SD)	17,6 (20,2)	18,4 (21,9)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	15,5 (17,6)	15,7 (20,7)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 9		
N[c]	243	213
Mittelwert (SD)	16,4 (20,1)	14,1 (18,2)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	249	225
Mittelwert (SD)	14,2 (17,3)	14,9 (19,3)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 18		
N[c]	212	188
Mittelwert (SD)	16,6 (21,1)	14,2 (18,0)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 24		
N[c]	193	152
Mittelwert (SD)	12,7 (16,4)	11,7 (16,4)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 75,0
Woche 30		
N[c]	178	135
Mittelwert (SD)	13,2 (19,5)	12,9 (18,3)
Median (Q1; Q3)	8,3 (0,0; 16,7)	8,3 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 100,0

EORTC QLQ-STO22 Einschränkungen beim Essen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	151	115
Mittelwert (SD)	11,6 (17,1)	12,0 (16,9)
Median (Q1; Q3)	8,3 (0,0; 16,7)	8,3 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	10,6 (16,0)	10,1 (16,7)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 16,7)
Min, Max	0,0; 91,7	0,0; 66,7
Woche 48		
N[c]	150	106
Mittelwert (SD)	11,9 (18,6)	9,7 (16,8)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

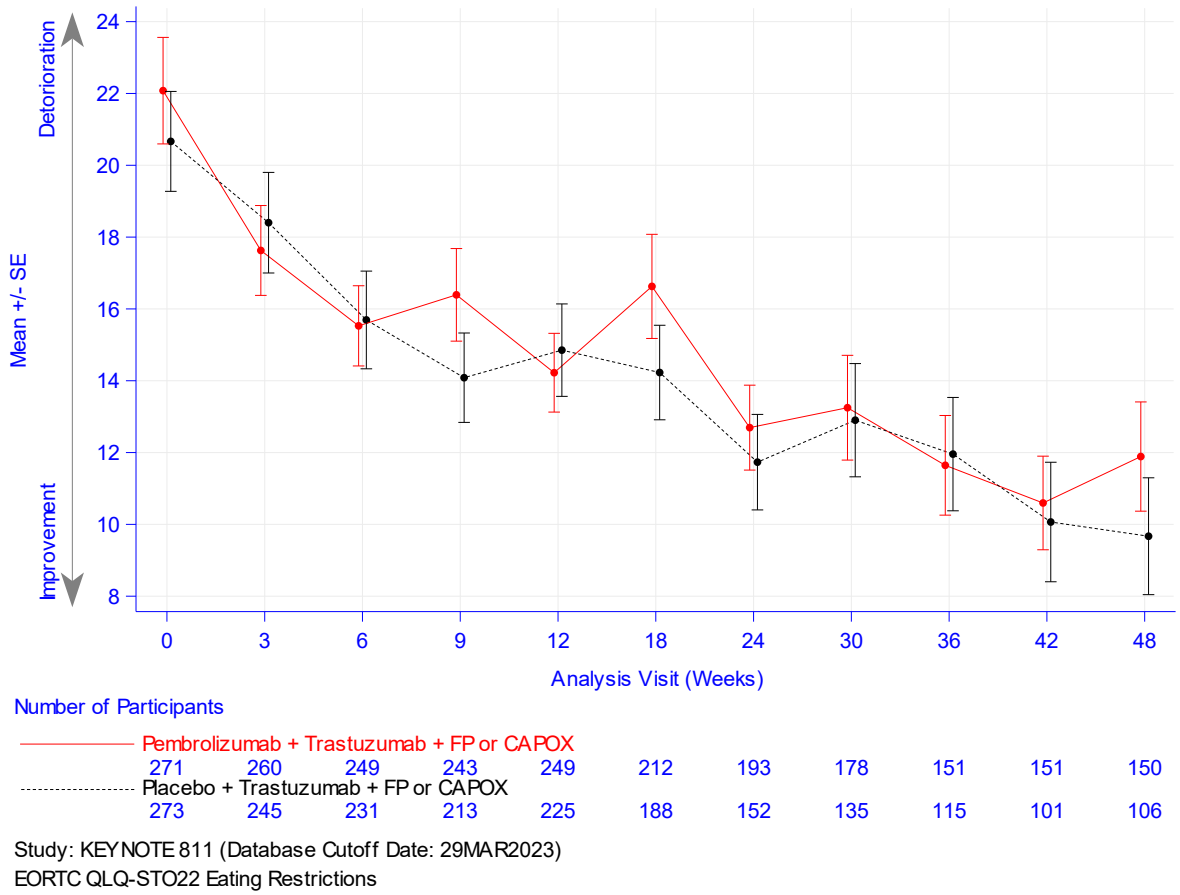

Abbildung 4G-13: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Einschränkungen beim Essen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Haarausfall

Tabelle 4G-17: Auswertung über den Studienverlauf der Symptomskala Haarausfall des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Haarausfall	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	11	21
Mittelwert (SD)	48,5 (43,1)	31,7 (32,4)
Median (Q1; Q3)	33,3 (0,0; 100,0)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	13	22
Mittelwert (SD)	25,6 (24,2)	13,6 (16,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)

EORTC QLQ-STO22 Haarausfall	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	0,0; 66,7	0,0; 33,3
Woche 6		
N[c]	29	37
Mittelwert (SD)	18,4 (22,9)	26,1 (33,5)
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]	34	29
Mittelwert (SD)	20,6 (29,6)	21,8 (32,5)
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 12		
N[c]	40	36
Mittelwert (SD)	20,0 (25,9)	33,3 (32,9)
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 18		
N[c]	33	32
Mittelwert (SD)	24,2 (32,6)	28,1 (32,9)
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 24		
N[c]	27	19
Mittelwert (SD)	27,2 (30,7)	33,3 (35,1)
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 30		
N[c]	20	26
Mittelwert (SD)	31,7 (27,5)	20,5 (26,8)
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 36		
N[c]	13	14
Mittelwert (SD)	17,9 (17,3)	23,8 (27,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 100,0
Woche 42		
N[c]	10	6
Mittelwert (SD)	23,3 (22,5)	22,2 (27,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 48		
N[c]	16	7
Mittelwert (SD)	25,0 (19,2)	33,3 (38,5)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 66,7	0,0; 100,0

EORTC QLQ-STO22 Haarausfall	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

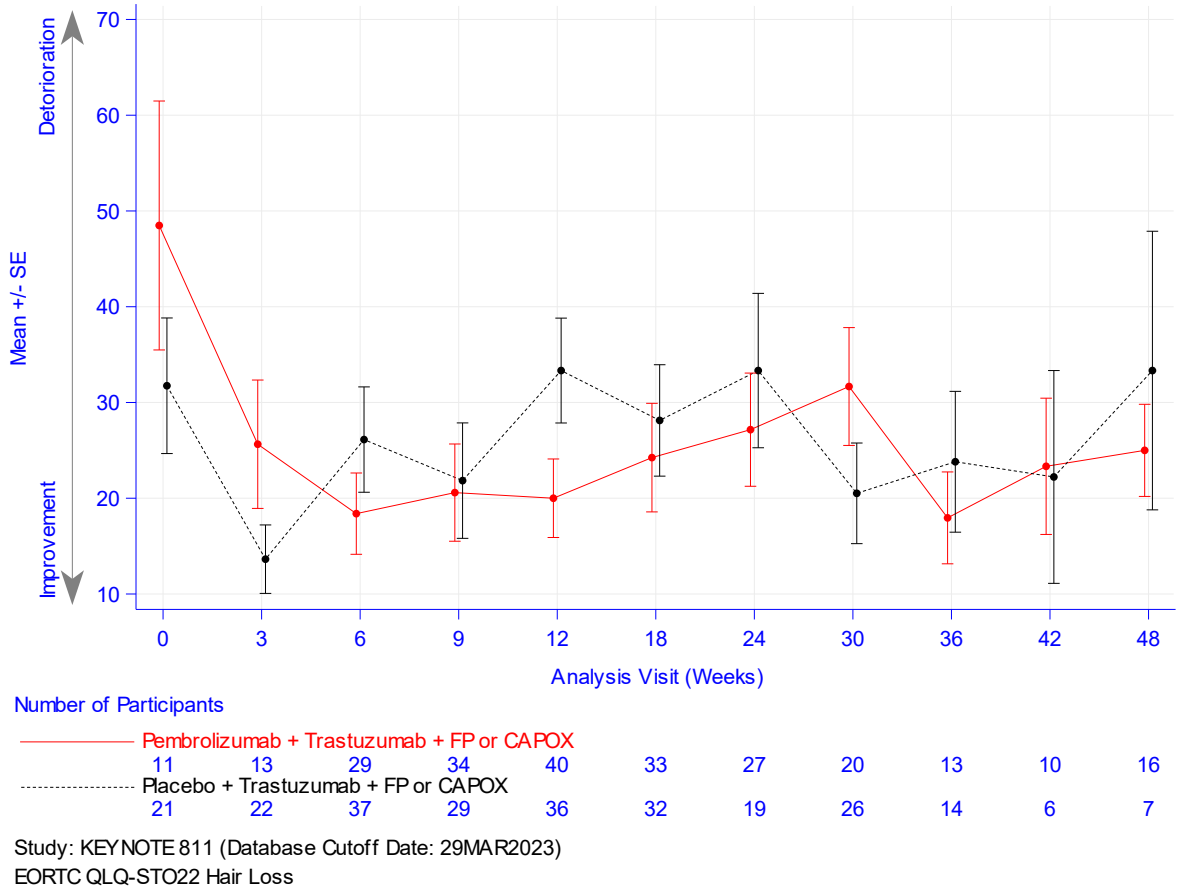

Abbildung 4G-14: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Haarausfall zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Schmerz

Tabelle 4G-18: Auswertung über den Studienverlauf der Symptomskala Schmerz des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Schmerzen	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	24,1 (21,2)	23,6 (21,4)
Median (Q1; Q3)	16,7 (8,3; 33,3)	16,7 (8,3; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	260	245
Mittelwert (SD)	16,8 (18,3)	18,1 (17,9)
Median (Q1; Q3)	8,3 (0,0; 25,0)	16,7 (0,0; 25,0)
Min, Max	0,0; 75,0	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	14,5 (15,6)	16,6 (19,3)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 75,0	0,0; 91,7
Woche 9		
N[c]	243	213
Mittelwert (SD)	16,2 (17,6)	13,8 (16,7)
Median (Q1; Q3)	16,7 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 12		
N[c]	249	225
Mittelwert (SD)	12,6 (15,6)	14,0 (17,8)
Median (Q1; Q3)	8,3 (0,0; 16,7)	8,3 (0,0; 25,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 18		
N[c]	212	188
Mittelwert (SD)	14,3 (16,7)	14,1 (17,3)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 91,7	0,0; 100,0
Woche 24		
N[c]	193	152
Mittelwert (SD)	13,8 (15,3)	12,7 (15,6)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 30		
N[c]	178	135
Mittelwert (SD)	14,1 (17,6)	14,0 (18,3)
Median (Q1; Q3)	8,3 (0,0; 25,0)	8,3 (0,0; 25,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-STO22 Schmerzen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 36		
N[c]	151	115
Mittelwert (SD)	12,4 (14,3)	11,8 (14,8)
Median (Q1; Q3)	8,3 (0,0; 16,7)	8,3 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 58,3
Woche 42		
N[c]	151	101
Mittelwert (SD)	11,5 (15,2)	12,2 (14,8)
Median (Q1; Q3)	8,3 (0,0; 16,7)	8,3 (0,0; 16,7)
Min, Max	0,0; 91,7	0,0; 66,7
Woche 48		
N[c]	150	106
Mittelwert (SD)	11,0 (15,9)	11,6 (16,1)
Median (Q1; Q3)	8,3 (0,0; 16,7)	4,2 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 58,3

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

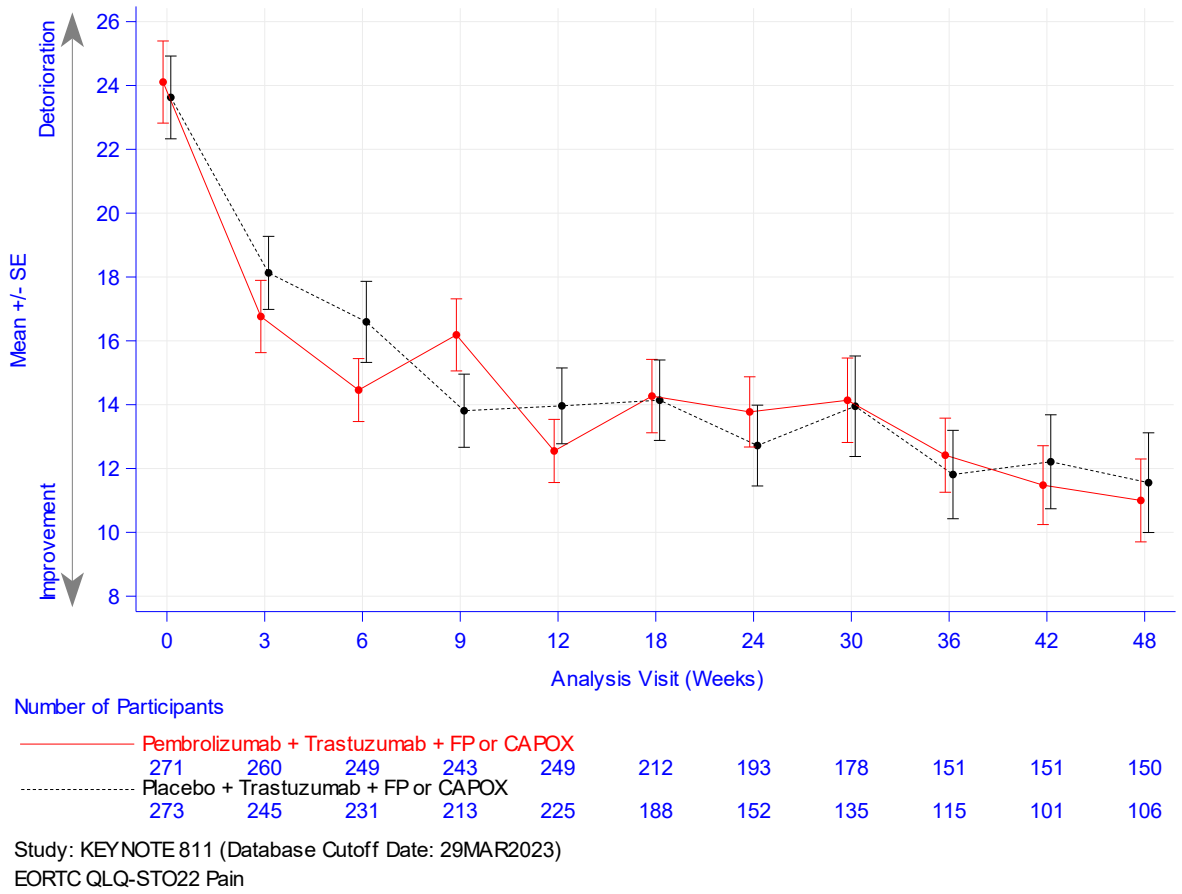

Abbildung 4G-15: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerz zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Reflux

Tabelle 4G-19: Auswertung über den Studienverlauf der Symptomskala Reflux des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Reflux	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	14,6 (18,5)	14,5 (19,7)
Median (Q1; Q3)	11,1 (0,0; 22,2)	11,1 (0,0; 22,2)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	260	245
Mittelwert (SD)	13,9 (18,0)	12,4 (17,6)
Median (Q1; Q3)	11,1 (0,0; 22,2)	11,1 (0,0; 22,2)

EORTC QLQ-STO22 Reflux	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
Min, Max	0,0; 88,9	0,0; 100,0
Woche 6		
N[c]	249	231
Mittelwert (SD)	11,9 (14,9)	12,4 (18,3)
Median (Q1; Q3)	11,1 (0,0; 22,2)	11,1 (0,0; 22,2)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	213
Mittelwert (SD)	12,1 (16,6)	11,4 (17,7)
Median (Q1; Q3)	11,1 (0,0; 22,2)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 12		
N[c]	249	225
Mittelwert (SD)	11,2 (15,4)	12,7 (19,6)
Median (Q1; Q3)	0,0 (0,0; 22,2)	0,0 (0,0; 22,2)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 18		
N[c]	212	188
Mittelwert (SD)	11,8 (16,7)	10,3 (16,4)
Median (Q1; Q3)	0,0 (0,0; 22,2)	0,0 (0,0; 11,1)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 24		
N[c]	193	152
Mittelwert (SD)	9,3 (13,1)	8,3 (12,6)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 77,8	0,0; 44,4
Woche 30		
N[c]	178	135
Mittelwert (SD)	9,9 (15,5)	8,8 (16,6)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	151	115
Mittelwert (SD)	9,6 (13,6)	7,0 (12,4)
Median (Q1; Q3)	0,0 (0,0; 22,2)	0,0 (0,0; 11,1)
Min, Max	0,0; 55,6	0,0; 77,8
Woche 42		
N[c]	151	101
Mittelwert (SD)	8,2 (12,2)	8,3 (13,0)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 55,6	0,0; 66,7
Woche 48		
N[c]	150	106
Mittelwert (SD)	8,7 (13,8)	8,4 (15,7)
Median (Q1; Q3)	0,0 (0,0; 11,1)	0,0 (0,0; 11,1)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-STO22 Reflux	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	Placebo + Trastuzumab + FP oder CAPOX N[b]= 286
a: Datenschnitt: 29. März 2023 b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1) c: Anzahl der Beobachtungen zu jedem Zeitpunkt 5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung		

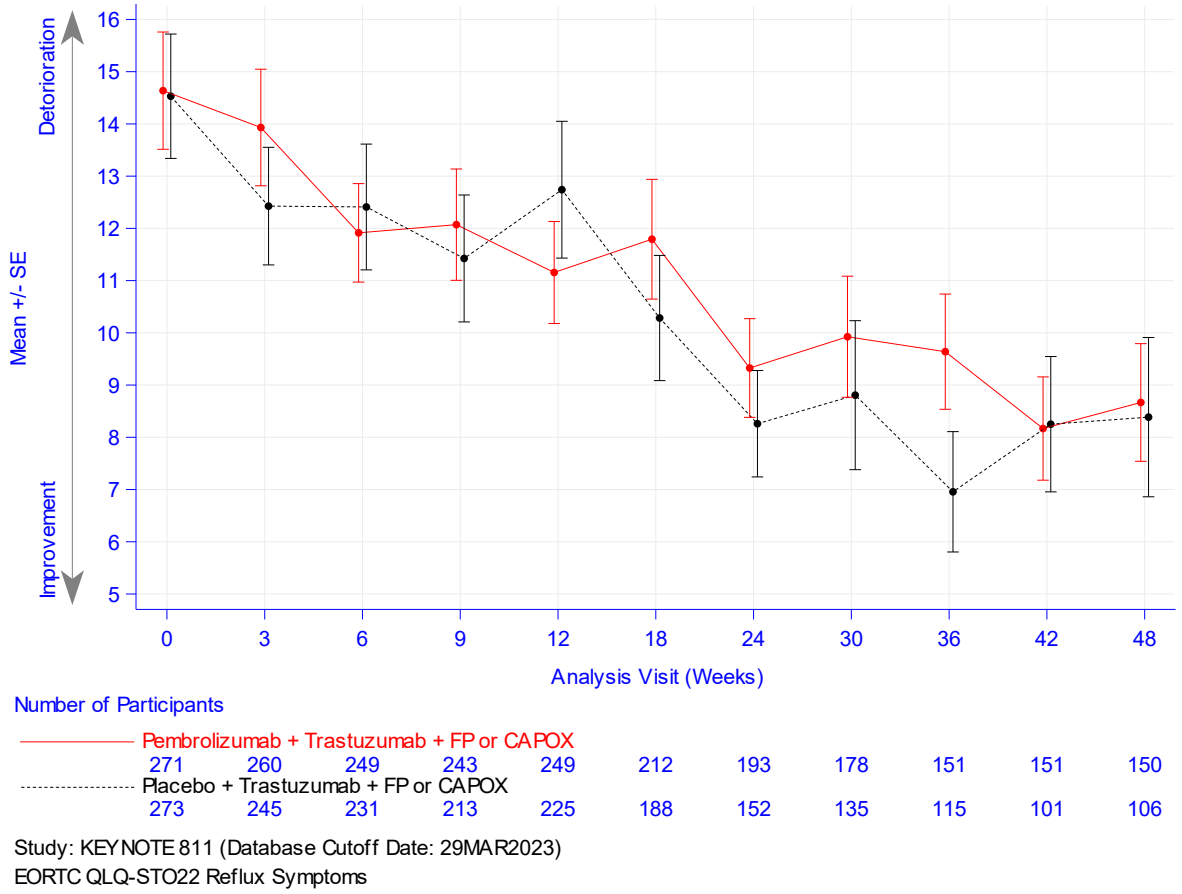

Abbildung 4G-16: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Reflux zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22: Symptomskala Geschmacksstörungen

Tabelle 4G-20: Auswertung über den Studienverlauf der Symptomskala Geschmacksstörungen des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-STO22 Geschmacksstörungen	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	271	273
Mittelwert (SD)	9,6 (21,6)	13,1 (23,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	260	245
Mittelwert (SD)	14,7 (24,3)	17,6 (26,6)
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]	249	231
Mittelwert (SD)	18,1 (25,0)	20,2 (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 9		
N[c]	243	213
Mittelwert (SD)	19,6 (23,7)	18,0 (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 12		
N[c]	249	225
Mittelwert (SD)	22,1 (26,1)	19,4 (27,2)
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 18		
N[c]	212	188
Mittelwert (SD)	22,2 (26,3)	17,7 (25,4)
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 24		
N[c]	193	152
Mittelwert (SD)	14,5 (22,5)	15,1 (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 30		
N[c]	178	135
Mittelwert (SD)	13,1 (20,7)	13,6 (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 36		

EORTC QLQ-STO22 Geschmacksstörungen	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
N[c]	151	115
Mittelwert (SD)	12,6 (19,9)	9,9 (17,6)
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 42		
N[c]	151	101
Mittelwert (SD)	10,8 (19,8)	9,9 (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 48		
N[c]	150	106
Mittelwert (SD)	10,4 (19,0)	8,2 (20,0)
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

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

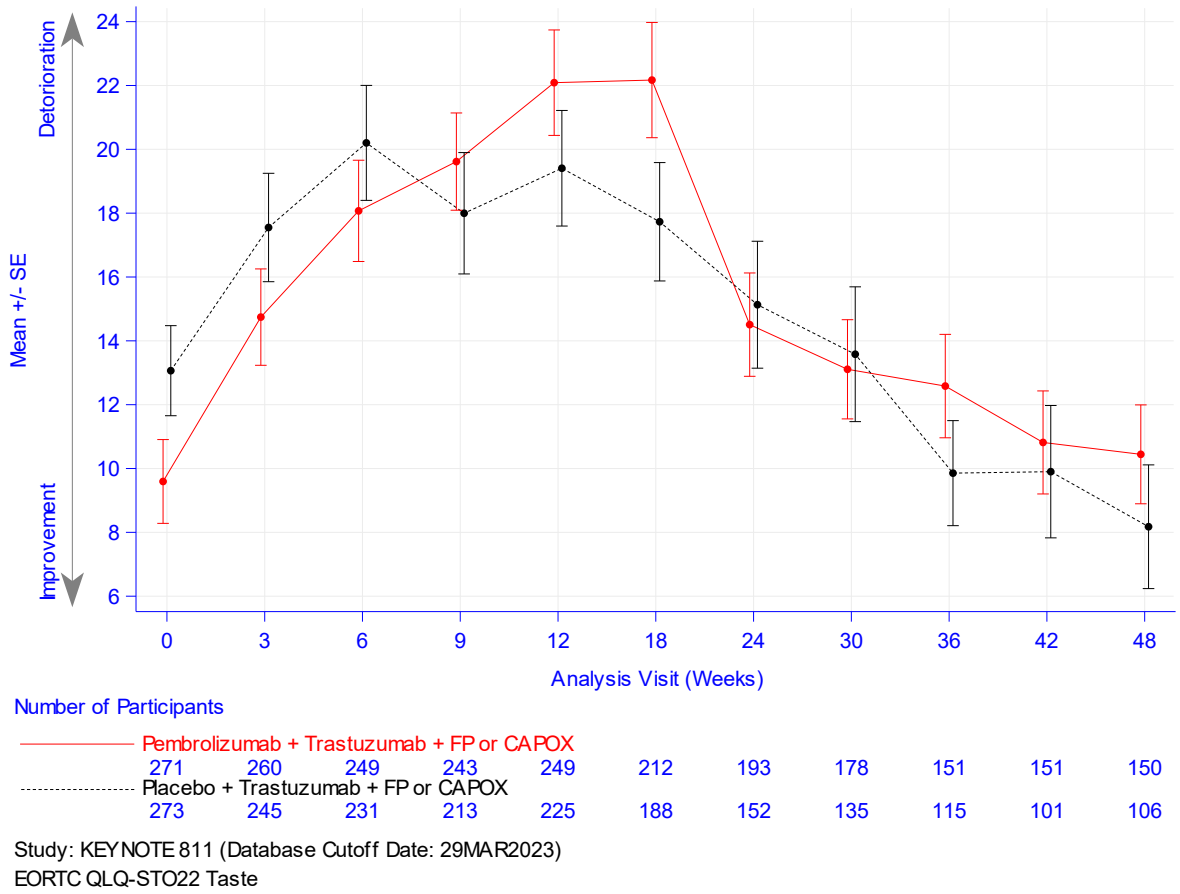

Abbildung 4G-17: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Geschmacksstörungen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-STO22 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EQ-5D VAS

Tabelle 4G-21: Auswertung über den Studienverlauf der EQ-5D VAS aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EQ-5D VAS	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	275	275
Mittelwert (SD)	76,5 (17,2)	75,3 (18,5)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (65,0; 90,0)
Min, Max	19,0; 100,0	0,0; 100,0
Woche 3		
N[c]	261	248
Mittelwert (SD)	77,8 (16,0)	76,7 (15,0)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (69,0; 89,0)
Min, Max	24,0; 100,0	20,0; 100,0

EQ-5D VAS	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 6		
N[c]	249	234
Mittelwert (SD)	78,0 (15,7)	77,1 (15,5)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (70,0; 90,0)
Min, Max	29,0; 100,0	10,0; 100,0
Woche 9		
N[c]	245	216
Mittelwert (SD)	78,1 (15,8)	78,2 (14,7)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (70,0; 90,0)
Min, Max	20,0; 100,0	13,0; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	79,2 (14,8)	78,1 (15,2)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (70,0; 90,0)
Min, Max	25,0; 100,0	20,0; 100,0
Woche 18		
N[c]	212	190
Mittelwert (SD)	77,6 (16,5)	77,4 (15,7)
Median (Q1; Q3)	80,0 (70,0; 90,0)	80,0 (70,0; 90,0)
Min, Max	11,0; 100,0	5,0; 100,0
Woche 24		
N[c]	196	152
Mittelwert (SD)	78,9 (15,0)	79,6 (14,8)
Median (Q1; Q3)	80,5 (70,0; 90,0)	81,0 (70,0; 90,0)
Min, Max	20,0; 100,0	29,0; 100,0
Woche 30		
N[c]	178	136
Mittelwert (SD)	77,1 (17,7)	78,4 (16,6)
Median (Q1; Q3)	80,0 (70,0; 90,0)	81,0 (70,0; 90,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	153	115
Mittelwert (SD)	79,8 (15,8)	80,0 (13,5)
Median (Q1; Q3)	83,0 (70,0; 91,0)	80,0 (70,0; 90,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 42		
N[c]	151	102
Mittelwert (SD)	78,5 (16,3)	79,8 (16,0)
Median (Q1; Q3)	80,0 (70,0; 90,0)	84,0 (73,0; 90,0)
Min, Max	0,0; 100,0	11,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	78,1 (16,5)	79,7 (15,8)
Median (Q1; Q3)	80,0 (70,0; 90,0)	81,0 (74,0; 90,0)
Min, Max	28,0; 100,0	10,0; 100,0

EQ-5D VAS	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286

a: Datenschnitt: 29. März 2023
b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)
c: Anzahl der Beobachtungen zu jedem Zeitpunkt
5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EQ-5D VAS: EuroQoL-5 Dimensions Visual Analogue Scale; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

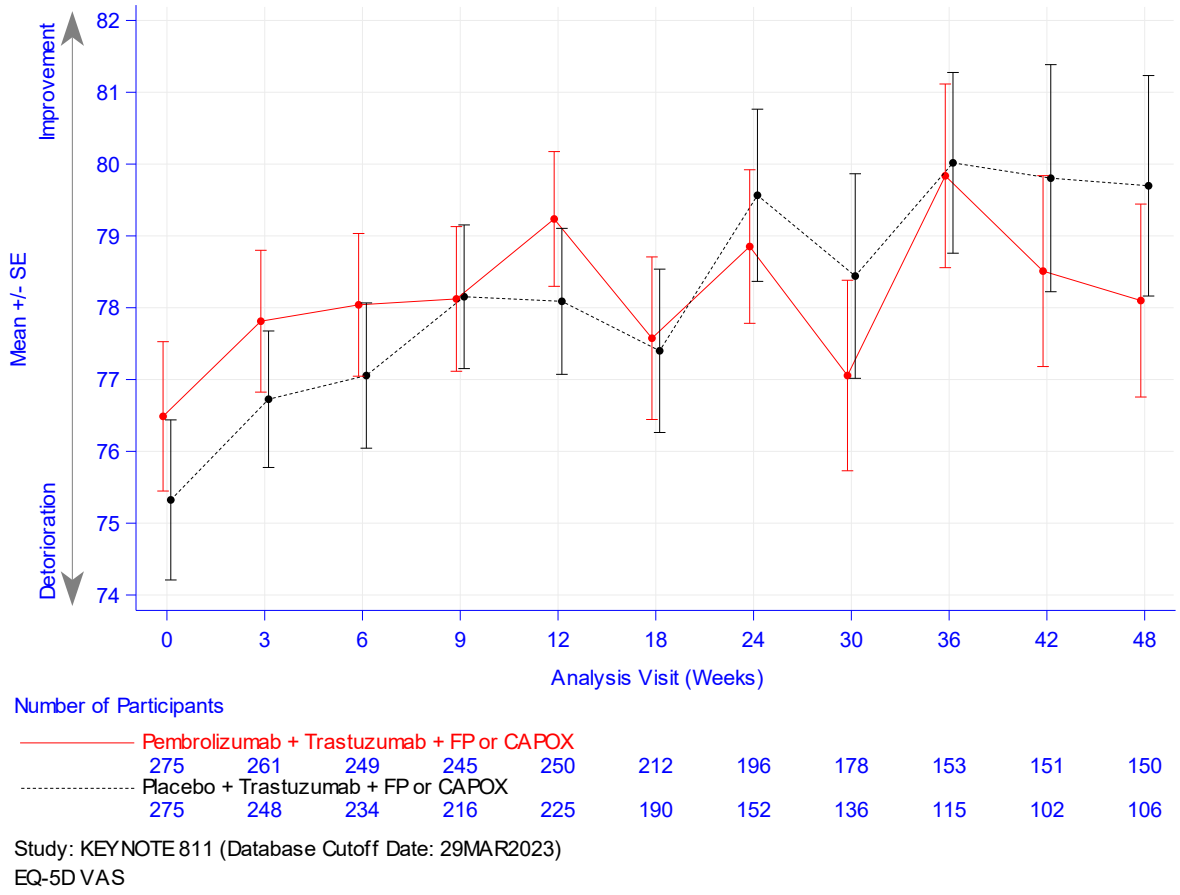

Abbildung 4G-18: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler des EQ-5D VAS zu den verschiedenen Erhebungszeitpunkten aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Anhang 4-G3: Auswertungen über den Studienverlauf für den Endpunkt Gesundheitsbezogene Lebensqualität anhand von EORTC QLQ-C30 (KEYNOTE 811)

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

Alle Ergebnisse beziehen sich auf den dritten Datenschnitt (29. März 2023).

Anhang 4-G3.1: Auswertungen über den Studienverlauf des EORTC QLQ-C30

EORTC QLQ-C30: Globaler Gesundheitsstatus

Tabelle 4G-22: Auswertung über den Studienverlauf des Globaler Gesundheitsstatus des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Globaler Gesundheitsstatus	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	69,6 (19,7)	66,9 (19,6)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 83,3)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	70,8 (18,5)	69,6 (18,9)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (58,3; 83,3)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	69,8 (19,0)	69,2 (19,1)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (58,3; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	70,5 (18,5)	70,9 (18,7)
Median (Q1; Q3)	66,7 (66,7; 83,3)	75,0 (54,2; 83,3)
Min, Max	16,7; 100,0	16,7; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	72,2 (17,5)	69,3 (19,1)
Median (Q1; Q3)	75,0 (66,7; 83,3)	66,7 (58,3; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	69,1 (19,6)	69,0 (18,0)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (58,3; 83,3)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 24		
N[c]	195	151

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Mittelwert (SD)	70,6 (17,6)	72,1 (17,0)
Median (Q1; Q3)	66,7 (66,7; 83,3)	75,0 (66,7; 83,3)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 30		
N[c]	178	134
Mittelwert (SD)	70,1 (18,9)	72,1 (17,3)
Median (Q1; Q3)	70,8 (66,7; 83,3)	75,0 (66,7; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	73,8 (18,3)	71,7 (17,3)
Median (Q1; Q3)	83,3 (66,7; 83,3)	75,0 (66,7; 83,3)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	73,7 (15,6)	71,0 (19,7)
Median (Q1; Q3)	75,0 (66,7; 83,3)	75,0 (58,3; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	73,7 (17,8)	72,3 (17,8)
Median (Q1; Q3)	79,2 (66,7; 83,3)	75,0 (66,7; 83,3)
Min, Max	0,0; 100,0	16,7; 100,0

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; QoL: Quality of Life; SD: Standardabweichung

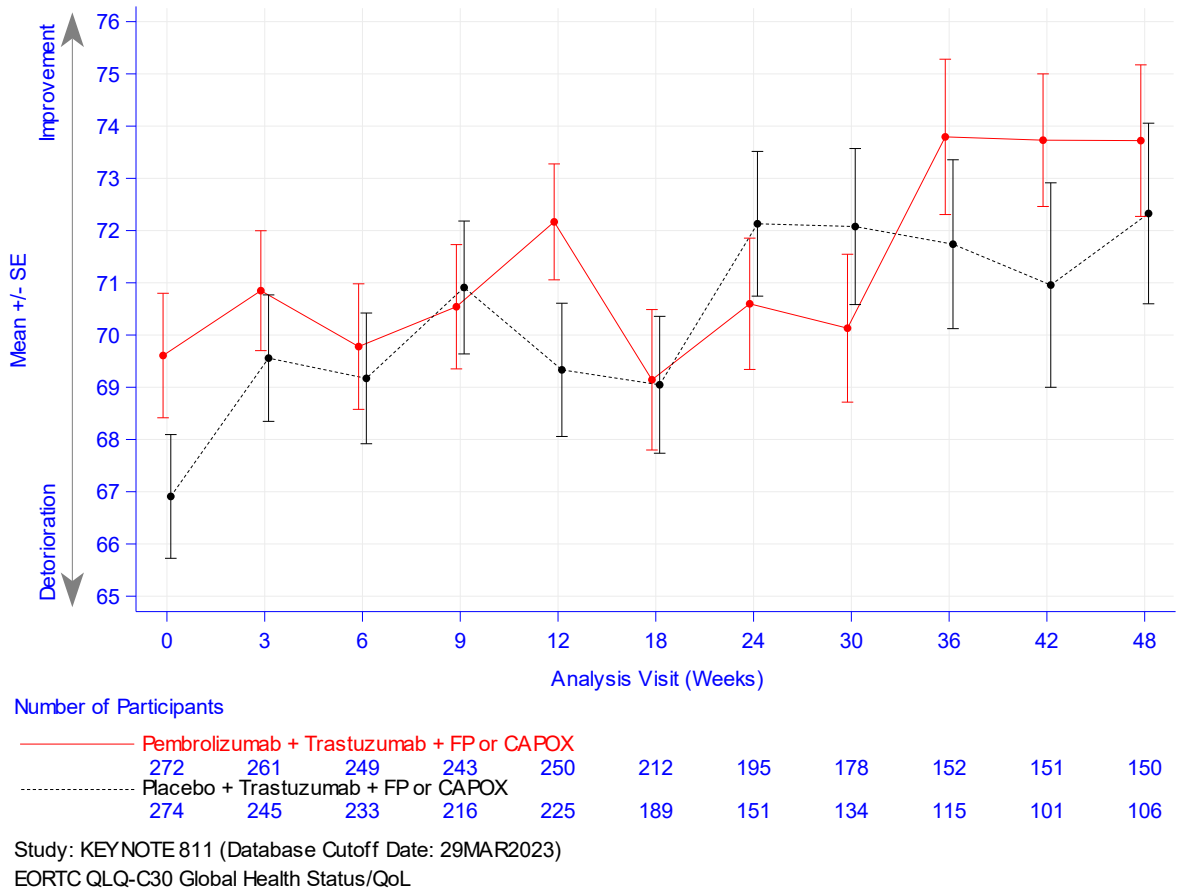

Abbildung 4G-19: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler des Globalen Gesundheitsstatus zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC-QLQ-C30: Funktionsskala Körperliche Funktion

Tabelle 4G-23: Auswertung über den Studienverlauf der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Körperliche Funktion	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	86,0 (17,6)	84,2 (18,1)
Median (Q1; Q3)	93,3 (80,0; 100,0)	86,7 (73,3; 100,0)
Min, Max	13,3; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	85,1 (17,0)	84,3 (16,0)
Median (Q1; Q3)	86,7 (80,0; 100,0)	86,7 (80,0; 100,0)

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	20,0; 100,0	6,7; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	84,7 (17,0)	83,3 (17,2)
Median (Q1; Q3)	86,7 (80,0; 100,0)	86,7 (80,0; 100,0)
Min, Max	13,3; 100,0	20,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	82,9 (19,0)	83,3 (18,7)
Median (Q1; Q3)	86,7 (73,3; 100,0)	86,7 (80,0; 100,0)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	84,5 (18,1)	83,3 (18,5)
Median (Q1; Q3)	86,7 (80,0; 100,0)	86,7 (80,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	82,8 (18,6)	83,6 (17,0)
Median (Q1; Q3)	86,7 (73,3; 100,0)	86,7 (80,0; 100,0)
Min, Max	13,3; 100,0	20,0; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	85,4 (14,8)	85,3 (16,8)
Median (Q1; Q3)	86,7 (80,0; 100,0)	86,7 (73,3; 100,0)
Min, Max	13,3; 100,0	20,0; 100,0
Woche 30		
N[c]	178	134
Mittelwert (SD)	84,8 (16,5)	85,2 (19,5)
Median (Q1; Q3)	86,7 (80,0; 100,0)	93,3 (80,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	86,7 (15,1)	86,2 (15,5)
Median (Q1; Q3)	93,3 (80,0; 100,0)	86,7 (80,0; 100,0)
Min, Max	33,3; 100,0	26,7; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	86,8 (15,0)	86,2 (17,8)
Median (Q1; Q3)	93,3 (80,0; 100,0)	93,3 (80,0; 100,0)
Min, Max	20,0; 100,0	26,7; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	85,0 (17,9)	86,3 (19,4)
Median (Q1; Q3)	90,0 (80,0; 100,0)	93,3 (80,0; 100,0)
Min, Max	6,7; 100,0	0,0; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

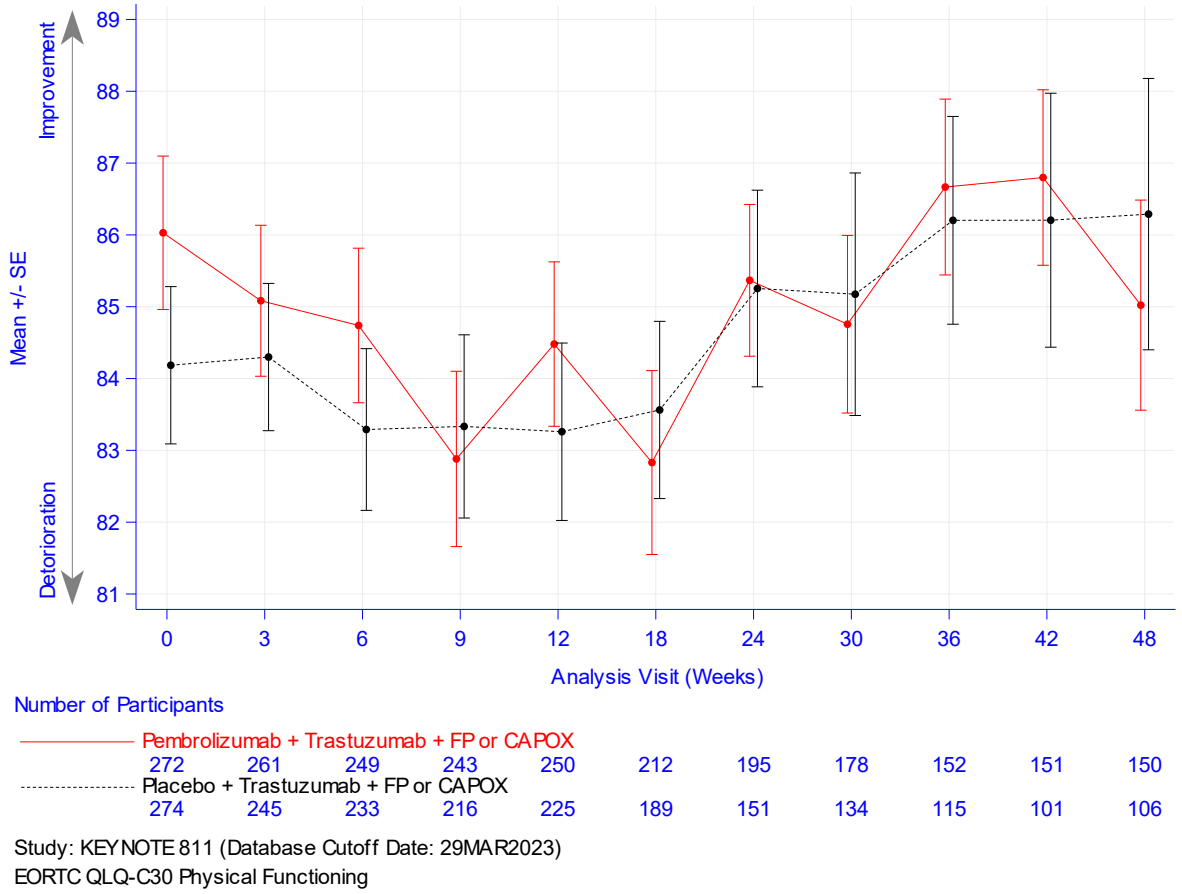

Abbildung 4G-20: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Körperliche Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Tabelle 4G-24: Auswertung über den Studienverlauf der Funktionsskala Rollenfunktion des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	83,3 (24,7)	80,2 (26,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	81,6 (23,4)	81,8 (23,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	81,1 (24,0)	81,3 (24,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	80,3 (25,4)	83,1 (25,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	83,2 (23,1)	81,9 (24,6)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	81,1 (25,0)	82,3 (23,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	81,3 (21,7)	84,2 (21,7)
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 30		
N[c]	178	134
Mittelwert (SD)	82,1 (23,5)	84,1 (23,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	82,6 (22,2)	85,7 (20,5)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)

EORTC QLQ-C30 Rollenfunktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	16,7; 100,0	0,0; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	83,8 (20,5)	85,0 (21,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	83,4 (23,5)	85,7 (23,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

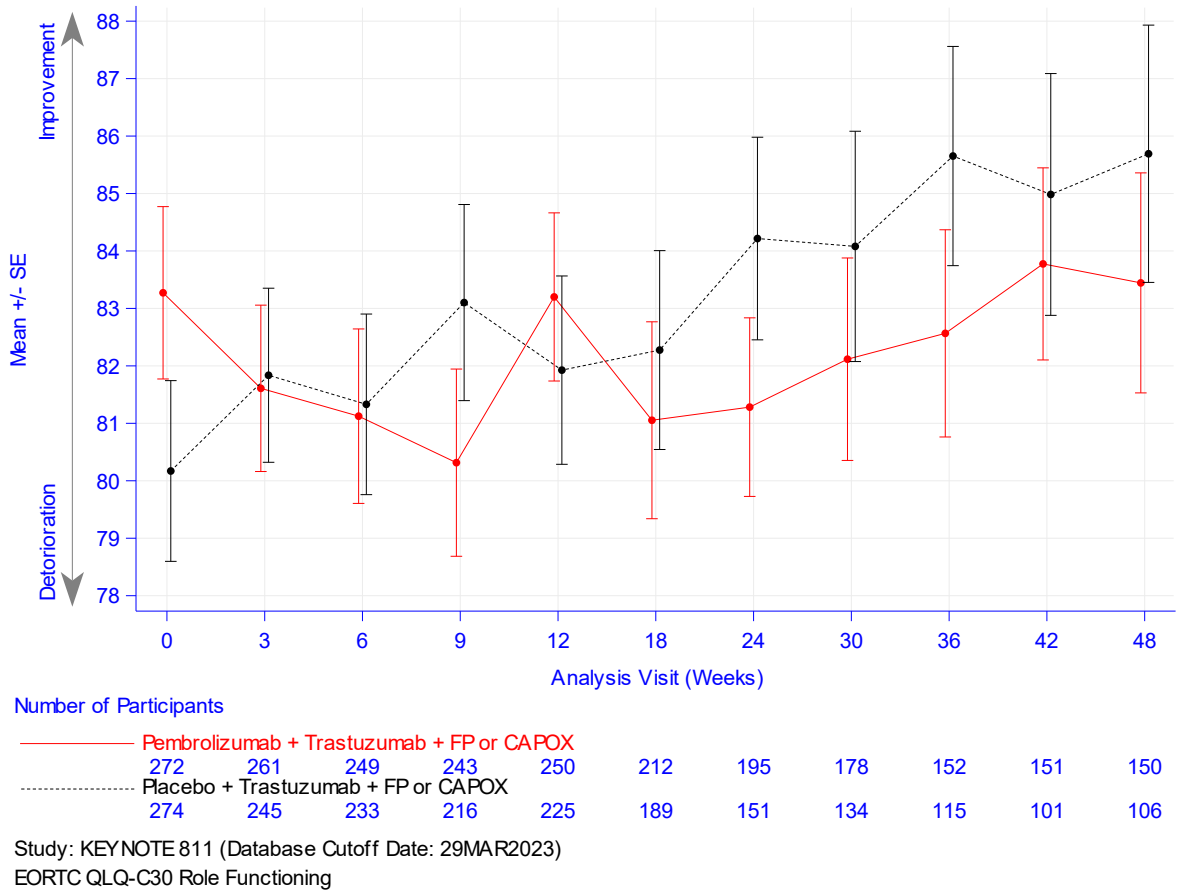

Abbildung 4G-21: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Rollenfunktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Tabelle 4G-25: Auswertung über den Studienverlauf der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Emotionale Funktion	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	81,0 (20,5)	80,7 (21,4)
Median (Q1; Q3)	83,3 (75,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	84,5 (18,4)	83,4 (18,2)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 6		
N[c]	249	233
Mittelwert (SD)	85,2 (16,9)	83,8 (19,6)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	84,2 (16,6)	84,1 (19,7)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	85,3 (18,1)	83,1 (19,5)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	83,5 (19,4)	82,6 (19,3)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	8,3; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	84,6 (19,5)	83,6 (20,5)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 30		
N[c]	178	134
Mittelwert (SD)	83,8 (22,0)	84,3 (19,7)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	85,1 (19,1)	85,4 (18,8)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	86,8 (16,8)	83,9 (21,0)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	85,0 (18,4)	85,5 (19,5)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

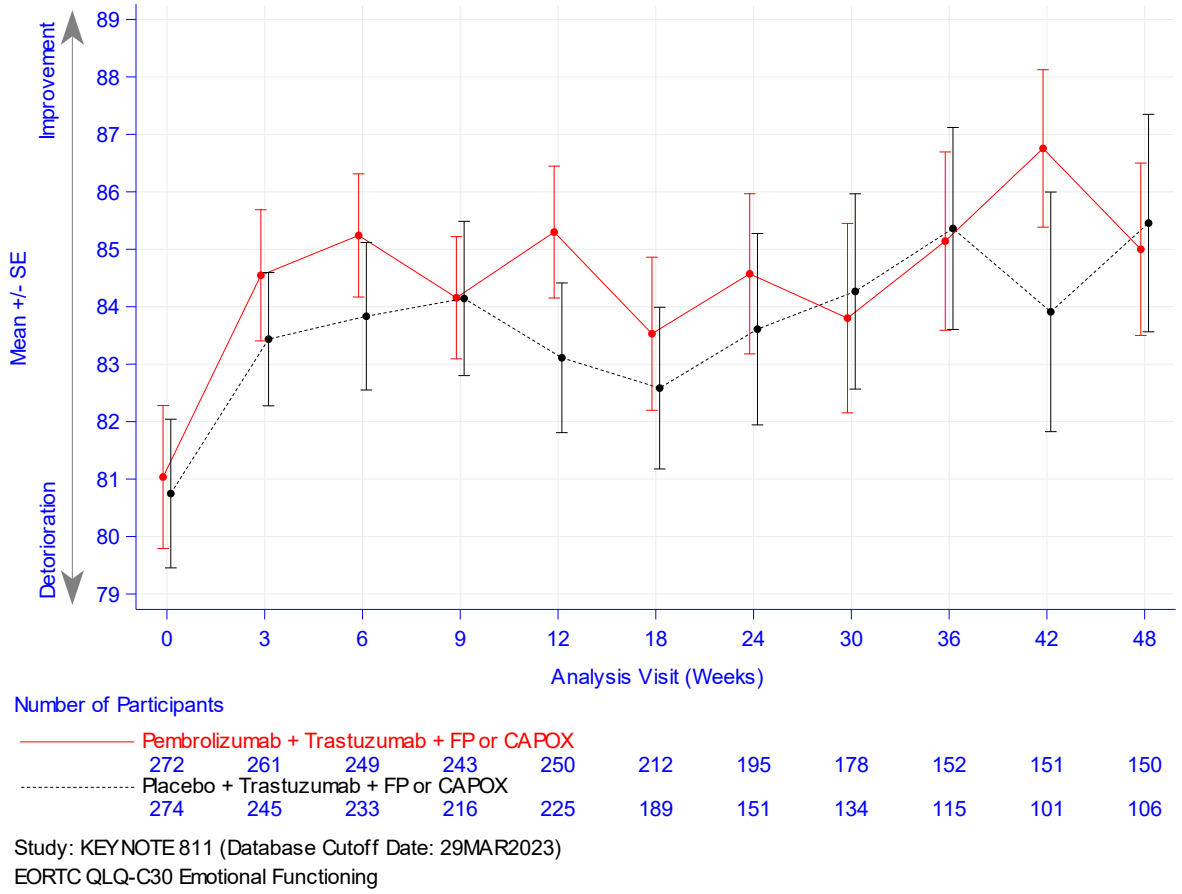

Abbildung 4G-22: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Emotionale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Tabelle 4G-26: Auswertung über den Studienverlauf der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Kognitive Funktion	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	90,3 (16,2)	90,5 (16,3)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N[c]	261	245
Mittelwert (SD)	90,2 (16,6)	91,3 (15,6)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 6		
N[c]	249	233
Mittelwert (SD)	90,5 (14,6)	90,5 (15,8)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	89,2 (17,2)	89,7 (17,9)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 12		
N[c]	250	225
Mittelwert (SD)	88,8 (17,5)	88,1 (17,1)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	87,8 (18,3)	89,5 (15,0)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 24		
N[c]	195	151
Mittelwert (SD)	89,2 (17,3)	89,6 (16,5)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 30		
N[c]	178	134
Mittelwert (SD)	89,6 (17,6)	88,2 (18,9)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	88,5 (16,9)	90,6 (14,7)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)

EORTC QLQ-C30 Kognitive Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Min, Max	16,7; 100,0	33,3; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	90,0 (15,2)	91,3 (16,4)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	90,0 (15,1)	89,5 (17,4)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	16,7; 100,0

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

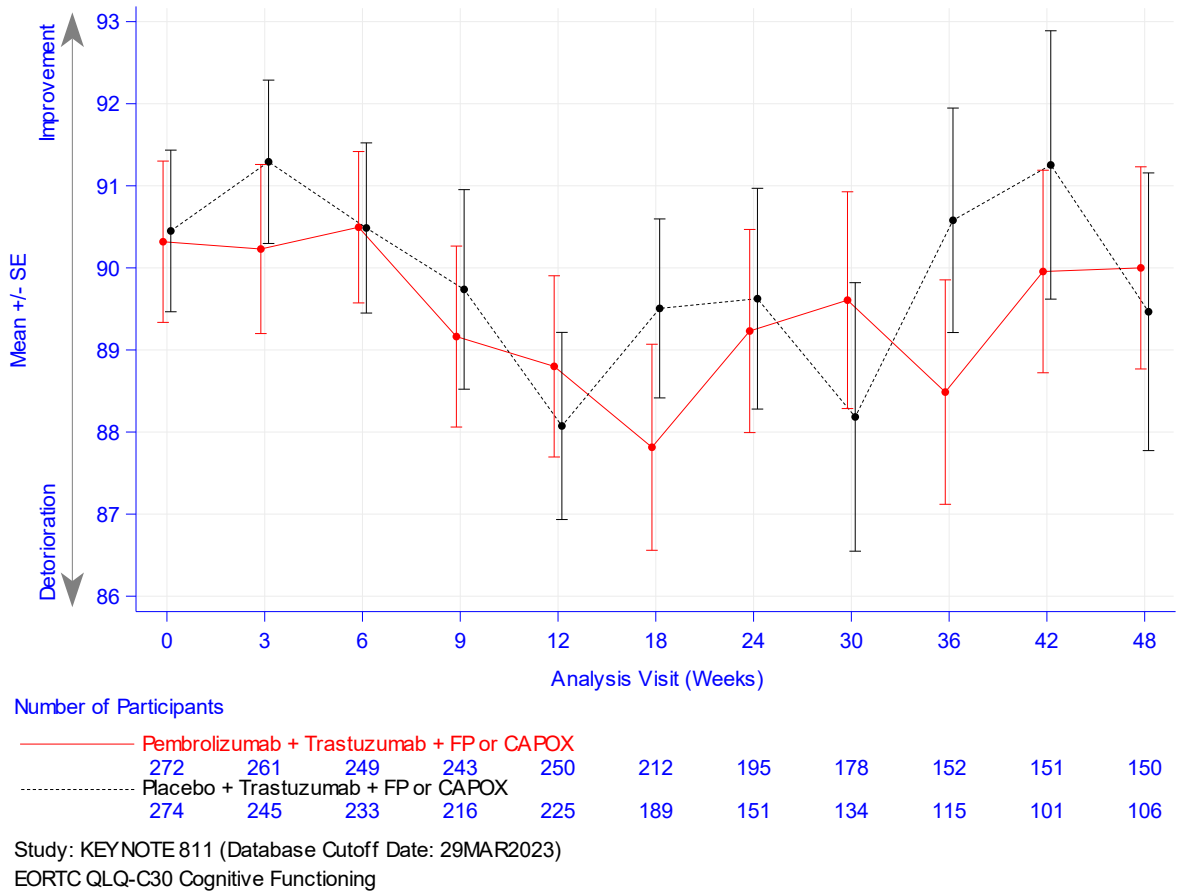

Abbildung 4G-23: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Kognitive Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Tabelle 4G-27: Auswertung über den Studienverlauf der Funktionsskala Soziale Funktion des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Soziale Funktion	**Studie: KEYNOTE 811[a]**	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Baseline		
N[c]	272	274
Mittelwert (SD)	83,0 (23,0)	81,7 (23,4)
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 3		
N[c]	261	245
Mittelwert (SD)	81,1 (23,3)	83,0 (21,9)
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 QLQ-C30 Soziale Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286
Woche 6		
N[c]	249	233
Mittelwert (SD)	82,0 (23,9)	82,5 (22,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N[c]	243	216
Mittelwert (SD)	81,2 (23,1)	83,7 (22,4)
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 12		
N[c]	250	225
Mittelwert (SD)	83,6 (21,2)	83,0 (24,1)
Median (Q1; Q3)	91,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 18		
N[c]	212	189
Mittelwert (SD)	82,1 (22,2)	82,9 (21,3)
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 24		
N[c]	195	151
Mittelwert (SD)	83,5 (20,5)	85,4 (21,5)
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 30		
N[c]	178	134
Mittelwert (SD)	84,1 (22,5)	84,3 (24,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 36		
N[c]	152	115
Mittelwert (SD)	83,0 (21,7)	86,7 (20,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 42		
N[c]	151	101
Mittelwert (SD)	87,0 (16,9)	88,3 (20,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 48		
N[c]	150	106
Mittelwert (SD)	86,0 (18,4)	86,9 (21,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: KEYNOTE 811[a]	
	Pembrolizumab + Trastuzumab + FP oder CAPOX N[b]= 291	**Placebo + Trastuzumab + FP oder CAPOX** N[b]= 286

a: Datenschnitt: 29. März 2023

b: Anzahl der Patient:innen: Full-Analysis-Set Population (CPS>=1)

c: Anzahl der Beobachtungen zu jedem Zeitpunkt

5-FU: 5-Fluorouracil; CAPOX: Capecitabin + Oxaliplatin; CPS: Combined Positive Score; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; FP: 5-FU + Cisplatin; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung

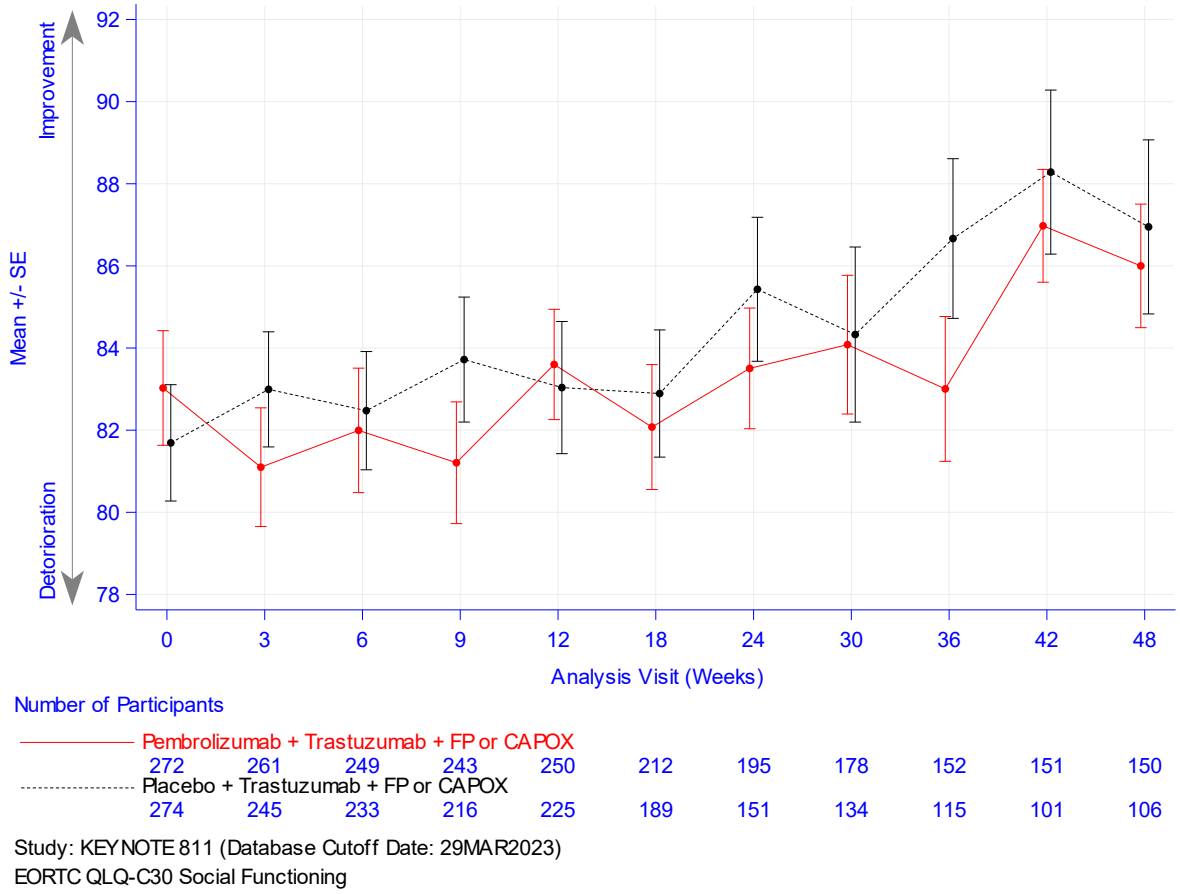

Abbildung 4G-24: Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Soziale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie KEYNOTE 811 mit dem zu bewertenden Arzneimittel

Anhang 4-G4: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest (p < 0,05) (KEYNOTE 811)

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.

Alle Ergebnisse beziehen sich auf den dritten Datenschnitt (29. März 2023).

Krankheitssymptomatik und Gesundheitszustand

EORTC QLQ-STO22: Symptomskala Reflux

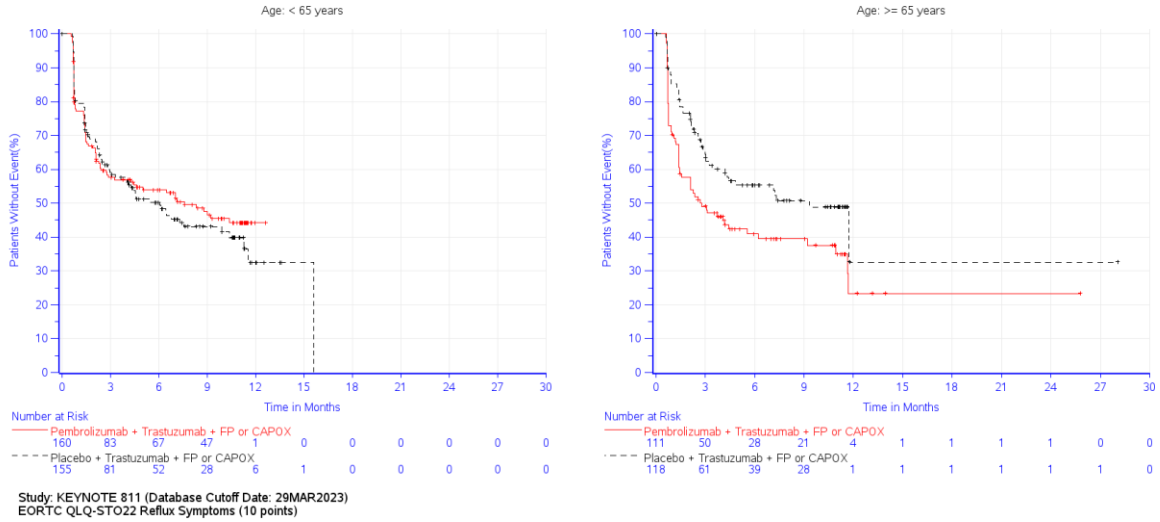

Abbildung 4G-25: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter (Jahre) (< 65 vs.≥ 65) für die Symptomskala Reflux des EORTC QLQ-STO22 der Studie KEYNOTE 811

Gesundheitsbezogene Lebensqualität

Gesundheitsbezogene Lebensqualität

EORTC QLQ-C30: Funktionsskala Kognitive Funktion

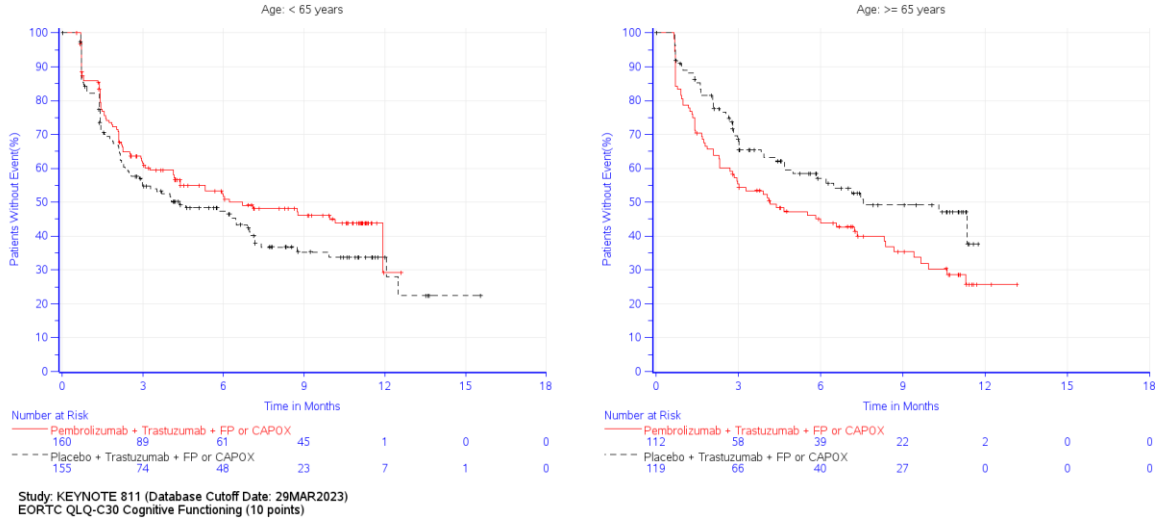

Abbildung 4G-26: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter (Jahre) (< 65 vs.≥ 65) für die Funktionsskala Kognitive Funktion des EORTC QLQ-C30 der Studie KEYNOTE 811

Nebenwirkungen

Unerwünschte Ereignisse Gesamtraten

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

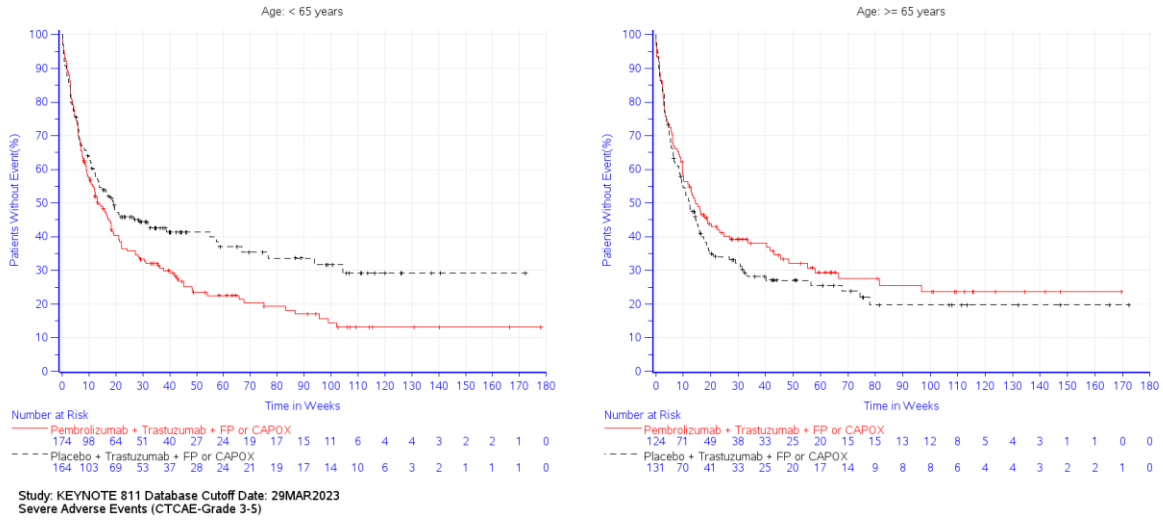

Abbildung 4G-27: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter (Jahre) (< 65 vs.≥ 65) für den Endpunkt schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) der Studie KEYNOTE 811

Therapieabbruch wegen Unerwünschter Ereignisse

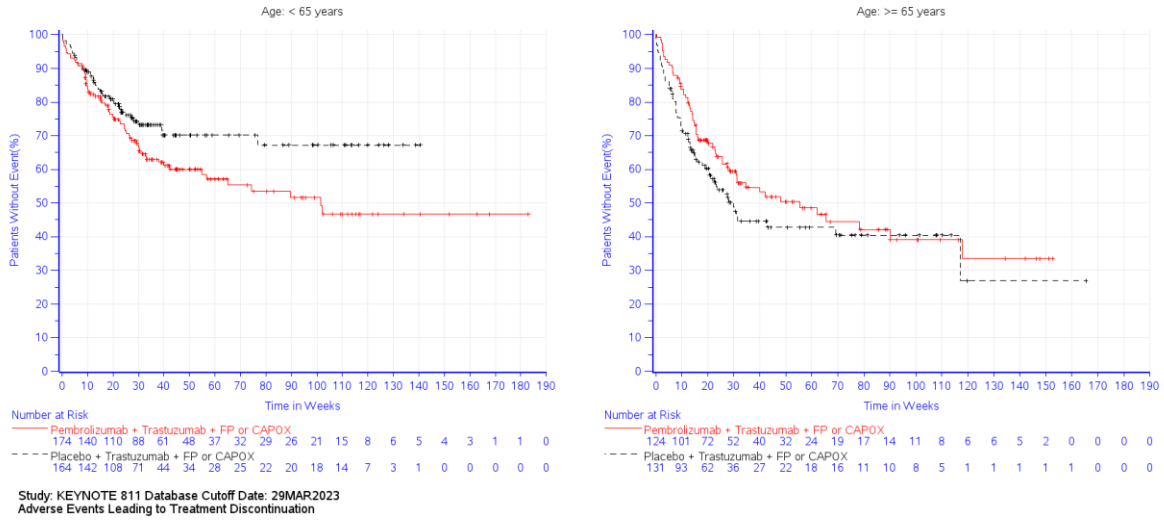

Abbildung 4G-28: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter (Jahre) (< 65 vs.≥ 65) für den Endpunkt Therapieabbruch wegen Unerwünschter Ereignisse der Studie KEYNOTE 811

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

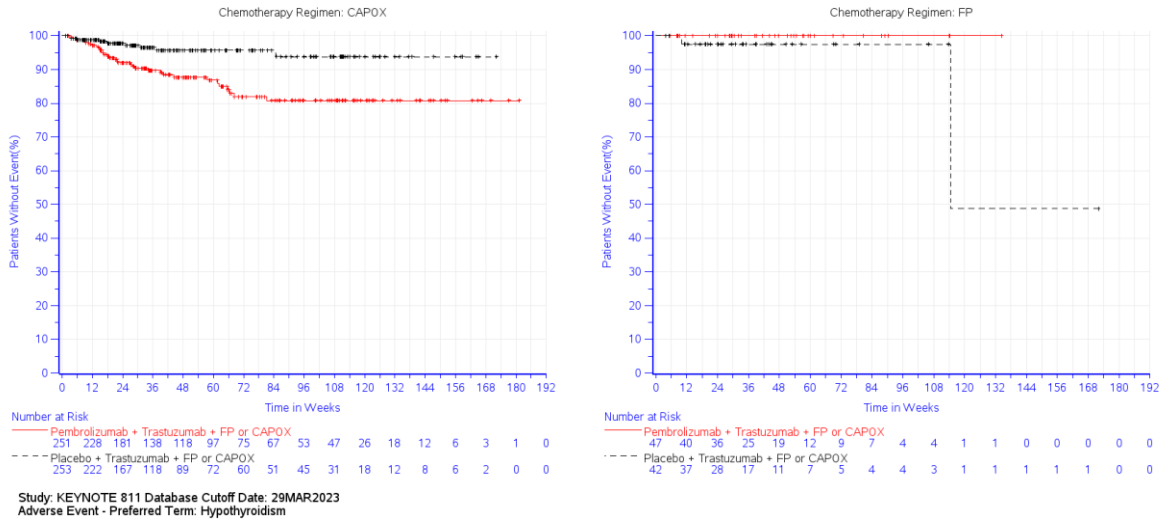

Abbildung 4G-29: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Chemotherapie (FP vs. CAPOX) für den Endpunkt Unerwünschte Ereignisse (gegliedert nach SOC und PT) für den PT Hypothyreose (SOC Endokrine Erkrankungen) der Studie KEYNOTE 811

Anhang 4-G5: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest (p ≥ 0,05) (KEYNOTE 811)

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

Alle Ergebnisse beziehen sich auf den dritten Datenschnitt (29. März 2023).

Mortalität

Gesamtüberleben

Tabelle 4G-28: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		p-Value for Interaction Test[f]
Overall Survival	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	240	166 (69.2)	19.9 [17.8; 22.2]	237	167 (70.5)	15.7 [13.5; 19.0]	0.88 [0.71; 1.09]	0.257	0.073
Female	58	38 (65.5)	24.5 [15.0; 37.6]	59	51 (86.4)	15.0 [10.4; 19.6]	0.52 [0.34; 0.81]	0.003	
Age									
< 65 years	174	115 (66.1)	20.3 [18.3; 25.7]	165	126 (76.4)	14.6 [11.8; 18.0]	0.69 [0.53; 0.88]	0.004	0.070
≥ 65 years	124	89 (71.8)	18.0 [14.4; 22.2]	131	92 (70.2)	17.2 [14.2; 20.4]	0.99 [0.74; 1.33]	0.971	
ECOG Performance Status									
0	127	85 (66.9)	21.7 [18.7; 25.5]	122	87 (71.3)	16.8 [13.1; 21.6]	0.78 [0.58; 1.06]	0.110	0.759
1	171	119 (69.6)	18.2 [15.5; 22.1]	174	131 (75.3)	15.1 [12.7; 18.1]	0.83 [0.64; 1.06]	0.135	
Geographic Region									
Asia	96	55 (57.3)	23.4 [19.5; 36.8]	96	53 (55.2)	31.1 [20.4; 42.3]	1.06 [0.73; 1.55]	0.746	0.064
Rest of World	105	73 (69.5)	19.9 [15.2; 24.3]	104	88 (84.6)	13.4 [10.4; 15.6]	0.59 [0.43; 0.81]	< 0.001	
Western Europe/Israel/North America/Australia	97	76 (78.4)	16.7 [14.1; 21.2]	96	77 (80.2)	12.1 [10.3; 15.7]	0.82 [0.60; 1.13]	0.229	
Chemotherapy Regimen									
CAPOX	251	164 (65.3)	21.2 [18.2; 24.3]	253	180 (71.1)	16.9 [14.5; 19.9]	0.80 [0.65; 0.99]	0.044	0.890
FP	47	40 (85.1)	16.4 [10.2; 20.1]	43	38 (88.4)	11.2 [8.2; 15.3]	0.77 [0.50; 1.21]	0.260	

MSI Status									
MSI High	6	4 (66.7)	n.c.	2	1 (50.0)	n.c.	n.c.	n.c.	n.c.
Non-MSI-High	282	192 (68.1)	n.c.	280	207 (73.9)	n.c.	n.c.	n.c.	
Primary location									
GEJ	97	71 (73.2)	18.3 [15.3; 22.1]	99	68 (68.7)	14.3 [10.5; 19.9]	0.97 [0.70; 1.36]	0.868	0.185
Stomach	201	133 (66.2)	21.5 [18.2; 24.4]	197	150 (76.1)	16.2 [14.2; 19.0]	0.73 [0.58; 0.93]	0.009	
Histological subtype									
Diffuse	54	40 (74.1)	17.6 [12.4; 27.9]	44	37 (84.1)	9.8 [7.2; 12.5]	0.55 [0.35; 0.86]	0.010	0.183
Intestinal	170	109 (64.1)	22.2 [18.8; 26.6]	159	110 (69.2)	19.6 [15.6; 22.2]	0.86 [0.66; 1.12]	0.273	
Indeterminate	73	54 (74.0)	17.9 [15.0; 22.7]	93	71 (76.3)	14.6 [11.8; 18.1]	0.86 [0.60; 1.22]	0.398	
Tumor Burden									
< Median	140	93 (66.4)	21.2 [17.9; 26.6]	139	97 (69.8)	18.6 [14.3; 24.2]	0.90 [0.68; 1.20]	0.467	0.300
≥ Median	146	102 (69.9)	20.1 [15.2; 22.7]	146	112 (76.7)	14.4 [11.7; 16.2]	0.73 [0.55; 0.95]	0.021	
Number of Metastases									
≤ 2	146	99 (67.8)	19.9 [16.7; 24.2]	171	124 (72.5)	15.6 [12.5; 18.6]	0.80 [0.62; 1.05]	0.106	0.915
≥ 3	152	105 (69.1)	20.1 [17.2; 24.2]	125	94 (75.2)	16.0 [13.6; 20.4]	0.81 [0.61; 1.07]	0.138	
Prior Gastrectomy									
Yes	32	17 (53.1)	24.3 [16.1; -]	43	29 (67.4)	19.9 [14.2; 37.8]	0.72 [0.39; 1.31]	0.282	0.735
No	266	187 (70.3)	20.0 [17.4; 22.2]	253	189 (74.7)	15.0 [12.7; 17.6]	0.80 [0.66; 0.98]	0.035	
Race 2									
Asian	97	56 (57.7)	23.4 [19.5; 36.8]	97	54 (55.7)	29.5 [20.4; 42.3]	1.06 [0.73; 1.55]	0.743	0.056
Non-Asian	201	148 (73.6)	18.7 [15.8; 21.2]	198	163 (82.3)	12.6 [11.1; 15.0]	0.70 [0.56; 0.87]	0.002	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: intention-to-treat population (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU; GEJ: Gastroesophageal Junction; MSI: Microsatellite Instability; 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)

Morbidität

Zeit bis zur ersten Folgetherapie oder Tod

Tabelle 4G-29: 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 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
Time to Subsequent Therapy[b] or Death	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Male	240	194 (80.8)	12.8 [10.4; 15.7]	237	205 (86.5)	9.1 [8.1; 10.6]	0.78 [0.64; 0.95]	0.013	0.055
Female	58	42 (72.4)	13.7 [10.2; 22.4]	59	55 (93.2)	8.7 [7.1; 10.3]	0.51 [0.34; 0.77]	0.001	
Age									
< 65 years	174	136 (78.2)	13.4 [10.6; 16.2]	165	146 (88.5)	9.0 [8.0; 10.3]	0.66 [0.52; 0.84]	< 0.001	0.368
≥ 65 years	124	100 (80.6)	12.6 [10.2; 16.1]	131	114 (87.0)	9.2 [7.1; 11.9]	0.79 [0.60; 1.03]	0.087	
ECOG Performance Status									
0	127	96 (75.6)	14.9 [11.5; 20.3]	122	101 (82.8)	10.3 [8.4; 11.8]	0.73 [0.55; 0.96]	0.025	0.985
1	171	140 (81.9)	12.2 [9.9; 14.4]	174	159 (91.4)	8.4 [7.7; 9.5]	0.71 [0.57; 0.89]	0.003	
Geographic Region									
Asia	96	70 (72.9)	14.6 [9.9; 22.1]	96	75 (78.1)	11.0 [8.0; 16.1]	0.84 [0.61; 1.16]	0.289	0.478
Rest of World	105	84 (80.0)	15.2 [12.2; 19.6]	104	94 (90.4)	9.4 [8.2; 11.4]	0.61 [0.45; 0.82]	0.001	
Western Europe/Israel/North America/Australia	97	82 (84.5)	10.0 [7.5; 13.0]	96	91 (94.8)	7.5 [6.7; 8.7]	0.69 [0.51; 0.93]	0.015	
Chemotherapy Regimen									
CAPOX	251	192 (76.5)	14.1 [11.8; 17.0]	253	218 (86.2)	9.3 [8.1; 10.6]	0.70 [0.58; 0.85]	< 0.001	0.574
FP	47	44 (93.6)	10.0 [7.2; 13.6]	43	42 (97.7)	8.2 [6.6; 9.9]	0.77 [0.50; 1.19]	0.237	

a: Database Cutoff Date: 29MAR2023

b: From clinical recommendation, systemic oncologic therapies recorded in the eCRF as neoadjuvant or adjuvant are not considered as subsequent oncology therapies

c: Number of participants: intention-to-treat population (Global Cohort - CPS>=1 Participants)

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate using Wald confidence interval

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; eCRF: Electronic Case Report Form; FP: Cisplatin plus 5-FU

Krankheitssymptomatik und Gesundheitszustand

EORTC QLQ-C30: Symptomskala Erschöpfung

Tabelle 4G-30: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Erschöpfung aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Fatigue (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	159 (71.9)	1.91 [1.41; 2.37]	223	133 (59.6)	2.79 [2.10; 4.40]	1.25 [0.99; 1.57]	0.0579	0.702
Female	51	32 (62.7)	2.33 [1.18; 4.86]	51	30 (58.8)	3.91 [1.64; 8.58]	1.13 [0.68; 1.86]	0.6370	
Age									
< 65 years	160	103 (64.4)	2.23 [1.58; 4.21]	155	95 (61.3)	3.06 [2.30; 4.63]	1.11 [0.84; 1.47]	0.4471	0.268
≥ 65 years	112	88 (78.6)	1.45 [0.99; 2.33]	119	68 (57.1)	2.17 [1.45; 5.62]	1.40 [1.02; 1.92]	0.0380	
ECOG Performance Status									
0	120	96 (80.0)	1.51 [1.25; 2.73]	115	74 (64.3)	2.27 [1.51; 3.02]	1.28 [0.95; 1.74]	0.1089	0.617
1	152	95 (62.5)	2.20 [1.58; 4.21]	159	89 (56.0)	4.30 [2.27; 6.97]	1.16 [0.87; 1.55]	0.3105	
Geographic Region									
Asia	89	66 (74.2)	2.04 [1.41; 4.44]	93	51 (54.8)	4.11 [2.10; -]	1.44 [1.00; 2.08]	0.0486	0.227
Rest of World	94	63 (67.0)	2.33 [1.45; 4.17]	95	59 (62.1)	2.14 [1.51; 4.04]	0.96 [0.67; 1.37]	0.8077	
Western Europe/Israel/North America/Australia	89	62 (69.7)	1.51 [0.79; 2.76]	86	53 (61.6)	3.06 [2.10; 5.65]	1.35 [0.94; 1.96]	0.1062	
Chemotherapy Regimen									
CAPOX	233	163 (70.0)	2.04 [1.45; 2.73]	239	137 (57.3)	2.79 [2.17; 4.63]	1.27 [1.01; 1.60]	0.0382	0.423
FP	39	28 (71.8)	2.33 [0.76; 3.25]	35	26 (74.3)	2.33 [0.95; 4.44]	1.01 [0.59; 1.73]	0.9660	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Übelkeit und Erbrechen

Tabelle 4G-31: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Übelkeit und Erbrechen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Nausea and Vomiting (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	123 (55.7)	2.99 [2.14; 6.18]	223	124 (55.6)	2.89 [2.17; 5.55]	0.94 [0.73; 1.21]	0.6308	0.553
Female	51	31 (60.8)	2.76 [1.61; 3.68]	51	28 (54.9)	2.53 [1.45; -]	1.11 [0.67; 1.85]	0.6869	
Age									
< 65 years	160	98 (61.3)	2.33 [1.91; 3.68]	155	88 (56.8)	2.86 [2.10; 6.01]	1.07 [0.80; 1.43]	0.6473	0.295
≥ 65 years	112	56 (50.0)	4.70 [2.27; -]	119	64 (53.8)	2.89 [2.07; 8.94]	0.84 [0.59; 1.20]	0.3436	
ECOG Performance Status									
0	120	74 (61.7)	2.14 [1.84; 4.17]	115	72 (62.6)	2.14 [1.45; 3.02]	0.90 [0.65; 1.24]	0.5142	0.525
1	152	80 (52.6)	4.07 [2.17; -]	159	80 (50.3)	4.24 [2.53; -]	1.03 [0.76; 1.40]	0.8498	
Geographic Region									
Asia	89	45 (50.6)	4.44 [2.76; -]	93	44 (47.3)	6.70 [3.94; -]	1.05 [0.70; 1.60]	0.8035	0.879
Rest of World	94	58 (61.7)	2.14 [1.58; 4.63]	95	56 (58.9)	2.50 [1.45; 4.21]	0.94 [0.65; 1.36]	0.7552	
Western Europe/Israel/North America/Australia	89	51 (57.3)	2.46 [1.45; 4.83]	86	52 (60.5)	2.10 [1.41; 2.92]	0.92 [0.63; 1.36]	0.6885	
Chemotherapy Regimen									
CAPOX	233	128 (54.9)	3.29 [2.14; 6.18]	239	130 (54.4)	3.06 [2.30; 5.88]	0.96 [0.75; 1.23]	0.7470	0.899
FP	39	26 (66.7)	1.84 [0.85; 3.25]	35	22 (62.9)	1.51 [0.76; -]	1.01 [0.57; 1.78]	0.9848	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Schmerzen

Tabelle 4G-32: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerzen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Pain (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	103 (46.6)	9.30 [6.01; -]	223	102 (45.7)	8.97 [5.55; 15.57]	0.96 [0.73; 1.27]	0.7888	0.323
Female	51	20 (39.2)	Not reached [6.01; -]	51	25 (49.0)	7.00 [2.10; -]	0.71 [0.39; 1.28]	0.2532	
Age									
< 65 years	160	71 (44.4)	11.30 [6.93; -]	155	72 (46.5)	9.20 [6.47; -]	0.90 [0.64; 1.25]	0.5128	0.877
≥ 65 years	112	52 (46.4)	7.33 [4.70; -]	119	55 (46.2)	6.74 [3.02; -]	0.92 [0.63; 1.34]	0.6524	
ECOG Performance Status									
0	120	60 (50.0)	6.93 [4.99; -]	115	56 (48.7)	6.74 [2.83; -]	0.89 [0.62; 1.28]	0.5360	0.950
1	152	63 (41.4)	11.30 [7.00; -]	159	71 (44.7)	9.89 [6.47; 15.57]	0.91 [0.65; 1.28]	0.5970	
Geographic Region									
Asia	89	38 (42.7)	9.46 [6.47; -]	93	41 (44.1)	11.04 [6.47; -]	0.95 [0.61; 1.48]	0.8267	0.658
Rest of World	94	42 (44.7)	11.30 [7.00; -]	95	46 (48.4)	9.20 [2.99; 15.57]	0.77 [0.51; 1.18]	0.2364	
Western Europe/Israel/North America/Australia	89	43 (48.3)	5.95 [4.17; -]	86	40 (46.5)	5.65 [4.27; -]	1.03 [0.67; 1.59]	0.8834	
Chemotherapy Regimen									
CAPOX	233	102 (43.8)	10.94 [6.93; -]	239	105 (43.9)	9.20 [6.47; 15.57]	0.93 [0.71; 1.23]	0.6290	0.490
FP	39	21 (53.8)	6.67 [3.02; -]	35	22 (62.9)	4.30 [1.54; 7.00]	0.73 [0.40; 1.34]	0.3115	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Dyspnoe

Tabelle 4G-33: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Dyspnoe aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Dyspnea (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	89 (40.3)	11.63 [9.30; -]	223	86 (38.6)	11.53 [8.97; -]	0.97 [0.72; 1.31]	0.8434	0.644
Female	51	24 (47.1)	10.61 [5.32; -]	51	21 (41.2)	Not reached [6.87; -]	1.13 [0.63; 2.04]	0.6735	
Age									
< 65 years	160	66 (41.3)	Not reached [7.13; -]	155	61 (39.4)	11.53 [8.81; -]	1.01 [0.71; 1.43]	0.9553	0.970
≥ 65 years	112	47 (42.0)	11.40 [7.49; 11.93]	119	46 (38.7)	11.73 [7.06; -]	0.97 [0.64; 1.45]	0.8655	
ECOG Performance Status									
0	120	53 (44.2)	11.40 [6.01; -]	115	53 (46.1)	9.89 [5.62; -]	0.84 [0.58; 1.23]	0.3794	0.249
1	152	60 (39.5)	11.63 [9.69; -]	159	54 (34.0)	Not reached [9.92; -]	1.13 [0.79; 1.64]	0.5024	
Geographic Region									
Asia	89	35 (39.3)	11.37 [8.54; -]	93	29 (31.2)	Not reached [11.04; -]	1.27 [0.78; 2.08]	0.3412	0.278
Rest of World	94	38 (40.4)	11.93 [7.66; -]	95	43 (45.3)	10.05 [6.14; 13.67]	0.77 [0.50; 1.20]	0.2467	
Western Europe/Israel/North America/Australia	89	40 (44.9)	8.64 [4.01; -]	86	35 (40.7)	7.56 [4.63; -]	1.08 [0.69; 1.70]	0.7388	
Chemotherapy Regimen									
CAPOX	233	90 (38.6)	11.66 [11.30; -]	239	88 (36.8)	11.73 [9.92; -]	0.96 [0.72; 1.29]	0.8080	0.607
FP	39	23 (59.0)	3.91 [2.79; 8.64]	35	19 (54.3)	4.63 [2.33; -]	1.14 [0.62; 2.09]	0.6809	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Schlaflosigkeit

Tabelle 4G-34: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Schlaflosigkeitaus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Insomnia (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	97 (43.9)	9.92 [8.31; -]	223	103 (46.2)	6.90 [5.45; -]	0.80 [0.61; 1.06]	0.1161	0.662
Female	51	18 (35.3)	11.66 [11.40; -]	51	22 (43.1)	Not reached [2.89; -]	0.71 [0.38; 1.33]	0.2854	
Age									
< 65 years	160	66 (41.3)	11.40 [9.20; -]	155	79 (51.0)	6.44 [4.63; 9.17]	0.68 [0.49; 0.94]	0.0197	0.195
≥ 65 years	112	49 (43.8)	9.92 [6.74; -]	119	46 (38.7)	11.73 [5.59; -]	0.96 [0.64; 1.44]	0.8448	
ECOG Performance Status									
0	120	53 (44.2)	11.14 [8.51; -]	115	55 (47.8)	7.23 [2.89; -]	0.72 [0.50; 1.06]	0.0957	0.626
1	152	62 (40.8)	11.66 [7.33; -]	159	70 (44.0)	7.00 [5.45; -]	0.84 [0.60; 1.18]	0.3191	
Geographic Region									
Asia	89	35 (39.3)	11.66 [9.13; -]	93	41 (44.1)	Not reached [5.49; -]	0.74 [0.47; 1.16]	0.1868	0.941
Rest of World	94	44 (46.8)	11.14 [4.57; -]	95	49 (51.6)	6.44 [3.02; 11.73]	0.78 [0.51; 1.17]	0.2244	
Western Europe/Israel/North America/Australia	89	36 (40.4)	11.50 [6.57; -]	86	35 (40.7)	7.00 [4.63; -]	0.85 [0.53; 1.36]	0.4997	
Chemotherapy Regimen									
CAPOX	233	101 (43.3)	11.40 [9.13; -]	239	107 (44.8)	7.75 [5.59; -]	0.81 [0.61; 1.06]	0.1250	0.589
FP	39	14 (35.9)	Not reached [5.78; -]	35	18 (51.4)	6.44 [2.37; -]	0.65 [0.32; 1.31]	0.2311	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Appetitverlust

Tabelle 4G-35: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Appetitverlustaus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Appetite Loss (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	118 (53.4)	5.09 [2.79; 11.34]	223	111 (49.8)	5.52 [3.02; 11.53]	1.03 [0.80; 1.34]	0.8081	0.841
Female	51	24 (47.1)	6.01 [2.27; -]	51	22 (43.1)	Not reached [2.73; -]	1.13 [0.64; 2.02]	0.6686	
Age									
< 65 years	160	74 (46.3)	9.20 [4.21; -]	155	73 (47.1)	9.23 [4.07; -]	0.98 [0.71; 1.36]	0.9225	0.582
≥ 65 years	112	68 (60.7)	2.92 [1.81; 5.09]	119	60 (50.4)	3.84 [2.17; 10.32]	1.13 [0.80; 1.59]	0.5036	
ECOG Performance Status									
0	120	69 (57.5)	3.02 [1.91; 11.34]	115	58 (50.4)	4.14 [2.10; 11.73]	1.08 [0.76; 1.53]	0.6688	0.707
1	152	73 (48.0)	7.13 [3.12; -]	159	75 (47.2)	6.21 [3.68; -]	0.99 [0.72; 1.36]	0.9368	
Geographic Region									
Asia	89	46 (51.7)	6.97 [2.69; -]	93	51 (54.8)	5.52 [2.76; -]	0.88 [0.59; 1.31]	0.5179	0.495
Rest of World	94	52 (55.3)	4.21 [1.74; -]	95	45 (47.4)	3.32 [1.61; -]	1.04 [0.70; 1.55]	0.8519	
Western Europe/Israel/North America/Australia	89	44 (49.4)	6.57 [2.07; -]	86	37 (43.0)	10.28 [4.14; -]	1.29 [0.83; 1.99]	0.2566	
Chemotherapy Regimen									
CAPOX	233	124 (53.2)	5.09 [2.83; 11.34]	239	118 (49.4)	5.52 [3.06; 11.53]	1.03 [0.80; 1.32]	0.8219	0.731
FP	39	18 (46.2)	Not reached [1.77; -]	35	15 (42.9)	Not reached [2.43; -]	1.17 [0.59; 2.32]	0.6546	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Verstopfung

Tabelle 4G-36: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Verstopfung aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Constipation (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	78 (35.3)	Not reached [-; -]	223	76 (34.1)	Not reached [10.19; -]	0.95 [0.69; 1.30]	0.7357	0.919
Female	51	19 (37.3)	Not reached [5.32; -]	51	20 (39.2)	8.97 [5.09; -]	0.89 [0.48; 1.67]	0.7232	
Age									
< 65 years	160	58 (36.3)	Not reached [11.27; -]	155	55 (35.5)	Not reached [8.97; -]	0.92 [0.64; 1.34]	0.6748	0.935
≥ 65 years	112	39 (34.8)	Not reached [-; -]	119	41 (34.5)	11.40 [8.77; -]	0.95 [0.61; 1.47]	0.8103	
ECOG Performance Status									
0	120	55 (45.8)	11.27 [4.27; -]	115	47 (40.9)	10.19 [6.14; -]	1.06 [0.72; 1.57]	0.7549	0.352
1	152	42 (27.6)	Not reached [-; -]	159	49 (30.8)	Not reached [10.22; -]	0.81 [0.54; 1.22]	0.3157	
Geographic Region									
Asia	89	33 (37.1)	Not reached [6.70; -]	93	34 (36.6)	Not reached [7.00; -]	0.94 [0.58; 1.52]	0.8128	0.706
Rest of World	94	34 (36.2)	Not reached [8.71; -]	95	29 (30.5)	11.40 [9.89; -]	1.07 [0.65; 1.76]	0.7867	
Western Europe/Israel/North America/Australia	89	30 (33.7)	Not reached [8.64; -]	86	33 (38.4)	9.66 [6.14; -]	0.80 [0.49; 1.32]	0.3791	
Chemotherapy Regimen									
CAPOX	233	80 (34.3)	Not reached [-; -]	239	77 (32.2)	Not reached [10.22; -]	0.97 [0.71; 1.32]	0.8319	0.556
FP	39	17 (43.6)	Not reached [2.27; -]	35	19 (54.3)	4.73 [2.14; -]	0.81 [0.42; 1.56]	0.5300	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Symptomskala Diarrhö

Tabelle 4G-37: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Diarrhö aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Diarrhea (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	132 (59.7)	2.86 [2.10; 4.67]	223	107 (48.0)	6.11 [3.06; -]	1.27 [0.98; 1.63]	0.0699	0.685
Female	51	34 (66.7)	2.76 [1.45; 6.57]	51	25 (49.0)	10.45 [1.38; -]	1.41 [0.84; 2.37]	0.1920	
Age									
< 65 years	160	99 (61.9)	3.02 [2.14; 5.03]	155	74 (47.7)	9.17 [3.06; -]	1.35 [1.00; 1.83]	0.0496	0.682
≥ 65 years	112	67 (59.8)	2.10 [1.41; 4.70]	119	58 (48.7)	4.83 [1.48; -]	1.21 [0.85; 1.73]	0.2803	
ECOG Performance Status									
0	120	85 (70.8)	2.14 [1.58; 3.52]	115	57 (49.6)	4.17 [1.51; -]	1.42 [1.02; 1.99]	0.0388	0.410
1	152	81 (53.3)	3.71 [2.10; 10.38]	159	75 (47.2)	6.47 [3.06; -]	1.17 [0.85; 1.60]	0.3276	
Geographic Region									
Asia	89	36 (40.4)	Not reached [9.89; -]	93	34 (36.6)	Not reached [7.36; -]	1.11 [0.69; 1.77]	0.6725	0.125
Rest of World	94	62 (66.0)	2.23 [1.58; 4.67]	95	54 (56.8)	2.43 [1.45; 5.78]	1.07 [0.74; 1.54]	0.7165	
Western Europe/Israel/North America/Australia	89	68 (76.4)	1.41 [0.85; 2.53]	86	44 (51.2)	3.06 [1.45; -]	1.78 [1.22; 2.60]	0.0030	
Chemotherapy Regimen									
CAPOX	233	139 (59.7)	2.76 [2.07; 4.70]	239	116 (48.5)	5.78 [2.37; -]	1.22 [0.95; 1.56]	0.1126	0.236
FP	39	27 (69.2)	3.25 [1.41; 4.99]	35	16 (45.7)	10.45 [4.17; -]	1.91 [1.03; 3.56]	0.0410	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Angst

Tabelle 4G-38: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Angst aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Anxiety (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	119 (54.1)	5.52 [2.96; 11.11]	223	126 (56.5)	3.71 [2.20; 5.75]	0.82 [0.64; 1.05]	0.1224	0.337
Female	51	29 (56.9)	3.25 [1.64; 10.84]	50	25 (50.0)	7.16 [1.45; -]	1.08 [0.63; 1.85]	0.7669	
Age									
< 65 years	160	85 (53.1)	6.41 [2.96; 11.30]	155	92 (59.4)	3.71 [1.77; 5.75]	0.77 [0.57; 1.03]	0.0812	0.241
≥ 65 years	111	63 (56.8)	3.19 [2.10; 10.84]	118	59 (50.0)	5.78 [2.20; 8.58]	1.02 [0.71; 1.46]	0.9152	
ECOG Performance Status									
0	120	63 (52.5)	5.52 [2.83; -]	114	67 (58.8)	2.79 [1.51; 6.28]	0.71 [0.51; 1.01]	0.0569	0.143
1	151	85 (56.3)	4.34 [2.27; 8.64]	159	84 (52.8)	5.26 [2.33; 7.33]	0.99 [0.74; 1.34]	0.9724	
Geographic Region									
Asia	89	48 (53.9)	6.01 [2.14; -]	93	50 (53.8)	4.30 [1.77; -]	0.91 [0.61; 1.36]	0.6424	0.590
Rest of World	93	54 (58.1)	6.41 [2.33; 11.30]	95	57 (60.0)	3.02 [1.48; 5.78]	0.71 [0.49; 1.03]	0.0716	
Western Europe/Israel/North America/Australia	89	46 (51.7)	4.70 [2.04; -]	85	44 (51.8)	5.55 [1.84; -]	0.99 [0.65; 1.50]	0.9599	
Chemotherapy Regimen									
CAPOX	232	130 (56.0)	4.60 [2.73; 7.56]	238	129 (54.2)	4.04 [2.33; 7.13]	0.91 [0.71; 1.16]	0.4563	0.250
FP	39	18 (46.2)	8.64 [2.10; -]	35	22 (62.9)	4.63 [1.38; 7.16]	0.61 [0.32; 1.14]	0.1205	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Körperbild

Tabelle 4G-39: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Körperbild aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Body Image (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	102 (46.4)	10.71 [4.63; -]	223	91 (40.8)	15.57 [6.47; -]	1.15 [0.86; 1.52]	0.3480	0.649
Female	51	28 (54.9)	5.91 [2.96; 10.84]	50	25 (50.0)	7.13 [1.41; -]	0.98 [0.57; 1.68]	0.9358	
Age									
< 65 years	160	76 (47.5)	8.77 [4.47; -]	155	70 (45.2)	8.41 [4.76; -]	1.05 [0.76; 1.46]	0.7686	0.540
≥ 65 years	111	54 (48.6)	6.74 [3.19; -]	118	46 (39.0)	Not reached [6.01; -]	1.21 [0.82; 1.80]	0.3341	
ECOG Performance Status									
0	120	57 (47.5)	10.84 [3.02; -]	114	51 (44.7)	8.58 [3.12; -]	0.99 [0.68; 1.44]	0.9453	0.359
1	151	73 (48.3)	7.56 [4.63; -]	159	65 (40.9)	15.57 [6.97; -]	1.23 [0.88; 1.73]	0.2208	
Geographic Region									
Asia	89	40 (44.9)	13.93 [4.44; -]	93	33 (35.5)	Not reached [-; -]	1.33 [0.83; 2.11]	0.2336	0.568
Rest of World	93	49 (52.7)	8.28 [4.27; -]	95	46 (48.4)	6.47 [4.44; -]	0.98 [0.66; 1.48]	0.9362	
Western Europe/Israel/North America/Australia	89	41 (46.1)	4.83 [2.96; -]	85	37 (43.5)	8.58 [3.06; -]	1.05 [0.67; 1.63]	0.8417	
Chemotherapy Regimen									
CAPOX	232	113 (48.7)	8.28 [4.63; -]	238	95 (39.9)	15.57 [7.13; -]	1.19 [0.91; 1.56]	0.2106	0.204
FP	39	17 (43.6)	Not reached [1.84; -]	35	21 (60.0)	6.44 [2.37; 8.41]	0.76 [0.40; 1.44]	0.4012	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Mundtrockenheit

Tabelle 4G-40: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Mundtrockenheit aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Dry Mouth (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	117 (53.2)	4.70 [3.06; 7.39]	223	104 (46.6)	5.59 [3.06; -]	1.06 [0.81; 1.38]	0.6641	0.428
Female	51	30 (58.8)	4.01 [2.10; 8.28]	50	22 (44.0)	Not reached [1.64; -]	1.36 [0.79; 2.36]	0.2712	
Age									
< 65 years	160	82 (51.3)	5.59 [3.94; -]	155	74 (47.7)	6.47 [2.60; -]	0.98 [0.71; 1.34]	0.8926	0.194
≥ 65 years	111	65 (58.6)	4.01 [2.27; 5.88]	118	52 (44.1)	7.75 [3.09; -]	1.35 [0.93; 1.94]	0.1107	
ECOG Performance Status									
0	120	71 (59.2)	3.75 [2.23; 5.29]	114	53 (46.5)	5.32 [2.66; -]	1.26 [0.88; 1.79]	0.2085	0.372
1	151	76 (50.3)	6.57 [4.17; -]	159	73 (45.9)	7.75 [3.09; -]	1.00 [0.73; 1.38]	0.9839	
Geographic Region									
Asia	89	36 (40.4)	Not reached [3.94; -]	93	36 (38.7)	Not reached [4.40; -]	1.06 [0.67; 1.69]	0.7964	0.979
Rest of World	93	57 (61.3)	4.40 [3.06; 7.13]	95	44 (46.3)	5.59 [2.07; -]	1.13 [0.76; 1.67]	0.5530	
Western Europe/Israel/North America/Australia	89	54 (60.7)	2.76 [2.07; 4.83]	85	46 (54.1)	2.79 [2.07; -]	1.09 [0.74; 1.62]	0.6630	
Chemotherapy Regimen									
CAPOX	232	128 (55.2)	4.40 [2.96; 7.13]	238	102 (42.9)	11.73 [4.34; -]	1.22 [0.94; 1.59]	0.1305	0.054
FP	39	19 (48.7)	6.57 [1.64; -]	35	24 (68.6)	2.14 [1.45; 5.32]	0.65 [0.35; 1.18]	0.1584	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Dysphagie

Tabelle 4G-41: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Dysphagie aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Dysphagia (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	102 (46.4)	9.89 [5.59; -]	223	94 (42.2)	9.89 [5.22; -]	1.03 [0.77; 1.36]	0.8610	0.333
Female	51	21 (41.2)	Not reached [3.25; -]	50	25 (50.0)	6.21 [2.30; -]	0.75 [0.42; 1.33]	0.3218	
Age									
< 65 years	160	65 (40.6)	Not reached [9.13; -]	155	69 (44.5)	9.89 [4.73; -]	0.83 [0.59; 1.16]	0.2801	0.173
≥ 65 years	111	58 (52.3)	4.96 [2.86; -]	118	50 (42.4)	8.77 [3.68; -]	1.18 [0.81; 1.72]	0.3977	
ECOG Performance Status									
0	120	64 (53.3)	5.88 [3.75; -]	114	55 (48.2)	8.31 [3.02; -]	0.97 [0.67; 1.39]	0.8629	0.848
1	151	59 (39.1)	Not reached [7.39; -]	159	64 (40.3)	Not reached [6.01; -]	0.93 [0.65; 1.32]	0.6750	
Geographic Region									
Asia	89	38 (42.7)	Not reached [4.44; -]	93	46 (49.5)	5.62 [2.30; -]	0.76 [0.49; 1.17]	0.2108	0.085
Rest of World	93	40 (43.0)	Not reached [5.88; -]	95	41 (43.2)	8.81 [4.73; -]	0.87 [0.56; 1.35]	0.5455	
Western Europe/Israel/North America/Australia	89	45 (50.6)	5.06 [2.96; -]	85	32 (37.6)	Not reached [7.16; -]	1.47 [0.93; 2.31]	0.0988	
Chemotherapy Regimen									
CAPOX	232	104 (44.8)	10.19 [6.05; -]	238	99 (41.6)	13.67 [6.21; -]	0.98 [0.74; 1.29]	0.8624	0.849
FP	39	19 (48.7)	6.93 [1.41; -]	35	20 (57.1)	6.01 [1.54; -]	0.93 [0.49; 1.74]	0.8110	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Einschränkungen beim Essen

Tabelle 4G-42: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Angst aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Eating Restrictions (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	88 (40.0)	13.93 [10.51; -]	223	91 (40.8)	11.53 [6.28; -]	0.92 [0.69; 1.24]	0.5816	0.485
Female	51	22 (43.1)	10.71 [4.63; -]	50	26 (52.0)	7.13 [2.76; -]	0.72 [0.41; 1.27]	0.2515	
Age									
< 65 years	160	52 (32.5)	Not reached [-; -]	155	59 (38.1)	11.53 [8.12; -]	0.80 [0.55; 1.17]	0.2514	0.489
≥ 65 years	111	58 (52.3)	5.26 [2.60; -]	118	58 (49.2)	5.59 [2.66; -]	0.96 [0.67; 1.38]	0.8147	
ECOG Performance Status									
0	120	58 (48.3)	10.51 [4.80; -]	114	56 (49.1)	5.88 [3.12; -]	0.82 [0.57; 1.19]	0.3076	0.879
1	151	52 (34.4)	Not reached [-; -]	159	61 (38.4)	15.57 [7.33; -]	0.87 [0.60; 1.26]	0.4711	
Geographic Region									
Asia	89	37 (41.6)	13.93 [7.59; -]	93	38 (40.9)	Not reached [6.31; -]	0.94 [0.60; 1.49]	0.8016	0.812
Rest of World	93	38 (40.9)	Not reached [5.09; -]	95	44 (46.3)	8.97 [4.04; -]	0.77 [0.50; 1.20]	0.2473	
Western Europe/Israel/North America/Australia	89	35 (39.3)	Not reached [4.80; -]	85	35 (41.2)	8.31 [4.40; -]	0.88 [0.55; 1.41]	0.5996	
Chemotherapy Regimen									
CAPOX	232	96 (41.4)	13.93 [9.20; -]	238	98 (41.2)	11.53 [6.47; -]	0.94 [0.71; 1.24]	0.6480	0.191
FP	39	14 (35.9)	Not reached [4.76; -]	35	19 (54.3)	4.73 [2.10; -]	0.59 [0.30; 1.19]	0.1404	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Haarausfall

Tabelle 4G-43: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Haarausfall aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Hair Loss (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	9	1 (11.1)	n.c.	12	1 (8.3)	n.c.	n.c.	n.c.	n.c.
Female	2	0 (0.0)	n.c.	9	2 (22.2)	n.c.	n.c.	n.c.	
Age									
< 65 years	6	0 (0.0)	n.c.	14	2 (14.3)	n.c.	n.c.	n.c.	n.c.
≥ 65 years	5	1 (20.0)	n.c.	7	1 (14.3)	n.c.	n.c.	n.c.	
ECOG Performance Status									
0	5	0 (0.0)	n.c.	7	2 (28.6)	n.c.	n.c.	n.c.	n.c.
1	6	1 (16.7)	n.c.	14	1 (7.1)	n.c.	n.c.	n.c.	
Geographic Region									
Asia	2	0 (0.0)	n.c.	2	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	5	0 (0.0)	n.c.	11	2 (18.2)	n.c.	n.c.	n.c.	
Western Europe/Israel/North America/Australia	4	1 (25.0)	n.c.	8	1 (12.5)	n.c.	n.c.	n.c.	
Chemotherapy Regimen									
CAPOX	10	1 (10.0)	n.c.	18	3 (16.7)	n.c.	n.c.	n.c.	n.c.
FP	1	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU; 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)

EORTC QLQ-STO22: Symptomskala Schmerz

Tabelle 4G-44: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Schmerz aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Pain (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	86 (39.1)	Not reached [9.13; -]	223	81 (36.3)	13.67 [10.32; -]	0.96 [0.71; 1.30]	0.8002	0.232
Female	51	11 (21.6)	Not reached [-; -]	50	15 (30.0)	Not reached [8.81; -]	0.57 [0.26; 1.24]	0.1582	
Age									
< 65 years	160	60 (37.5)	Not reached [9.86; -]	155	61 (39.4)	13.67 [8.35; -]	0.85 [0.59; 1.22]	0.3760	0.632
≥ 65 years	111	37 (33.3)	Not reached [9.53; -]	118	35 (29.7)	Not reached [-; -]	0.99 [0.62; 1.57]	0.9622	
ECOG Performance Status									
0	120	48 (40.0)	Not reached [9.13; -]	114	47 (41.2)	13.67 [6.11; -]	0.77 [0.51; 1.15]	0.1997	0.369
1	151	49 (32.5)	Not reached [-; -]	159	49 (30.8)	15.57 [15.57; -]	0.99 [0.66; 1.47]	0.9610	
Geographic Region									
Asia	89	30 (33.7)	Not reached [9.13; -]	93	31 (33.3)	Not reached [-; -]	0.94 [0.57; 1.56]	0.8196	0.893
Rest of World	93	34 (36.6)	Not reached [9.04; -]	95	35 (36.8)	13.67 [6.70; -]	0.82 [0.51; 1.32]	0.4067	
Western Europe/Israel/North America/Australia	89	33 (37.1)	Not reached [8.64; -]	85	30 (35.3)	Not reached [7.39; -]	0.93 [0.56; 1.52]	0.7612	
Chemotherapy Regimen									
CAPOX	232	82 (35.3)	Not reached [11.20; -]	238	79 (33.2)	13.67 [13.67; -]	0.94 [0.69; 1.28]	0.6943	0.331
FP	39	15 (38.5)	Not reached [4.14; -]	35	17 (48.6)	6.70 [2.14; -]	0.68 [0.34; 1.36]	0.2729	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Symptomskala Reflux

Tabelle 4G-45: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Reflux aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Reflux Symptoms (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	121 (55.0)	4.44 [2.37; 9.00]	223	110 (49.3)	6.47 [4.30; 11.27]	1.19 [0.92; 1.55]	0.1805	0.566
Female	51	26 (51.0)	7.03 [2.27; -]	50	24 (48.0)	7.33 [2.14; -]	1.00 [0.57; 1.74]	0.9872	
ECOG Performance Status									
0	120	69 (57.5)	4.27 [2.10; 8.77]	114	56 (49.1)	6.77 [2.83; -]	1.17 [0.82; 1.66]	0.3880	0.909
1	151	78 (51.7)	6.47 [2.37; -]	159	78 (49.1)	7.16 [4.30; 11.73]	1.15 [0.84; 1.57]	0.3920	
Geographic Region									
Asia	89	51 (57.3)	6.47 [2.27; 10.35]	93	39 (41.9)	Not reached [4.53; -]	1.40 [0.93; 2.13]	0.1104	0.505
Rest of World	93	49 (52.7)	4.27 [1.54; -]	95	48 (50.5)	6.14 [2.83; 11.73]	1.11 [0.75; 1.67]	0.5955	
Western Europe/Israel/North America/Australia	89	47 (52.8)	3.71 [2.04; 11.70]	85	47 (55.3)	4.30 [2.79; 7.56]	1.01 [0.67; 1.51]	0.9794	
Chemotherapy Regimen									
CAPOX	232	124 (53.4)	6.24 [2.56; 9.20]	238	106 (44.5)	9.89 [6.05; 15.57]	1.25 [0.97; 1.62]	0.0887	0.101
FP	39	23 (59.0)	3.12 [0.85; -]	35	28 (80.0)	2.33 [1.41; 4.30]	0.72 [0.41; 1.26]	0.2514	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

EORTC QLQ-STO22: Geschmacksstörungen

Tabelle 4G-46: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Symptomskala Geschmacksstörungen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-STO22 Taste (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	220	125 (56.8)	3.19 [2.37; 5.55]	223	111 (49.8)	5.59 [2.96; 9.89]	1.12 [0.87; 1.44]	0.3893	0.612
Female	51	33 (64.7)	2.30 [1.51; 4.40]	50	27 (54.0)	2.99 [1.51; -]	1.25 [0.75; 2.09]	0.3873	
Age									
< 65 years	160	86 (53.8)	4.63 [2.37; 10.09]	155	79 (51.0)	5.55 [2.79; -]	1.05 [0.77; 1.42]	0.7639	0.321
≥ 65 years	111	72 (64.9)	2.40 [2.07; 2.96]	118	59 (50.0)	5.59 [2.46; 10.35]	1.32 [0.94; 1.87]	0.1101	
ECOG Performance Status									
0	120	80 (66.7)	2.10 [1.61; 2.79]	114	66 (57.9)	2.66 [1.51; 6.05]	1.15 [0.83; 1.60]	0.3959	0.984
1	151	78 (51.7)	4.90 [2.83; -]	159	72 (45.3)	8.94 [4.40; -]	1.15 [0.83; 1.58]	0.4064	
Geographic Region									
Asia	89	45 (50.6)	9.46 [2.79; -]	93	48 (51.6)	6.31 [2.33; -]	0.88 [0.58; 1.32]	0.5263	0.253
Rest of World	93	56 (60.2)	4.14 [2.10; 6.93]	95	41 (43.2)	9.89 [4.04; -]	1.37 [0.92; 2.05]	0.1252	
Western Europe/Israel/North America/Australia	89	57 (64.0)	2.10 [1.48; 2.76]	85	49 (57.6)	2.79 [1.51; 5.72]	1.28 [0.87; 1.88]	0.2020	
Chemotherapy Regimen									
CAPOX	232	132 (56.9)	2.86 [2.37; 5.42]	238	115 (48.3)	6.31 [2.86; -]	1.17 [0.91; 1.51]	0.2106	0.734
FP	39	26 (66.7)	2.10 [1.41; 5.55]	35	23 (65.7)	3.02 [1.48; 5.72]	1.02 [0.58; 1.80]	0.9363	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-STO22: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Gastric Cancer 22 items; FP: Cisplatin plus 5-FU

Gesundheitszustand: EQ-5D VAS

Tabelle 4G-47: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Gesundheitszustand: EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EQ-5D VAS (15 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	224	95 (42.4)	14.26 [10.15; -]	224	93 (41.5)	22.01 [7.39; -]	0.89 [0.67; 1.19]	0.4287	0.658
Female	51	19 (37.3)	Not reached [6.67; -]	51	21 (41.2)	8.81 [6.21; -]	0.83 [0.44; 1.54]	0.5497	
Age									
< 65 years	163	60 (36.8)	25.89 [12.75; -]	156	62 (39.7)	24.18 [7.59; -]	0.78 [0.54; 1.11]	0.1627	0.400
≥ 65 years	112	54 (48.2)	8.08 [5.95; -]	119	52 (43.7)	12.75 [5.16; -]	0.99 [0.67; 1.44]	0.9444	
ECOG Performance Status									
0	121	57 (47.1)	12.75 [7.49; 39.29]	116	54 (46.6)	8.77 [5.16; 26.12]	0.82 [0.57; 1.20]	0.3058	0.798
1	154	57 (37.0)	26.65 [11.11; -]	159	60 (37.7)	22.01 [9.89; -]	0.89 [0.62; 1.28]	0.5225	
Geographic Region									
Asia	89	40 (44.9)	12.75 [6.74; -]	93	30 (32.3)	Not reached [22.01; -]	1.34 [0.84; 2.16]	0.2207	0.060
Rest of World	95	42 (44.2)	15.97 [10.12; -]	95	46 (48.4)	8.31 [4.30; -]	0.63 [0.41; 0.97]	0.0348	
Western Europe/Israel/North America/Australia	91	32 (35.2)	25.89 [7.33; -]	87	38 (43.7)	8.54 [6.21; -]	0.75 [0.47; 1.20]	0.2269	
Chemotherapy Regimen									
CAPOX	235	97 (41.3)	18.20 [10.58; -]	240	96 (40.0)	22.01 [8.54; -]	0.89 [0.67; 1.18]	0.4268	0.680
FP	40	17 (42.5)	11.30 [6.57; -]	35	18 (51.4)	7.16 [3.71; -]	0.75 [0.38; 1.47]	0.4004	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EQ-5D VAS: European Quality of Life 5 Dimensions Visual Analogue Scale; FP: Cisplatin plus 5-FU

Gesundheitsbezogene Lebensqualität

EORTC QLQ-C30: Globaler Gesundheitsstatus

Tabelle 4G-48: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den globalen Gesundheitsstatus aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Global Health Status/QoL (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	124 (56.1)	4.37 [2.27; 6.93]	223	117 (52.5)	4.73 [3.06; 9.23]	1.03 [0.80; 1.33]	0.7955	0.612
Female	51	24 (47.1)	9.82 [2.27; -]	51	27 (52.9)	4.21 [2.14; -]	0.89 [0.51; 1.54]	0.6744	
Age									
< 65 years	160	83 (51.9)	6.05 [2.96; 11.30]	155	82 (52.9)	6.11 [4.07; 9.89]	0.98 [0.72; 1.34]	0.9211	0.841
≥ 65 years	112	65 (58.0)	4.17 [2.04; 6.57]	119	62 (52.1)	3.52 [2.20; 9.96]	1.02 [0.72; 1.45]	0.8969	
ECOG Performance Status									
0	120	78 (65.0)	4.14 [2.10; 6.01]	115	62 (53.9)	3.06 [2.14; 9.23]	1.12 [0.80; 1.57]	0.4995	0.348
1	152	70 (46.1)	11.56 [4.17; -]	159	82 (51.6)	6.01 [3.94; 9.92]	0.90 [0.65; 1.24]	0.5066	
Geographic Region									
Asia	89	48 (53.9)	5.26 [2.10; -]	93	43 (46.2)	7.13 [3.52; -]	1.17 [0.77; 1.76]	0.4595	0.673
Rest of World	94	50 (53.2)	7.10 [2.79; 11.56]	95	50 (52.6)	5.26 [2.99; 9.92]	0.91 [0.61; 1.35]	0.6381	
Western Europe/Israel/North America/Australia	89	50 (56.2)	4.17 [1.61; 6.93]	86	51 (59.3)	3.06 [2.17; 6.11]	0.95 [0.64; 1.40]	0.7852	
Chemotherapy Regimen									
CAPOX	233	125 (53.6)	5.52 [2.56; 9.13]	239	119 (49.8)	6.47 [3.52; 9.96]	1.05 [0.82; 1.35]	0.6955	0.372
FP	39	23 (59.0)	4.37 [2.04; 11.30]	35	25 (71.4)	3.09 [2.10; 4.73]	0.74 [0.42; 1.33]	0.3136	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU; QoL: Quality of Life

EORTC QLQ-C30: Funktionsskala Körperliche Funktion

Tabelle 4G-49: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperliche Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Physical Functioning (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	133 (60.2)	4.40 [3.91; 5.78]	223	112 (50.2)	5.26 [3.68; 9.63]	1.11 [0.86; 1.43]	0.4144	0.548
Female	51	29 (56.9)	2.33 [1.58; -]	51	31 (60.8)	4.44 [2.27; 7.33]	0.93 [0.56; 1.54]	0.7672	
Age									
< 65 years	160	86 (53.8)	5.78 [3.98; 10.15]	155	77 (49.7)	7.00 [4.21; 9.92]	1.01 [0.74; 1.37]	0.9662	0.552
≥ 65 years	112	76 (67.9)	3.29 [2.17; 4.30]	119	66 (55.5)	3.52 [2.23; 5.78]	1.16 [0.83; 1.61]	0.3854	
ECOG Performance Status									
0	120	73 (60.8)	4.37 [2.86; 6.34]	115	62 (53.9)	4.70 [2.56; 7.75]	0.99 [0.70; 1.38]	0.9336	0.563
1	152	89 (58.6)	4.21 [2.79; 7.06]	159	81 (50.9)	5.78 [3.29; 11.73]	1.13 [0.84; 1.53]	0.4207	
Geographic Region									
Asia	89	52 (58.4)	5.26 [2.86; 9.92]	93	45 (48.4)	6.47 [3.98; -]	1.22 [0.82; 1.83]	0.3253	0.356
Rest of World	94	64 (68.1)	4.14 [2.73; 5.55]	95	51 (53.7)	5.22 [2.43; 9.04]	1.15 [0.80; 1.67]	0.4471	
Western Europe/Israel/North America/Australia	89	46 (51.7)	4.60 [2.17; -]	86	47 (54.7)	3.06 [1.64; 7.39]	0.85 [0.56; 1.27]	0.4225	
Chemotherapy Regimen									
CAPOX	233	138 (59.2)	4.37 [3.22; 5.68]	239	120 (50.2)	5.26 [3.29; 8.58]	1.10 [0.86; 1.40]	0.4573	0.640
FP	39	24 (61.5)	4.17 [2.10; 8.64]	35	23 (65.7)	4.44 [1.64; 8.58]	0.96 [0.54; 1.70]	0.8903	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Funktionsskala Rollenfunktion

Tabelle 4G-50: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Funktionsskala Rollenfunktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Role Functioning (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	142 (64.3)	3.78 [2.33; 4.63]	223	119 (53.4)	4.60 [2.89; 7.75]	1.20 [0.94; 1.53]	0.1413	0.770
Female	51	32 (62.7)	2.96 [1.41; 7.82]	51	30 (58.8)	4.37 [2.30; 9.04]	1.08 [0.65; 1.78]	0.7632	
Age									
< 65 years	160	100 (62.5)	3.12 [2.33; 5.65]	155	82 (52.9)	6.01 [3.68; 9.92]	1.27 [0.95; 1.70]	0.1133	0.469
≥ 65 years	112	74 (66.1)	3.02 [2.07; 4.63]	119	67 (56.3)	3.12 [2.23; 5.09]	1.07 [0.77; 1.49]	0.6921	
ECOG Performance Status									
0	120	88 (73.3)	2.79 [2.07; 4.34]	115	67 (58.3)	2.89 [2.10; 5.22]	1.16 [0.84; 1.59]	0.3597	0.956
1	152	86 (56.6)	4.40 [2.33; 7.82]	159	82 (51.6)	5.85 [4.04; 9.92]	1.15 [0.85; 1.56]	0.3571	
Geographic Region									
Asia	89	53 (59.6)	5.55 [2.14; 7.59]	93	46 (49.5)	6.67 [2.83; -]	1.19 [0.80; 1.76]	0.3912	0.265
Rest of World	94	67 (71.3)	2.56 [2.10; 4.21]	95	50 (52.6)	5.78 [3.12; 9.92]	1.45 [1.00; 2.10]	0.0490	
Western Europe/Israel/North America/Australia	89	54 (60.7)	2.96 [2.10; 6.24]	86	53 (61.6)	2.66 [1.64; 4.37]	0.94 [0.64; 1.37]	0.7510	
Chemotherapy Regimen									
CAPOX	233	149 (63.9)	3.09 [2.33; 4.63]	239	124 (51.9)	5.09 [3.06; 8.31]	1.24 [0.98; 1.57]	0.0781	0.260
FP	39	25 (64.1)	3.91 [1.64; 8.64]	35	25 (71.4)	2.99 [1.45; 4.63]	0.88 [0.51; 1.53]	0.6549	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Funktionsskala Emotionale Funktion

Tabelle 4G-51: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Emotionale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Emotional Functioning (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	89 (40.3)	Not reached [8.81; -]	223	102 (45.7)	8.31 [5.98; -]	0.80 [0.60; 1.06]	0.1171	0.627
Female	51	21 (41.2)	11.66 [7.56; -]	51	25 (49.0)	8.31 [3.02; -]	0.65 [0.36; 1.16]	0.1458	
Age									
< 65 years	160	60 (37.5)	Not reached [9.82; -]	155	78 (50.3)	7.39 [5.26; 11.53]	0.64 [0.46; 0.89]	0.0092	0.100
≥ 65 years	112	50 (44.6)	11.50 [6.57; -]	119	49 (41.2)	11.34 [5.88; -]	0.98 [0.66; 1.45]	0.9070	
ECOG Performance Status									
0	120	49 (40.8)	Not reached [8.81; -]	115	53 (46.1)	7.95 [5.75; -]	0.79 [0.53; 1.16]	0.2287	0.926
1	152	61 (40.1)	11.66 [8.31; -]	159	74 (46.5)	8.31 [5.26; -]	0.75 [0.54; 1.06]	0.1044	
Geographic Region									
Asia	89	29 (32.6)	Not reached [11.66; -]	93	35 (37.6)	Not reached [7.39; -]	0.79 [0.48; 1.29]	0.3458	0.934
Rest of World	94	45 (47.9)	9.82 [4.50; -]	95	51 (53.7)	5.88 [3.02; 9.89]	0.71 [0.48; 1.06]	0.0943	
Western Europe/Israel/North America/Australia	89	36 (40.4)	11.50 [5.75; -]	86	41 (47.7)	6.21 [3.15; -]	0.78 [0.50; 1.23]	0.2889	
Chemotherapy Regimen									
CAPOX	233	95 (40.8)	11.66 [9.40; -]	239	106 (44.4)	8.51 [6.31; -]	0.81 [0.62; 1.08]	0.1475	0.238
FP	39	15 (38.5)	Not reached [4.60; -]	35	21 (60.0)	5.45 [2.07; -]	0.54 [0.28; 1.05]	0.0715	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Funktionsskala Kognitive Funktion
Tabelle 4G-52: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Funktionsskala Kognitive Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Cognitive Functioning (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	119 (53.8)	6.01 [4.14; 9.40]	223	107 (48.0)	6.47 [4.70; 10.32]	1.07 [0.82; 1.39]	0.6262	0.744
Female	51	32 (62.7)	2.96 [2.10; 8.67]	51	33 (64.7)	3.52 [1.64; 7.00]	1.00 [0.61; 1.63]	0.9843	
ECOG Performance Status									
0	120	66 (55.0)	5.82 [2.92; 9.66]	115	63 (54.8)	4.37 [2.79; 7.56]	0.94 [0.67; 1.33]	0.7294	0.405
1	152	85 (55.9)	5.95 [3.02; 9.40]	159	77 (48.4)	6.97 [4.37; 12.06]	1.13 [0.83; 1.54]	0.4335	
Geographic Region									
Asia	89	47 (52.8)	8.74 [3.09; 11.30]	93	42 (45.2)	10.32 [5.85; -]	1.22 [0.80; 1.84]	0.3587	0.612
Rest of World	94	57 (60.6)	4.11 [2.33; 8.31]	95	52 (54.7)	4.70 [2.83; 7.16]	1.00 [0.69; 1.46]	0.9954	
Western Europe/Israel/North America/Australia	89	47 (52.8)	5.32 [2.56; 10.61]	86	46 (53.5)	4.37 [2.66; 7.46]	0.93 [0.62; 1.40]	0.7218	
Chemotherapy Regimen									
CAPOX	233	130 (55.8)	5.95 [3.02; 8.74]	239	115 (48.1)	6.90 [4.07; 10.32]	1.13 [0.88; 1.45]	0.3388	0.089
FP	39	21 (53.8)	5.32 [3.91; -]	35	25 (71.4)	3.52 [1.41; 6.44]	0.68 [0.38; 1.22]	0.1902	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

EORTC QLQ-C30: Funktionsskala Soziale Funktion

Tabelle 4G-53: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die Funktionsskala Soziale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
EORTC QLQ-C30 Social Functioning (10 points)	**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]**	**p-Value for Interaction Test[f]**
Sex									
Male	221	137 (62.0)	3.42 [2.17; 4.44]	223	121 (54.3)	5.22 [3.71; 6.90]	1.21 [0.94; 1.54]	0.1335	0.352
Female	51	35 (68.6)	2.10 [1.38; 2.96]	51	28 (54.9)	7.13 [1.45; -]	1.52 [0.92; 2.51]	0.0996	
Age									
< 65 years	160	99 (61.9)	3.02 [2.00; 5.52]	155	91 (58.7)	4.60 [2.83; 6.90]	1.11 [0.83; 1.48]	0.4775	0.172
≥ 65 years	112	73 (65.2)	2.96 [2.10; 4.17]	119	58 (48.7)	5.88 [3.58; 10.58]	1.52 [1.07; 2.14]	0.0182	
ECOG Performance Status									
0	120	90 (75.0)	2.10 [1.41; 3.12]	115	67 (58.3)	2.96 [2.07; 5.85]	1.38 [1.01; 1.89]	0.0456	0.399
1	152	82 (53.9)	4.34 [2.27; 10.74]	159	82 (51.6)	6.90 [4.63; 9.73]	1.14 [0.84; 1.55]	0.4082	
Geographic Region									
Asia	89	48 (53.9)	5.95 [2.96; -]	93	45 (48.4)	7.13 [4.50; -]	1.19 [0.79; 1.79]	0.4040	0.823
Rest of World	94	63 (67.0)	2.79 [2.07; 4.21]	95	55 (57.9)	4.70 [2.89; 9.20]	1.22 [0.85; 1.75]	0.2916	
Western Europe/Israel/North America/Australia	89	61 (68.5)	2.10 [1.25; 4.14]	86	49 (57.0)	2.96 [2.17; 6.24]	1.38 [0.95; 2.01]	0.0936	
Chemotherapy Regimen									
CAPOX	233	147 (63.1)	3.12 [2.10; 4.34]	239	124 (51.9)	5.78 [4.04; 7.43]	1.31 [1.03; 1.67]	0.0258	0.405
FP	39	25 (64.1)	2.17 [1.41; 4.14]	35	25 (71.4)	2.66 [1.38; 8.58]	1.01 [0.58; 1.76]	0.9751	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: full-analysis-set population with baseline (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FP: Cisplatin plus 5-FU

Nebenwirkungen

Unerwünschte Ereignisse

Unerwünschte Ereignisse gesamt

Tabelle 4G-54: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Unerwünschte Ereignisse gesamt aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
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-Value for Interaction Test[f]**
Sex									
Male	240	238 (99.2)	0.36 [0.29; 0.57]	236	236 (100.0)	0.43 [0.29; 0.71]	1.02 [0.85; 1.22]	0.8524	0.981
Female	58	58 (100.0)	0.29 [0.29; 0.57]	59	59 (100.0)	0.29 [0.29; 0.86]	0.99 [0.68; 1.42]	0.9431	
Age									
< 65 years	174	173 (99.4)	0.29 [0.29; 0.43]	164	164 (100.0)	0.36 [0.29; 0.71]	1.11 [0.90; 1.38]	0.3263	0.193
≥ 65 years	124	123 (99.2)	0.57 [0.29; 0.86]	131	131 (100.0)	0.57 [0.29; 0.71]	0.89 [0.70; 1.14]	0.3649	
ECOG Performance Status									
0	127	125 (98.4)	0.29 [0.14; 0.43]	121	121 (100.0)	0.29 [0.29; 0.43]	0.97 [0.75; 1.24]	0.7889	0.572
1	171	171 (100.0)	0.43 [0.29; 0.71]	174	174 (100.0)	0.71 [0.43; 1.00]	1.05 [0.85; 1.30]	0.6378	
Geographic Region									
Asia	96	95 (99.0)	0.29 [0.14; 0.29]	96	96 (100.0)	0.29 [0.14; 0.29]	0.93 [0.70; 1.24]	0.6139	0.298
Rest of World	105	105 (100.0)	1.00 [0.57; 2.29]	103	103 (100.0)	1.71 [0.86; 2.57]	1.19 [0.90; 1.56]	0.2229	
Western Europe/Israel/North America/Australia	97	96 (99.0)	0.29 [0.14; 0.43]	96	96 (100.0)	0.29 [0.14; 0.29]	0.91 [0.68; 1.21]	0.5011	
Chemotherapy Regimen									
CAPOX	251	250 (99.6)	0.29 [0.29; 0.43]	253	253 (100.0)	0.43 [0.29; 0.57]	1.02 [0.86; 1.22]	0.8017	0.885
FP	47	46 (97.9)	0.57 [0.29; 1.14]	42	42 (100.0)	0.71 [0.29; 1.43]	1.02 [0.67; 1.55]	0.9346	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-55: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
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-Value for Interaction Test[f]**
Sex									
Male	240	117 (48.8)	66.57 [45.29; -]	236	117 (49.6)	58.43 [27.00; -]	0.90 [0.70; 1.16]	0.4262	0.879
Female	58	26 (44.8)	142.14 [31.00; -]	59	24 (40.7)	Not reached [32.00; -]	0.95 [0.54; 1.66]	0.8491	
Age									
< 65 years	174	89 (51.1)	69.14 [43.29; 98.86]	164	74 (45.1)	68.71 [33.43; -]	1.03 [0.76; 1.40]	0.8514	0.188
≥ 65 years	124	54 (43.5)	Not reached [42.14; -]	131	67 (51.1)	56.57 [19.57; -]	0.76 [0.53; 1.09]	0.1328	
ECOG Performance Status									
0	127	54 (42.5)	Not reached [60.14; -]	121	54 (44.6)	Not reached [27.00; -]	0.83 [0.57; 1.22]	0.3482	0.517
1	171	89 (52.0)	52.00 [31.00; 98.86]	174	87 (50.0)	56.57 [27.00; 117.14]	0.97 [0.72; 1.31]	0.8612	
Geographic Region									
Asia	96	42 (43.8)	142.14 [52.00; -]	96	32 (33.3)	Not reached [-; -]	1.30 [0.82; 2.06]	0.2625	0.142
Rest of World	105	42 (40.0)	90.29 [65.57; -]	103	38 (36.9)	117.14 [67.86; -]	0.87 [0.56; 1.36]	0.5488	
Western Europe/Israel/North America/Australia	97	59 (60.8)	22.14 [9.14; 57.86]	96	71 (74.0)	12.43 [6.43; 22.29]	0.73 [0.52; 1.03]	0.0763	
Chemotherapy Regimen									
CAPOX	251	120 (47.8)	76.14 [49.86; -]	253	120 (47.4)	68.71 [32.86; -]	0.91 [0.71; 1.18]	0.4778	0.951
FP	47	23 (48.9)	57.86 [22.86; -]	42	21 (50.0)	55.00 [19.57; -]	0.88 [0.48; 1.60]	0.6728	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

Tabelle 4G-56: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
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]**	**p-Value for Interaction Test[f]**
Sex									
Male	240	176 (73.3)	16.00 [11.71; 19.29]	236	153 (64.8)	16.14 [12.14; 19.57]	1.11 [0.90; 1.38]	0.3290	0.950
Female	58	44 (75.9)	12.00 [7.71; 18.14]	59	41 (69.5)	12.14 [6.29; 21.00]	1.10 [0.72; 1.68]	0.6693	
ECOG Performance Status									
0	127	88 (69.3)	15.57 [10.71; 35.71]	121	75 (62.0)	17.57 [10.71; 29.14]	1.08 [0.79; 1.47]	0.6304	0.815
1	171	132 (77.2)	13.71 [9.57; 18.29]	174	119 (68.4)	14.57 [10.86; 19.00]	1.14 [0.89; 1.46]	0.3139	
Geographic Region									
Asia	96	58 (60.4)	28.86 [14.14; 66.57]	96	51 (53.1)	31.86 [16.57; -]	1.11 [0.76; 1.61]	0.6008	0.972
Rest of World	105	84 (80.0)	18.29 [13.00; 23.14]	103	66 (64.1)	16.71 [12.43; 32.00]	1.13 [0.82; 1.56]	0.4532	
Western Europe/Israel/North America/Australia	97	78 (80.4)	6.14 [3.86; 9.14]	96	77 (80.2)	6.43 [4.86; 10.86]	1.09 [0.79; 1.49]	0.6003	
Chemotherapy Regimen									
CAPOX	251	181 (72.1)	16.00 [12.00; 21.14]	253	166 (65.6)	16.00 [12.14; 19.43]	1.07 [0.86; 1.31]	0.5571	0.331
FP	47	39 (83.0)	9.86 [4.57; 16.00]	42	28 (66.7)	10.43 [6.14; 29.14]	1.37 [0.84; 2.22]	0.2090	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU

Therapieabbruch wegen unerwünschter Ereignisse

Tabelle 4G-57: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
Adverse Events Leading to Treatment Discontinuation	**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-Value for Interaction Test[f]**
Sex									
Male	240	98 (40.8)	89.43 [47.86; -]	236	86 (36.4)	117.14 [69.14; -]	1.04 [0.78; 1.39]	0.7907	0.764
Female	58	29 (50.0)	56.71 [25.14; 102.00]	59	22 (37.3)	Not reached [23.43; -]	1.11 [0.63; 1.94]	0.7212	
ECOG Performance Status									
0	127	57 (44.9)	55.29 [31.14; -]	121	52 (43.0)	69.14 [24.43; -]	0.92 [0.63; 1.34]	0.6639	0.346
1	171	70 (40.9)	78.14 [54.86; -]	174	56 (32.2)	117.14 [117.14; -]	1.18 [0.83; 1.68]	0.3530	
Geographic Region									
Asia	96	43 (44.8)	55.29 [30.86; -]	96	38 (39.6)	Not reached [27.14; -]	1.07 [0.69; 1.65]	0.7665	0.419
Rest of World	105	44 (41.9)	89.43 [56.71; -]	103	29 (28.2)	117.14 [76.71; -]	1.27 [0.80; 2.04]	0.3151	
Western Europe/Israel/North America/Australia	97	40 (41.2)	118.00 [27.57; -]	96	41 (42.7)	Not reached [22.43; -]	0.87 [0.56; 1.34]	0.5270	
Chemotherapy Regimen									
CAPOX	251	113 (45.0)	62.14 [39.86; 102.00]	253	101 (39.9)	117.14 [39.00; -]	1.00 [0.77; 1.31]	0.9830	0.199
FP	47	14 (29.8)	90.14 [90.14; -]	42	7 (16.7)	Not reached [-; -]	1.91 [0.77; 4.74]	0.1618	

a: Database Cutoff Date: 29MAR2023

b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)

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)

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

Tabelle 4G-58: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	**Pembrolizumab + Trastuzumab + FP or CAPOX**			**Placebo + Trastuzumab + FP or CAPOX**			**Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX**		
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-Value for Interaction Test[f]**
SOC[g]: Endocrine disorders									
Sex									
Male	240	34 (14.2)	Not reached [-; -]	236	15 (6.4)	Not reached [-; -]	1.98 [1.08; 3.65]	0.027	0.801
Female	58	17 (29.3)	Not reached [61.7; -]	59	7 (11.9)	Not reached [-; -]	2.46 [1.02; 5.93]	0.045	
Age									
< 65 years	174	30 (17.2)	Not reached [-; -]	164	15 (9.1)	Not reached [-; -]	1.63 [0.87; 3.03]	0.125	0.243
≥ 65 years	124	21 (16.9)	Not reached [-; -]	131	7 (5.3)	Not reached [-; -]	3.01 [1.28; 7.08]	0.012	
ECOG Performance Status									
0	127	21 (16.5)	Not reached [-; -]	121	5 (4.1)	Not reached [-; -]	3.57 [1.34; 9.47]	0.011	0.151
1	171	30 (17.5)	Not reached [-; -]	174	17 (9.8)	Not reached [-; -]	1.65 [0.91; 2.99]	0.101	
Geographic Region									
Asia	96	13 (13.5)	Not reached [-; -]	96	10 (10.4)	Not reached [-; -]	1.28 [0.56; 2.93]	0.554	0.231
Rest of World	105	24 (22.9)	Not reached [-; -]	103	9 (8.7)	Not reached [114.4; -]	2.14 [0.99; 4.60]	0.053	
Western Europe/Israel/North America/Australia	97	14 (14.4)	Not reached [-; -]	96	3 (3.1)	Not reached [-; -]	4.34 [1.25; 15.10]	0.021	
Chemotherapy Regimen									
CAPOX	251	48 (19.1)	Not reached [-; -]	253	20 (7.9)	Not reached [-; -]	2.20 [1.31; 3.71]	0.003	0.573
FP	47	3 (6.4)	Not reached [-; -]	42	2 (4.8)	114.4 [114.4; -]	2.48 [0.26; 24.09]	0.433	
SOC[g]: Infections and infestations									
Sex									
Male	240	113 (47.1)	53.3 [42.3; 80.0]	236	62 (26.3)	112.9 [105.1; 161.1]	1.85 [1.36; 2.52]	< 0.001	0.402
Female	58	26 (44.8)	73.7 [40.4; 115.3]	59	17 (28.8)	71.7 [41.7; -]	1.29 [0.70; 2.40]	0.417	
Age									
< 65 years	174	86 (49.4)	64.6 [37.9; 94.1]	164	40 (24.4)	112.9 [105.1; -]	2.02 [1.39; 2.94]	< 0.001	0.320
≥ 65 years	124	53 (42.7)	57.7 [41.9; 84.6]	131	39 (29.8)	85.3 [56.6; -]	1.52 [1.00; 2.30]	0.051	

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]
ECOG Performance Status									
0	127	62 (48.8)	66.6 [36.1; 84.6]	121	31 (25.6)	110.4 [76.1; -]	2.05 [1.33; 3.17]	0.001	0.406
1	171	77 (45.0)	57.7 [42.3; 115.3]	174	48 (27.6)	149.1 [76.7; -]	1.58 [1.10; 2.27]	0.013	
Geographic Region									
Asia	96	39 (40.6)	79.4 [42.3; -]	96	21 (21.9)	161.1 [110.4; -]	2.08 [1.22; 3.54]	0.007	0.542
Rest of World	105	47 (44.8)	78.6 [48.0; 103.1]	103	27 (26.2)	112.9 [76.1; -]	1.36 [0.84; 2.18]	0.209	
Western Europe/Israel/North America/Australia	97	53 (54.6)	34.3 [23.1; 66.6]	96	31 (32.3)	60.9 [43.3; -]	1.85 [1.18; 2.89]	0.007	
Chemotherapy Regimen									
CAPOX	251	121 (48.2)	53.3 [43.1; 80.0]	253	67 (26.5)	112.9 [85.3; -]	1.81 [1.35; 2.45]	< 0.001	0.495
FP	47	18 (38.3)	64.6 [34.3; -]	42	12 (28.6)	111.3 [43.3; -]	1.61 [0.74; 3.53]	0.231	
SOC[g]: Renal and urinary disorders									
Sex									
Male	240	32 (13.3)	Not reached [-; -]	236	12 (5.1)	Not reached [-; -]	2.52 [1.30; 4.90]	0.006	0.974
Female	58	6 (10.3)	Not reached [-; -]	59	2 (3.4)	Not reached [-; -]	2.07 [0.41; 10.45]	0.380	
Age									
< 65 years	174	23 (13.2)	Not reached [-; -]	164	9 (5.5)	Not reached [-; -]	2.21 [1.02; 4.79]	0.045	0.593
≥ 65 years	124	15 (12.1)	Not reached [-; -]	131	5 (3.8)	Not reached [-; -]	3.01 [1.09; 8.28]	0.033	
ECOG Performance Status									
0	127	15 (11.8)	Not reached [-; -]	121	6 (5.0)	Not reached [-; -]	2.12 [0.82; 5.48]	0.120	0.648
1	171	23 (13.5)	Not reached [-; -]	174	8 (4.6)	Not reached [-; -]	2.77 [1.24; 6.21]	0.013	
Geographic Region									
Asia	96	9 (9.4)	Not reached [-; -]	96	4 (4.2)	Not reached [-; -]	2.29 [0.71; 7.44]	0.168	0.869
Rest of World	105	12 (11.4)	Not reached [121.6; -]	103	3 (2.9)	Not reached [-; -]	3.06 [0.86; 10.91]	0.085	
Western Europe/Israel/North America/Australia	97	17 (17.5)	Not reached [-; -]	96	7 (7.3)	Not reached [107.6; -]	2.23 [0.92; 5.38]	0.076	
Chemotherapy Regimen									
CAPOX	251	30 (12.0)	Not reached [-; -]	253	12 (4.7)	Not reached [-; -]	2.31 [1.18; 4.51]	0.015	0.609
FP	47	8 (17.0)	Not reached [69.6; -]	42	2 (4.8)	Not reached [-; -]	3.47 [0.74; 16.37]	0.116	

a: Database Cutoff Date: 29MAR2023
b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)
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

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]
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 ≥10% or (incidence ≥1% and in at least 10 participants) in one or more treament 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									
5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU; SOC: System Organ Class									

Tabelle 4G-59: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für PT aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]
SOC: Blood and lymphatic system disorders - PT[g]: Leukopenia									
Sex									
Male	240	6 (2.5)	Not reached [-; -]	236	15 (6.4)	Not reached [-; -]	0.37 [0.14; 0.95]	0.038	0.356
Female	58	5 (8.6)	Not reached [-; -]	59	6 (10.2)	Not reached [106.1; -]	0.69 [0.21; 2.30]	0.543	
Age									
< 65 years	174	6 (3.4)	Not reached [-; -]	164	8 (4.9)	Not reached [-; -]	0.63 [0.22; 1.83]	0.399	0.455
≥ 65 years	124	5 (4.0)	Not reached [-; -]	131	13 (9.9)	Not reached [-; -]	0.37 [0.13; 1.04]	0.059	
ECOG Performance Status									
0	127	6 (4.7)	Not reached [-; -]	121	8 (6.6)	Not reached [-; -]	0.64 [0.22; 1.84]	0.405	0.443
1	171	5 (2.9)	Not reached [-; -]	174	13 (7.5)	Not reached [-; -]	0.37 [0.13; 1.03]	0.057	
Geographic Region									
Asia	96	1 (1.0)	Not reached [-; -]	96	3 (3.1)	Not reached [-; -]	0.31 [0.03; 3.02]	0.315	0.365
Rest of World	105	9 (8.6)	Not reached [-; -]	103	12 (11.7)	Not reached [-; -]	0.63 [0.26; 1.49]	0.292	
Western Europe/Israel/North America/Australia	97	1 (1.0)	Not reached [-; -]	96	6 (6.3)	Not reached [-; -]	0.16 [0.02; 1.31]	0.087	
Chemotherapy Regimen									
CAPOX	251	10 (4.0)	Not reached [-; -]	253	18 (7.1)	Not reached [-; -]	0.51 [0.23; 1.10]	0.088	0.623
FP	47	1 (2.1)	Not reached [-; -]	42	3 (7.1)	Not reached [-; -]	0.29 [0.03; 2.77]	0.281	

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]
SOC: Endocrine disorders - PT[g]: Hypothyroidism									
Sex									
Male	240	21 (8.8)	Not reached [-; -]	236	7 (3.0)	Not reached [-; -]	2.62 [1.11; 6.16]	0.028	0.910
Female	58	11 (19.0)	Not reached [-; -]	59	4 (6.8)	Not reached [-; -]	2.73 [0.87; 8.60]	0.085	
Age									
< 65 years	174	19 (10.9)	Not reached [-; -]	164	7 (4.3)	Not reached [-; -]	2.17 [0.91; 5.18]	0.081	0.579
≥ 65 years	124	13 (10.5)	Not reached [-; -]	131	4 (3.1)	Not reached [-; -]	3.22 [1.05; 9.88]	0.041	
ECOG Performance Status									
0	127	14 (11.0)	Not reached [-; -]	121	4 (3.3)	Not reached [-; -]	2.90 [0.95; 8.81]	0.061	0.766
1	171	18 (10.5)	Not reached [-; -]	174	7 (4.0)	Not reached [-; -]	2.36 [0.98; 5.66]	0.054	
Geographic Region									
Asia	96	8 (8.3)	Not reached [-; -]	96	6 (6.3)	Not reached [-; -]	1.30 [0.45; 3.75]	0.627	0.224
Rest of World	105	16 (15.2)	Not reached [-; -]	103	4 (3.9)	Not reached [114.4; -]	3.18 [1.06; 9.52]	0.039	
Western Europe/Israel/North America/Australia	97	8 (8.2)	Not reached [-; -]	96	1 (1.0)	Not reached [-; -]	7.22 [0.90; 57.80]	0.063	
SOC: General disorders and administration site conditions - PT[g]: Asthenia									
Sex									
Male	240	30 (12.5)	Not reached [-; -]	236	43 (18.2)	Not reached [-; -]	0.63 [0.39; 1.00]	0.051	0.957
Female	58	9 (15.5)	Not reached [-; -]	59	12 (20.3)	Not reached [-; -]	0.65 [0.27; 1.55]	0.331	
Age									
< 65 years	174	22 (12.6)	Not reached [-; -]	164	31 (18.9)	Not reached [-; -]	0.61 [0.35; 1.05]	0.072	0.756
≥ 65 years	124	17 (13.7)	Not reached [-; -]	131	24 (18.3)	Not reached [-; -]	0.69 [0.37; 1.28]	0.241	
ECOG Performance Status									
0	127	15 (11.8)	Not reached [-; -]	121	24 (19.8)	Not reached [-; -]	0.52 [0.27; 1.00]	0.049	0.428
1	171	24 (14.0)	Not reached [-; -]	174	31 (17.8)	Not reached [-; -]	0.73 [0.43; 1.25]	0.252	
Geographic Region									
Asia	96	2 (2.1)	Not reached [-; -]	96	3 (3.1)	Not reached [-; -]	0.66 [0.11; 3.96]	0.651	0.899
Rest of World	105	14 (13.3)	Not reached [-; -]	103	18 (17.5)	Not reached [-; -]	0.70 [0.35; 1.41]	0.315	
Western Europe/Israel/North America/Australia	97	23 (23.7)	Not reached [-; -]	96	34 (35.4)	Not reached [41.7; -]	0.56 [0.33; 0.95]	0.031	

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		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]	
Chemotherapy Regimen									
CAPOX	251	26 (10.4)	Not reached [-; -]	253	40 (15.8)	Not reached [-; -]	0.60 [0.37; 0.99]	0.043	0.941
FP	47	13 (27.7)	Not reached [56.0; -]	42	15 (35.7)	Not reached [3.9; -]	0.62 [0.30; 1.31]	0.213	
SOC: Nervous system disorders - PT[g]: Polyneuropathy									
Sex									
Male	240	2 (0.8)	Not reached [-; -]	236	10 (4.2)	Not reached [-; -]	0.18 [0.04; 0.82]	0.027	0.565
Female	58	0 (0.0)	Not reached [-; -]	59	1 (1.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.317	
Age									
< 65 years	174	1 (0.6)	n.c.	164	4 (2.4)	n.c.	n.c.	n.c.	n.c.
≥ 65 years	124	1 (0.8)	n.c.	131	7 (5.3)	n.c.	n.c.	n.c.	
ECOG Performance Status									
0	127	0 (0.0)	Not reached [-; -]	121	3 (2.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.069	0.266
1	171	2 (1.2)	Not reached [-; -]	174	8 (4.6)	Not reached [-; -]	0.23 [0.05; 1.10]	0.066	
Geographic Region									
Asia	96	0 (0.0)	Not reached [-; -]	96	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	0.710
Rest of World	105	2 (1.9)	Not reached [-; -]	103	9 (8.7)	Not reached [-; -]	0.18 [0.04; 0.86]	0.031	
Western Europe/Israel/North America/Australia	97	0 (0.0)	Not reached [-; -]	96	2 (2.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.147	
Chemotherapy Regimen									
CAPOX	251	2 (0.8)	Not reached [-; -]	253	11 (4.3)	Not reached [-; -]	0.17 [0.04; 0.76]	0.021	0.998
FP	47	0 (0.0)	Not reached [-; -]	42	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
SOC: Psychiatric disorders - PT[g]: Depression									
Sex									
Male	240	1 (0.4)	Not reached [-; -]	236	9 (3.8)	Not reached [-; -]	0.10 [0.01; 0.78]	0.028	0.051
Female	58	2 (3.4)	Not reached [-; -]	59	1 (1.7)	Not reached [-; -]	1.92 [0.17; 21.15]	0.595	
Age									
< 65 years	174	1 (0.6)	n.c.	164	5 (3.0)	n.c.	n.c.	n.c.	n.c.
≥ 65 years	124	2 (1.6)	n.c.	131	5 (3.8)	n.c.	n.c.	n.c.	

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]**
ECOG Performance Status									
0	127	2 (1.6)	n.c.	121	5 (4.1)	n.c.	n.c.	n.c.	n.c.
1	171	1 (0.6)	n.c.	174	5 (2.9)	n.c.	n.c.	n.c.	
Geographic Region									
Asia	96	0 (0.0)	n.c.	96	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	105	3 (2.9)	n.c.	103	2 (1.9)	n.c.	n.c.	n.c.	
Western Europe/Israel/North America/Australia	97	0 (0.0)	n.c.	96	8 (8.3)	n.c.	n.c.	n.c.	
Chemotherapy Regimen									
CAPOX	251	3 (1.2)	Not reached [-; -]	253	8 (3.2)	Not reached [-; -]	0.34 [0.09; 1.28]	0.111	0.261
FP	47	0 (0.0)	Not reached [-; -]	42	2 (4.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.120	
SOC: Respiratory, thoracic and mediastinal disorders - PT[g]: Pneumonitis									
Sex									
Male	240	18 (7.5)	Not reached [-; -]	236	2 (0.8)	Not reached [-; -]	8.19 [1.90; 35.30]	0.005	0.651
Female	58	1 (1.7)	Not reached [-; -]	59	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.309	
Age									
< 65 years	174	9 (5.2)	Not reached [-; -]	164	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.006	0.143
≥ 65 years	124	10 (8.1)	Not reached [-; -]	131	2 (1.5)	Not reached [-; -]	4.96 [1.09; 22.62]	0.039	
ECOG Performance Status									
0	127	7 (5.5)	Not reached [-; -]	121	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.014	0.208
1	171	12 (7.0)	Not reached [-; -]	174	2 (1.1)	Not reached [-; -]	5.71 [1.28; 25.53]	0.023	
Geographic Region									
Asia	96	4 (4.2)	Not reached [-; -]	96	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.051	0.603
Rest of World	105	9 (8.6)	Not reached [-; -]	103	1 (1.0)	Not reached [-; -]	7.66 [0.97; 60.50]	0.053	
Western Europe/Israel/North America/Australia	97	6 (6.2)	Not reached [-; -]	96	1 (1.0)	Not reached [-; -]	5.51 [0.66; 45.85]	0.114	
Chemotherapy Regimen									
CAPOX	251	17 (6.8)	Not reached [-; -]	253	2 (0.8)	Not reached [-; -]	7.82 [1.81; 33.86]	0.006	0.531
FP	47	2 (4.3)	Not reached [-; -]	42	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.182	

a: Database Cutoff Date: 29MAR2023
b: Number of participants: all-participants-as-treated population (Global Cohort - CPS>=1 Participants)
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

Study: KEYNOTE 811[a]	Pembrolizumab + Trastuzumab + FP or CAPOX			Placebo + Trastuzumab + FP or CAPOX			Pembrolizumab + Trastuzumab + FP or CAPOX vs. Placebo + Trastuzumab + FP or CAPOX		
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-Value for Interaction Test[f]

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 ≥10% or (incidence ≥1% and in at least 10 participants) in one or more treament 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

5-FU: 5-Fluorouracil; CAPOX: Oxaliplatin plus Capecitabine; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; FP: Cisplatin plus 5-FU; 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); PT: Preferred Term; SOC: System Organ Class

Anhang 4-G6: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT

Tabelle 4G-60 Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT in der Studie KEYNOTE 811

AEOSI	**Preferred Terms**	**Immune-mediated (Yes/No)**
Pneumonitis	Acute interstitial pneumonitis Autoimmune lung disease Interstitial lung disease Pneumonitis Idiopathic pneumonia syndrome Organising pneumonia Immune-mediated lung disease	Yes
Colitis	Colitis Colitis microscopic Enterocolitis Enterocolitis haemorrhagic Necrotising colitis Colitis erosive Autoimmune colitis Immune-mediated enterocolitis	Yes
Hepatitis	Hepatitis Immune-mediated hepatitis Autoimmune hepatitis Hepatitis acute Hepatitis fulminant Drug-induced liver injury	Yes

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	Yes
Adrenal Insufficiency	Adrenal insufficiency Adrenocortical insufficiency acute Secondary adrenocortical insufficiency Primary adrenal insufficiency Addison's disease Immune-mediated adrenal insufficiency	Yes
Hypophysitis	Hypophysitis Hypopituitarism Lymphocytic hypophysitis Immune-mediated hypophysitis	Yes
Hyperthyroidism	Hyperthyroidism Basedow's disease Thyrotoxic crisis Immune-mediated hyperthyroidism	Yes
Hypothyroidism	Hypothyroidism Hypothyroidic goitre Myxoedema Myxoedema coma Primary hypothyroidism Autoimmune hypothyroidism Immune-mediated hypothyroidism	Yes
Thyroiditis	Thyroid disorder Thyroiditis Autoimmune thyroiditis Thyroiditis acute Silent thyroiditis Autoimmune thyroid disorder Immune-mediated thyroiditis	Yes

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	Yes
Skin Reactions or Severe Skin Reactions (CTCAE-Grade 3-5)*	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 Rash* Rash erythematous* Rash maculo-papular* Rash pruritic* Rash pustular* Pruritus* Pruritus genital* Lichen planus* Oral lichen planus* Cutaneous vasculitis* Vasculitic rash*	Yes
Uveitis	Iritis Uveitis Cyclitis Autoimmune uveitis Iridocyclitis Vogt-Koyanagi-Harada disease Chorioretinitis Choroiditis Immune-mediated uveitis Choroidal effusion Choroidal detachment Serous retinal detachment	Yes

Pancreatitis	Pancreatitis Autoimmune pancreatitis Pancreatitis acute Pancreatitis haemorrhagic Pancreatitis necrotising Immune-mediated pancreatitis	Yes
Myositis	Myositis Necrotising myositis Polymyositis Immune-mediated myositis Rhabdomyolysis Myopathy Dermatomyositis Autoimmune myositis	Yes
Guillain-Barre Syndrome	Demyelinating polyneuropathy Guillain-Barre syndrome Axonal neuropathy Multifocal motor neuropathy Polyneuropathy idiopathic progressive Miller Fisher syndrome Subacute inflammatory demyelinating polyneuropathy	Yes
Myocarditis	Myocarditis Autoimmune myocarditis Hypersensitivity myocarditis Immune-mediated myocarditis	Yes
Encephalitis	Encephalitis Encephalitis autoimmune Limbic encephalitis Noninfective encephalitis Immune-mediated encephalitis	Yes
Sarcoidosis	Sarcoidosis Cutaneous sarcoidosis Ocular sarcoidosis Pulmonary sarcoidosis Sarcoidosis of lymph node	Yes
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	No

Myasthenic Syndrome	Myasthenic syndrome Myasthenia gravis Myasthenia gravis crisis Ocular myasthenia	Yes
Myelitis	Myelitis Myelitis transverse Acute necrotising myelitis	Yes
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	Yes
Cholangitis Sclerosing	Cholangitis sclerosing Autoimmune cholangitis Immune-mediated cholangitis	Yes
Hypoparathyroidism	Hypoparathyroidism Primary hypoparathyroidism	Yes