Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4 A Anhang 4-G

Behandlung des primär fortgeschrittenen oder rezidivierenden Endometriumkarzinoms

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

Stand: 14.11.2024

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Anhang 4-G1: Ergänzende Analysen

Anhang 4-G1.1 Ergänzende Darstellung der Ergebnisse zu den Endpunkten Zeit bis zum Ansprechen, Dauer und Auswertung des Ansprechens

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.4 die Ergebnisse zu den Ergänzenden Morbiditätsendpunkten Zeit bis zum Ansprechen, Dauer und Auswertung des Ansprechens tabellarisch dargestellt.

Alle Ergebnisse beziehen sich auf den Datenschnitt des Regulatory Update Reports (18. August 2023).

Tabelle 4G-1: Ergebnisse für die Endpunkte Zeit bis zum Ansprechen, Dauer und Auswertung des Ansprechens aus RCT mit dem zu bewertenden Arzneimittel

Response Evaluation	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo		
	n	%	95% CI[a]	n	%	95% CI[a]
Participants in population	319			334		
Complete Response (CR)	62	19.4	(15.2, 24.2)	33	9.9	(6.9, 13.6)
Partial Response (PR)	178	55.8	(50.2, 61.3)	176	52.7	(47.2, 58.2)
Overall Response (CR+PR)	**240**	**75.2**	**(70.1, 79.9)**	**209**	**62.6**	**(57.1, 67.8)**
Stable Disease (SD)	33	10.3	(7.2, 14.2)	71	21.3	(17.0, 26.0)
Disease Control (CR+PR+SD≥8Weeks)	**268**	**84.0**	**(79.5, 87.9)**	**273**	**81.7**	**(77.2, 85.7)**
Clinical Benefit (CR+PR+ SD≥23Weeks)	**253**	**79.3**	**(74.4, 83.6)**	**231**	**69.2**	**(63.9, 74.1)**
Progressive Disease (PD)	20	6.3	(3.9, 9.5)	22	6.6	(4.2, 9.8)
NE	2	0.6	(0.1, 2.2)	3	0.9	(0.2, 2.6)
No Assessment	24	7.5	(4.9, 11.0)	29	8.7	(5.9, 12.2)

[a] Based on binomial exact confidence interval method.
Non-evaluable: Post-baseline assessment(s) available, but not evaluable.
No Assessment: No post-baseline assessment available for response evaluation.
Patients who enter the study with no measurable disease are excluded from the calculation.
Database Cutoff Date: 18AUG2023

Anhang 4-G1.2 Behandlungs- und Beobachtungsdauer

Tabelle 4G-2: Behandlungs- und Beobachtungsdauer

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab	Paclitaxel + Carboplatin + Placebo
Duration of Treatment (months)[b]		
N[c]	391	388
Mean (SD)	9.6 (6.4)	6.1 (4.3)
Median (Q1; Q3)	8.3 (5.1; 13.6)	5.5 (3.5; 7.4)
Min; Max	0.0; 24.2	0.0; 22.8
Observation Period		
Overall Survival (months)[d]		
N[e]	408	411
Mean (SD)	16.6 (9.1)	15.4 (8.8)
Median (Q1; Q3)	14.7 (10.6; 22.0)	14.2 (9.0; 20.9)
Min; Max	0.0; 44.7	0.0; 44.3
Progression-Free Survival (months)[f]		
N[e]	408	411
Mean (SD)	13.2 (8.9)	10.1 (7.1)
Median (Q1; Q3)	11.2 (6.9; 17.2)	8.5 (5.9; 12.0)
Min; Max	0.0; 44.7	0.0; 44.3
Adverse Events (months)[g]		
N[c]	391	388
Mean (SD)	10.4 (6.3)	7.1 (4.3)
Median (Q1; Q3)	8.8 (6.0; 14.0)	6.5 (4.5; 8.4)
Min; Max	0.2; 25.1	0.9; 23.8
Serious Adverse Events (months)[g]		
N[c]	391	388
Mean (SD)	11.6 (6.1)	8.9 (4.4)
Median (Q1; Q3)	10.4 (7.3; 14.5)	8.2 (6.4; 10.3)
Min; Max	0.2; 26.9	0.9; 25.7
FACT Questionnaire (months)[h]		
N[i]	268	266
Mean (SD)	5.7 (4.4)	5.7 (4.4)
Median (Q1; Q3)	5.0 (1.4; 7.7)	4.5 (1.4; 8.0)
Min; Max	0.0; 14.6	0.0; 14.5
PROMIS Questionnaire (months)[h]		
N[i]	267	265
Mean (SD)	5.7 (4.4)	5.7 (4.4)
Median (Q1; Q3)	4.9 (1.4; 7.6)	4.5 (1.4; 8.0)
Min; Max	0.0; 14.1	0.0; 14.5

a: Database Cutoff Date: 18AUG2023 for efficacy and safety endpoints, 06DEC2022 for PRO endpoints

b: Calculated from date of first dose until date of last dose

c: Number of participants: all-participants-as-treated population

d: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date if the participant is still alive

e: Number of participants: intention-to-treat population

f: Calculated from date of randomization until the earliest of the date of first PD as determined by investigator review of radiographic disease assessment per RECIST 1.1, date of death or last known alive date

g: Adverse event follow-up duration is defined as the time from first dose to the earliest of the last dose + planned safety follow-up time, date of death, date of last contact or the database cutoff date if the participant is still alive

h: Calculated from date of first dose until date of last questionnaire assessment. For participants without post-baseline assessments, the observation period is set to 1 day

i: Number of participants: full-analysis-set population

FACT: Functional Assessment of Cancer Therapy; Max: Maximum; Min: Minimum; PROMIS: Patient Reported Outcomes Measurement Information System; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Anhang 4-G2: Rücklaufquoten des PROMIS Erschöpfung SF 7a, PROMIS Körperliche Funktionsfähigkeit SF 8c, FACT-En TOI, Belastung durch Nebenwirkungen der Krebstherapie und Neuropathie [FACT/GOG-Ntx-4]

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.3 die Rücklaufquoten des PROMIS Erschöpfung SF 7a, PROMIS Körperliche Funktionsfähigkeit SF 8c, FACT-En TOI, Belastung durch Nebenwirkungen der Krebstherapie (Single-item GP5 des FACT) und Neuropathie [FACT/GOG-Ntx-4] dargestellt.

Alle Ergebnisse beziehen sich auf den Datenschnitt der Interimsanalyse (dMMR 16. Dezember 2022, pMMR 06. Dezember 2022).

Tabelle 4G-3: Gründe für das Fehlen von Werten der FACT und PROMIS Fragebögen

		Paclitaxel + Carboplatin + Pembrolizumab N=268		Paclitaxel + Carboplatin + Placebo N=266	
Treatment Visit	Category	n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**264**	**(98.5)**	**260**	**(97.7)**
	Completed	260	(97.0)	257	(96.6)
	Compliance (% in those expected to complete questionnaires)	260	(98.5)	257	(98.8)
	Not completed	4	(1.5)	3	(1.1)
	With visit, no record	4	(1.5)	3	(1.1)
	Missing by Design	**4**	**(1.5)**	**6**	**(2.3)**
	Discontinued due to other	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	4	(1.5)	6	(2.3)
	Discontinued due to alternative therapy (in absence of progression)	0	(0.0)	0	(0.0)
	Discontinued due to patient off-treatment for other complicating disease	0	(0.0)	0	(0.0)
	Discontinued due to patient withdrawal/refusal after beginning protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to adverse event/side effects/complications	0	(0.0)	0	(0.0)
	Discontinued due to death on study	0	(0.0)	0	(0.0)
	Discontinued due to disease progression, relapse during active treatment	0	(0.0)	0	(0.0)
	Discontinued due to symptomatic deterioration	0	(0.0)	0	(0.0)
WEEK 6	**Expected to Complete Questionnaires**	**234**	**(87.3)**	**236**	**(88.7)**
	Completed	221	(82.5)	225	(84.6)
	Compliance (% in those expected to complete questionnaires)	221	(94.4)	225	(95.3)
	Not completed	13	(4.9)	11	(4.1)
	With visit, no record	13	(4.9)	11	(4.1)
	Missing by Design	**34**	**(12.7)**	**30**	**(11.3)**

Treatment Visit	Category	Paclitaxel + Carboplatin + Pembrolizumab N=268		Paclitaxel + Carboplatin + Placebo N=266	
		n	(%)	n	(%)
	Discontinued due to other	1	(0.4)	1	(0.4)
	Visit not reached	12	(4.5)	9	(3.4)
WEEK 6	Visit not scheduled	10	(3.7)	4	(1.5)
	Discontinued due to alternative therapy (in absence of progression)	0	(0.0)	2	(0.8)
	Discontinued due to patient off-treatment for other complicating disease	0	(0.0)	0	(0.0)
	Discontinued due to patient withdrawal/refusal after beginning protocol therapy	2	(0.7)	5	(1.9)
	Discontinued due to adverse event/side effects/complications	3	(1.1)	5	(1.9)
	Discontinued due to death on study	2	(0.7)	0	(0.0)
	Discontinued due to disease progression, relapse during active treatment	4	(1.5)	4	(1.5)
	Discontinued due to symptomatic deterioration	0	(0.0)	0	(0.0)
WEEK 18	**Expected to Complete Questionnaires**	**189**	**(70.5)**	**187**	**(70.3)**
	Completed	169	(63.1)	173	(65.0)
	Compliance (% in those expected to complete questionnaires)	169	(89.4)	173	(92.5)
	Not completed	20	(7.5)	14	(5.3)
	With visit, no record	20	(7.5)	14	(5.3)
	Missing by Design	**79**	**(29.5)**	**79**	**(29.7)**
	Discontinued due to other	2	(0.7)	5	(1.9)
	Visit not reached	36	(13.4)	34	(12.8)
	Visit not scheduled	9	(3.4)	5	(1.9)
	Discontinued due to alternative therapy (in absence of progression)	0	(0.0)	1	(0.4)
	Discontinued due to patient off-treatment for other complicating disease	1	(0.4)	1	(0.4)
	Discontinued due to patient withdrawal/refusal after beginning protocol therapy	5	(1.9)	6	(2.3)
	Discontinued due to adverse event/side effects/complications	11	(4.1)	6	(2.3)
	Discontinued due to death on study	3	(1.1)	2	(0.8)
	Discontinued due to disease progression, relapse during active treatment	11	(4.1)	17	(6.4)
	Discontinued due to symptomatic deterioration	1	(0.4)	2	(0.8)
WEEK 30	**Expected to Complete Questionnaires**	**133**	**(49.6)**	**129**	**(48.5)**
	Completed	124	(46.3)	114	(42.9)
	Compliance (% in those expected to complete questionnaires)	124	(93.2)	114	(88.4)
	Not completed	9	(3.4)	15	(5.6)
	With visit, no record	9	(3.4)	15	(5.6)
	Missing by Design	**135**	**(50.4)**	**137**	**(51.5)**
	Discontinued due to other	2	(0.7)	16	(6.0)
	Visit not reached	70	(26.1)	61	(22.9)

Treatment Visit	Category	Paclitaxel + Carboplatin + Pembrolizumab N=268		Paclitaxel + Carboplatin + Placebo N=266	
		n	(%)	n	(%)
	Visit not scheduled	3	(1.1)	3	(1.1)
	Discontinued due to alternative therapy (in absence of progression)	1	(0.4)	2	(0.8)
	Discontinued due to patient off-treatment for other complicating disease	2	(0.7)	1	(0.4)
	Discontinued due to patient withdrawal/refusal after beginning protocol therapy	7	(2.6)	8	(3.0)
	Discontinued due to adverse event/side effects/complications	17	(6.3)	11	(4.1)
	Discontinued due to death on study	6	(2.2)	2	(0.8)
	Discontinued due to disease progression, relapse during active treatment	26	(9.7)	31	(11.7)
	Discontinued due to symptomatic deterioration	1	(0.4)	2	(0.8)
WEEK 54	**Expected to Complete Questionnaires**	**73**	**(27.2)**	**68**	**(25.6)**
	Completed	62	(23.1)	63	(23.7)
	Compliance (% in those expected to complete questionnaires)	62	(84.9)	63	(92.6)
	Not completed	11	(4.1)	5	(1.9)
	With visit, no record	11	(4.1)	5	(1.9)
	Missing by Design	**195**	**(72.8)**	**198**	**(74.4)**
	Discontinued due to other	4	(1.5)	14	(5.3)
	Visit not reached	93	(34.7)	84	(31.6)
WEEK 54	Visit not scheduled	1	(0.4)	1	(0.4)
	Discontinued due to alternative therapy (in absence of progression)	1	(0.4)	2	(0.8)
	Discontinued due to patient off-treatment for other complicating disease	1	(0.4)	1	(0.4)
	Discontinued due to patient withdrawal/refusal after beginning protocol therapy	10	(3.7)	11	(4.1)
	Discontinued due to adverse event/side effects/complications	24	(9.0)	13	(4.9)
	Discontinued due to death on study	6	(2.2)	2	(0.8)
	Discontinued due to disease progression, relapse during active treatment	53	(19.8)	68	(25.6)
	Discontinued due to symptomatic deterioration	2	(0.7)	2	(0.8)

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

Compliance is the proportion of participants 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 participants in the analysis population (N)

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment , investigator's decision to discontinue the participant, noncompliance with study treatment or procedure requirements or administrative reasons requiring cessation of treatment), and translation not available

Database Cutoff Date: 06DEC2022

Anhang 4-G3: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest (p < 0,05)

Im Folgenden werden für Time-To-Event-Endpunkte 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.

Aufgrund der längeren Beobachtungsdauer wird der Regulatory Update Report (18. August 2023) für alle Wirksamkeitsendpunkte (außer die patientenberichteten Endpunkte zur Krankheitssymptomatik) sowie unerwünschte Ereignisse herangezogen. Für alle patientenberichteten Endpunkte wird die Interimsanalyse (dMMR 16. Dezember 2022, pMMR 06. Dezember 2022) herangezogen, da diese die längste Beobachtungsdauer für die patientenberichteten Endpunkte darstellt und zudem eine Entblindung nach dem ersten Datenschnitt (Entblindung zum 06. Februar 2023) stattfand.

Anhang 4-G3.1: Mortalität

Gesamtüberleben

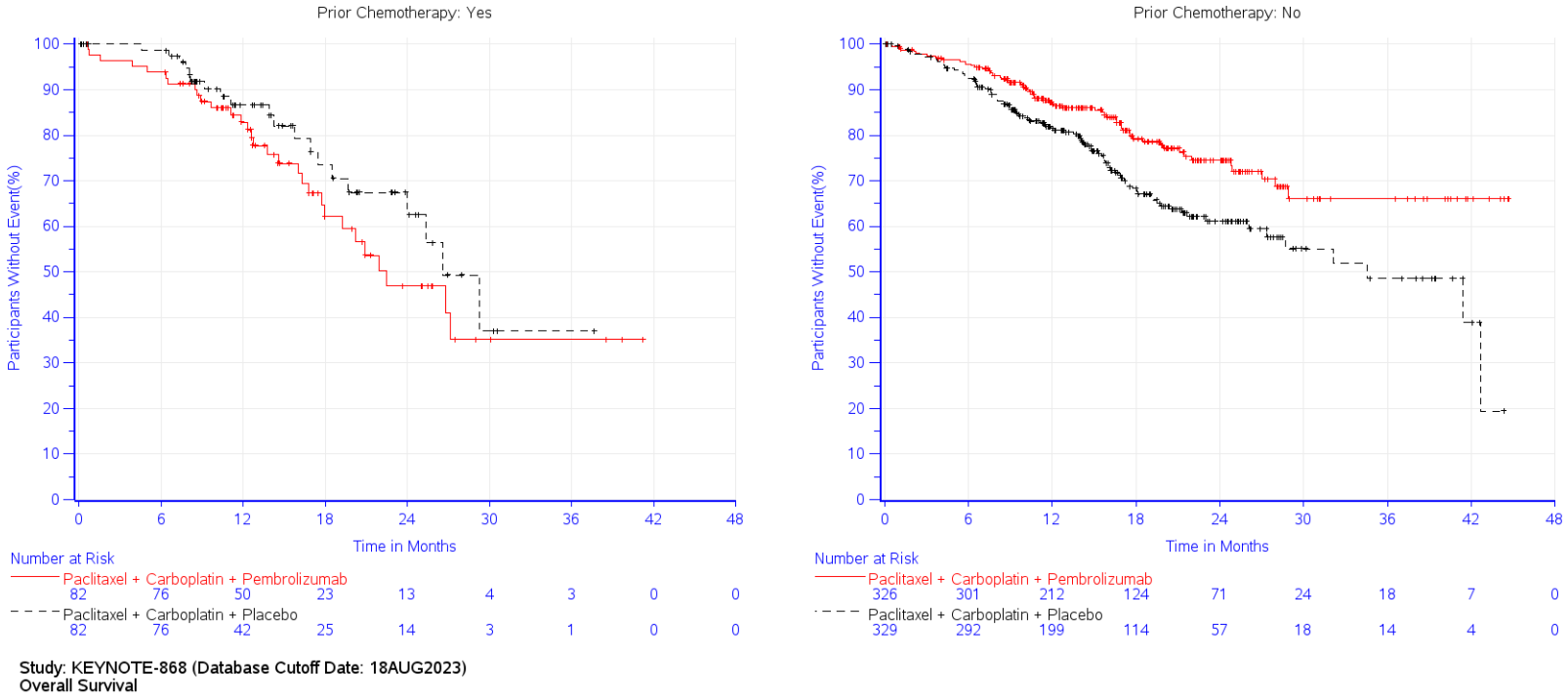


Abbildung 1: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Gesamtüberleben der Studie KEYNOTE 868

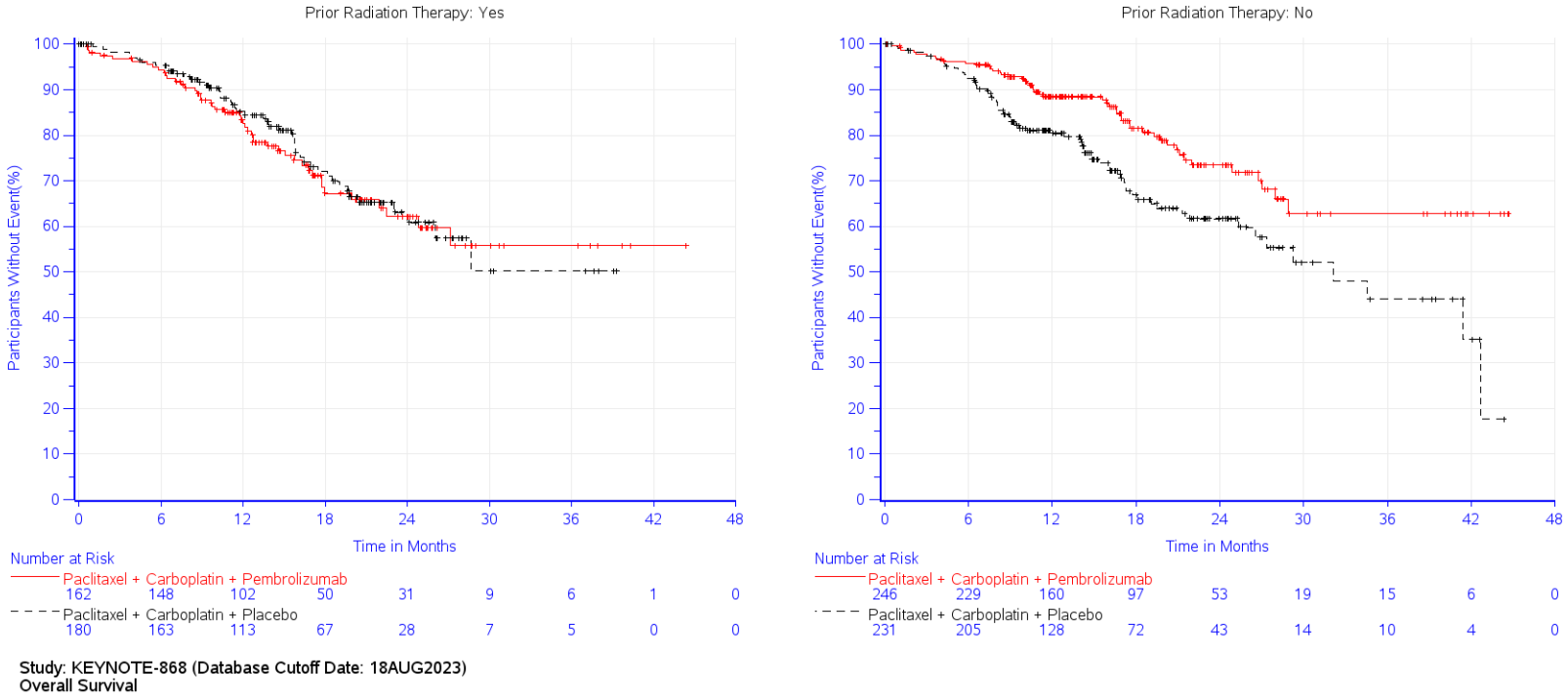


Abbildung 2: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Radiotherapie für den Endpunkt Gesamtüberleben der Studie KEYNOTE 868

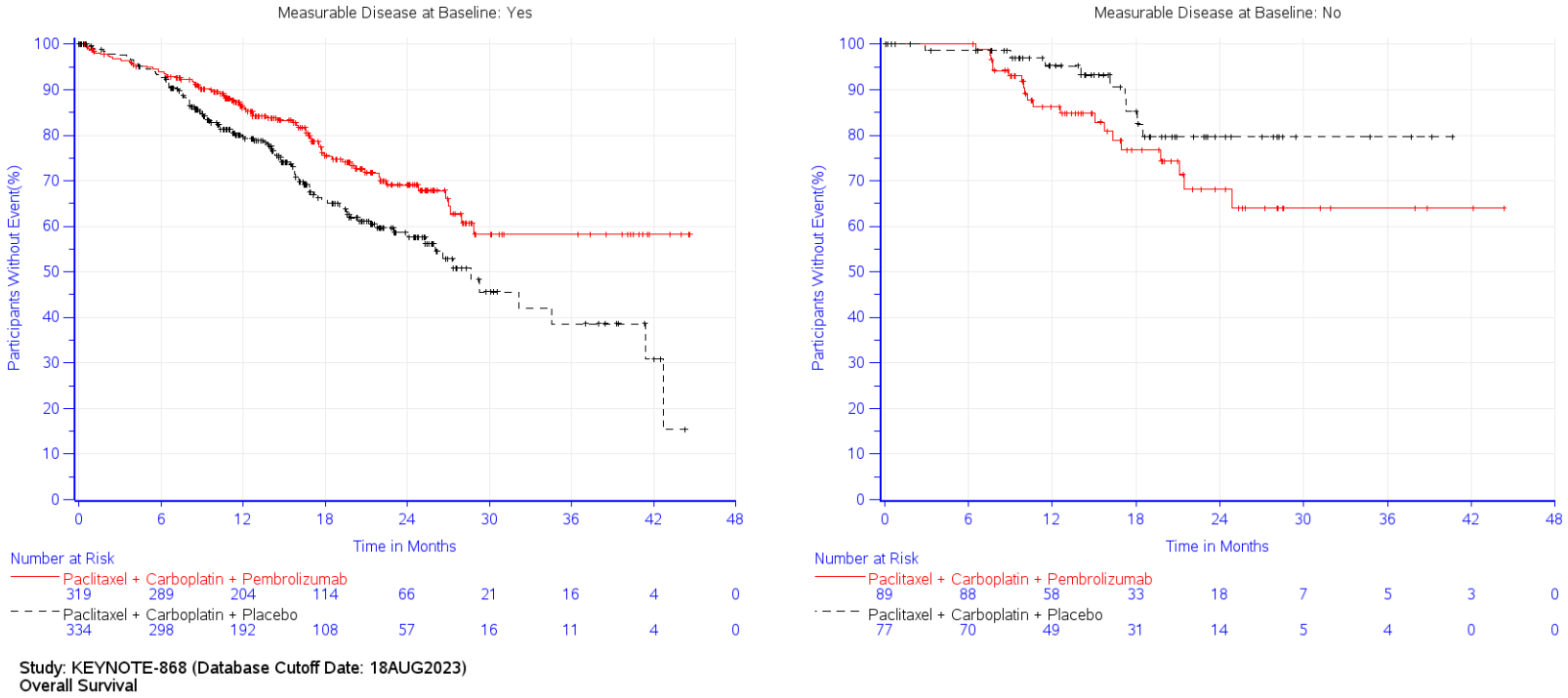


Abbildung 3: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Messbarer Erkrankung zu Baseline für den Endpunkt Gesamtüberleben der Studie KEYNOTE 868

Anhang 4-G3.2: Morbidität

Progressionsfreies Überleben

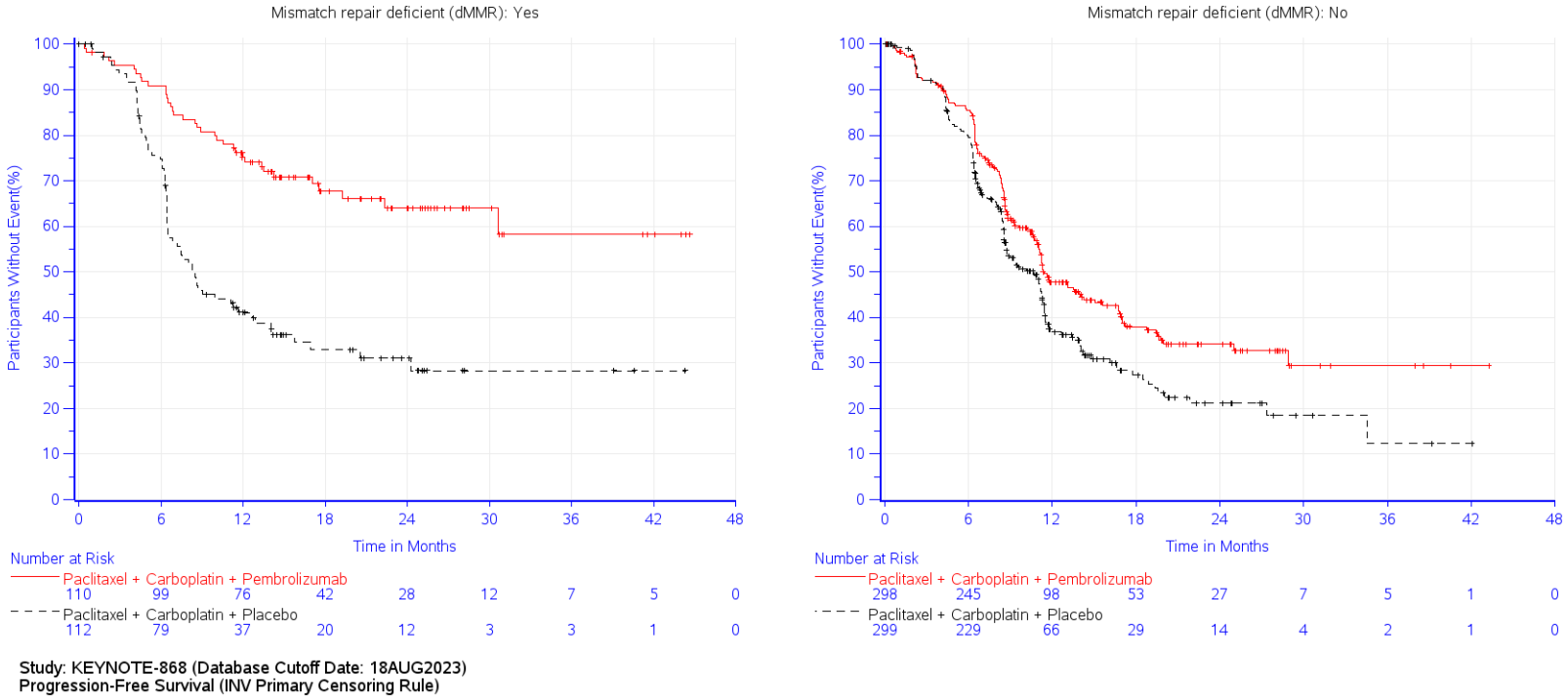


Abbildung 4: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Progressionsfreies Überleben der Studie KEYNOTE 868

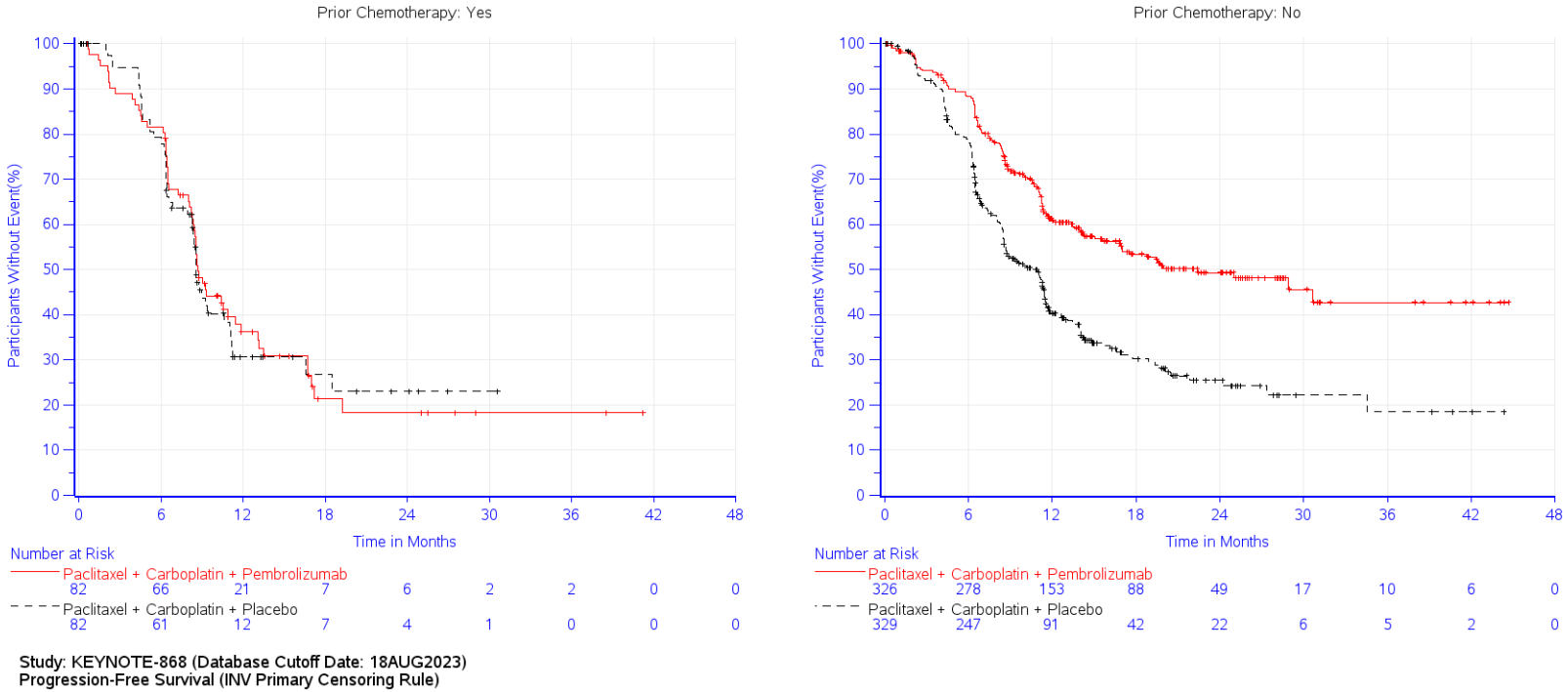


Abbildung 5: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Progressionsfreies Überleben der Studie KEYNOTE 868

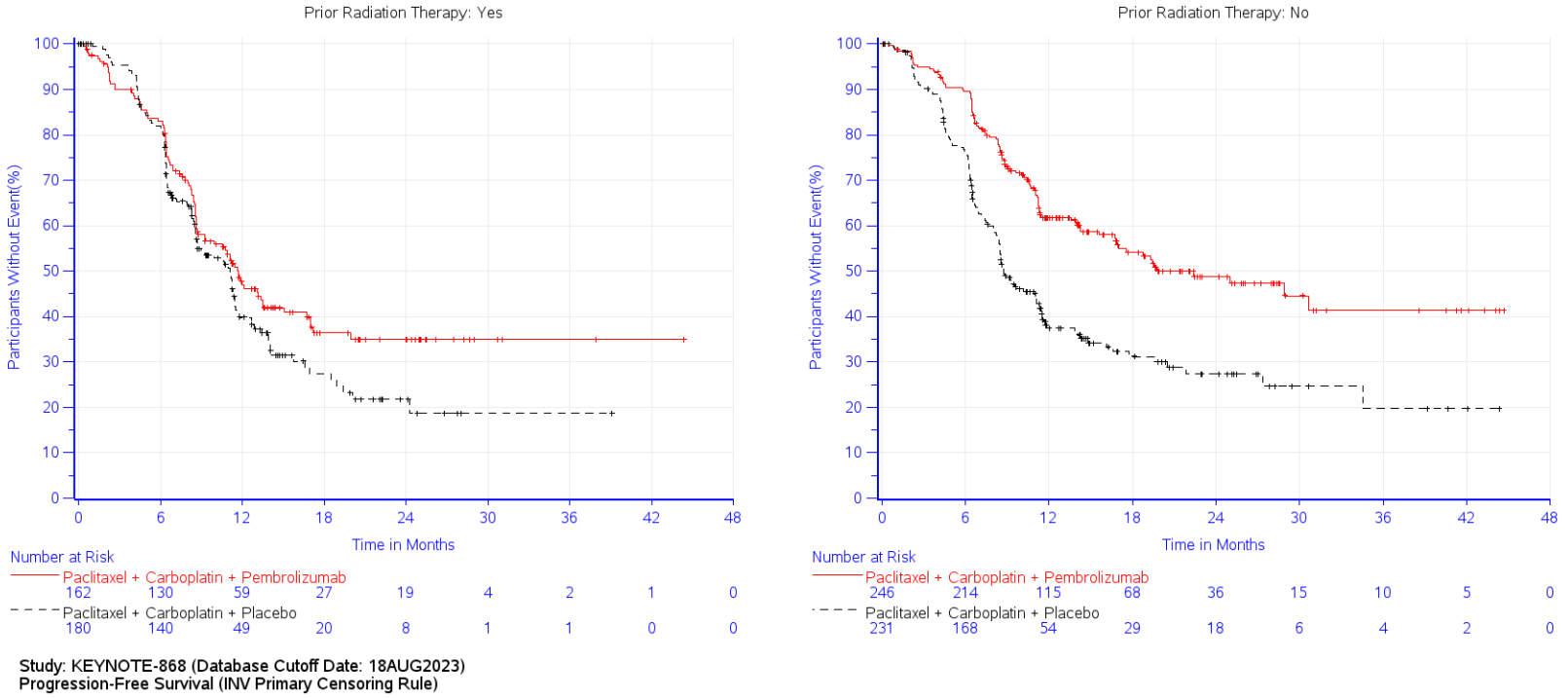


Abbildung 6: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Radiotherapie für den Endpunkt Progressionsfreies Überleben der Studie KEYNOTE 868

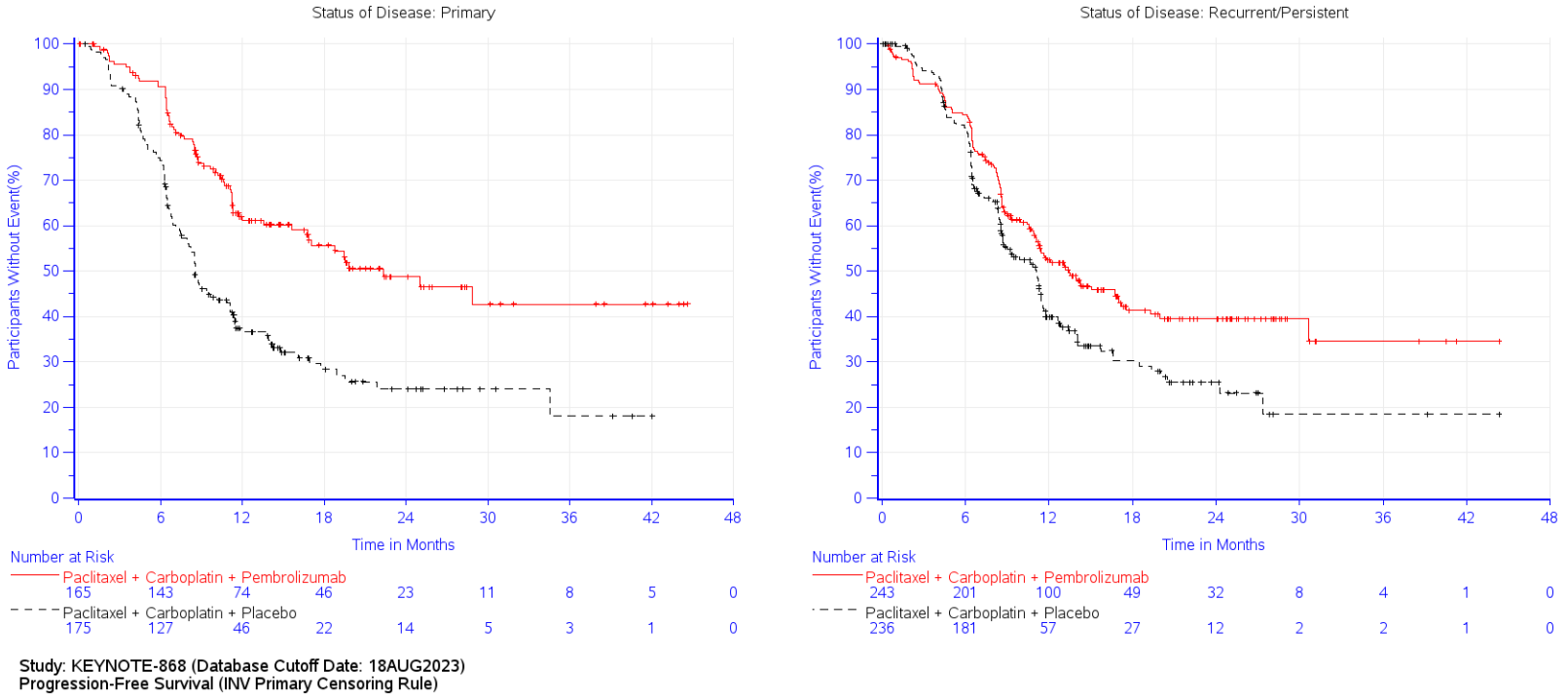


Abbildung 7: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Krankheitsstadium für den Endpunkt Progressionsfreies Überleben der Studie KEYNOTE 868

Zeit bis zur ersten Folgetherapie oder Tod

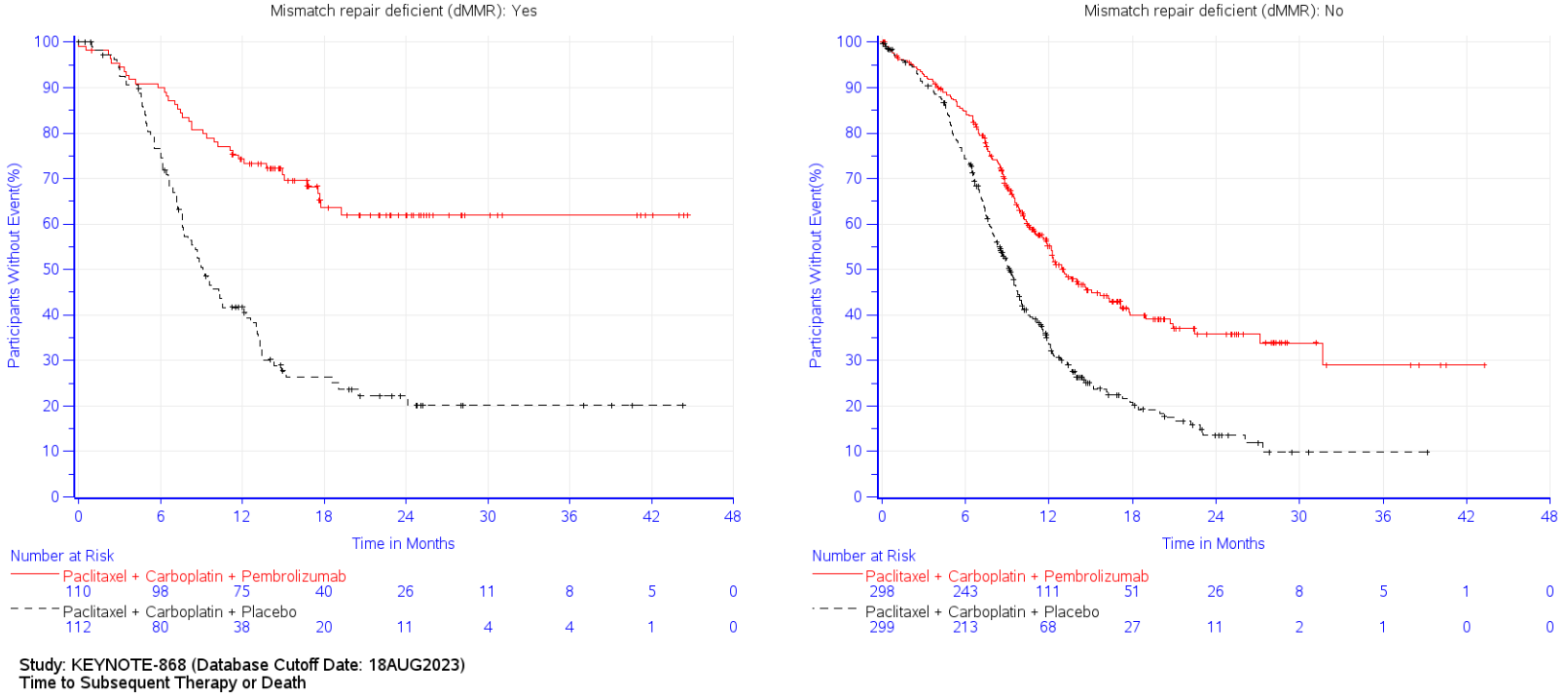


Abbildung 8: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Zeit bis zu ersten Folgetherapie oder Tod der Studie KEYNOTE 868

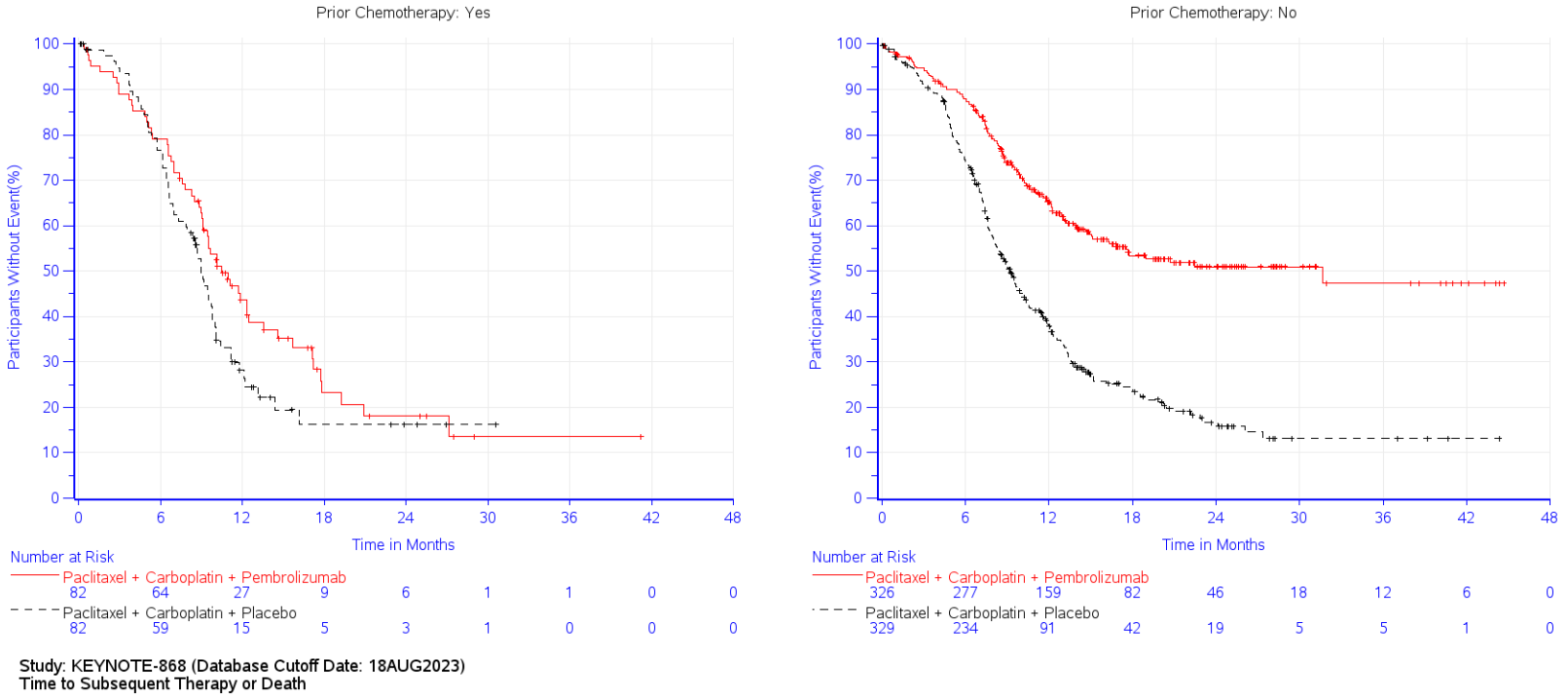


Abbildung 9: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Zeit bis zu ersten Folgetherapie oder Tod der Studie KEYNOTE 868

Anhang 4-G3.3: Nebenwirkungen

Unerwünschte Ereignisse Gesamtraten

Unerwünschte Ereignisse gesamt

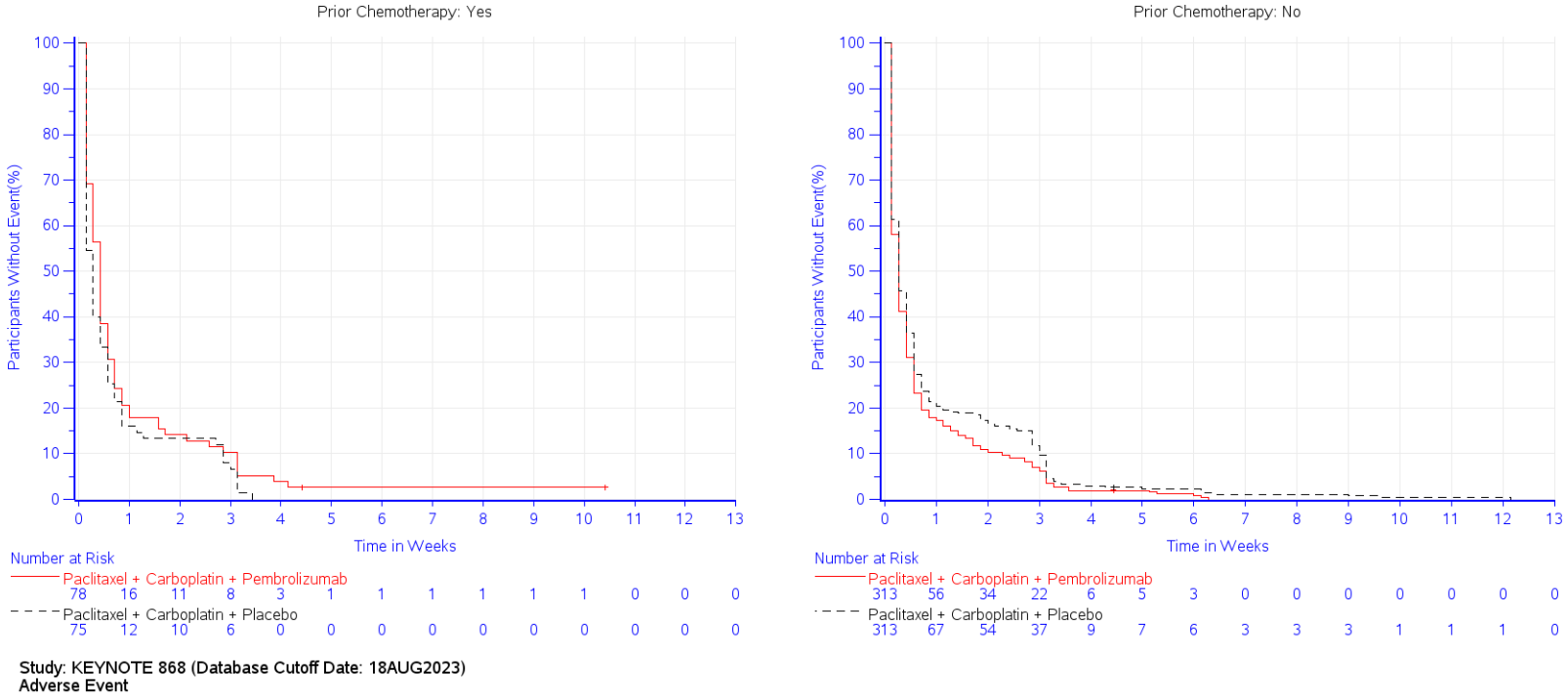


Abbildung 10: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Unerwünschte Ereignisse gesamt der Studie KEYNOTE 868

Therapieabbruch wegen unerwünschter Ereignisse/ Nebenwirkungen/ Komplikationen

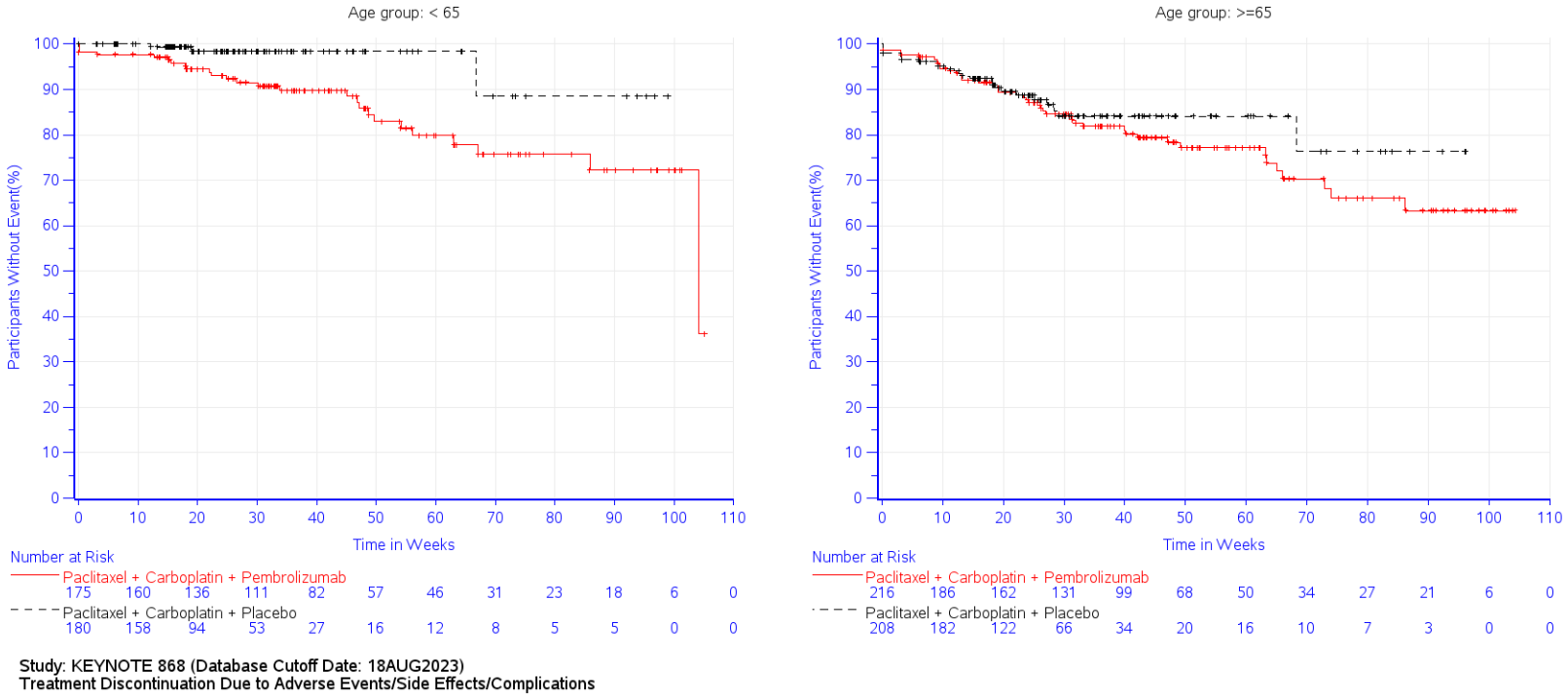


Abbildung 11: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Alter für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse/ Nebenwirkungen/ Komplikationen der Studie KEYNOTE 868

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

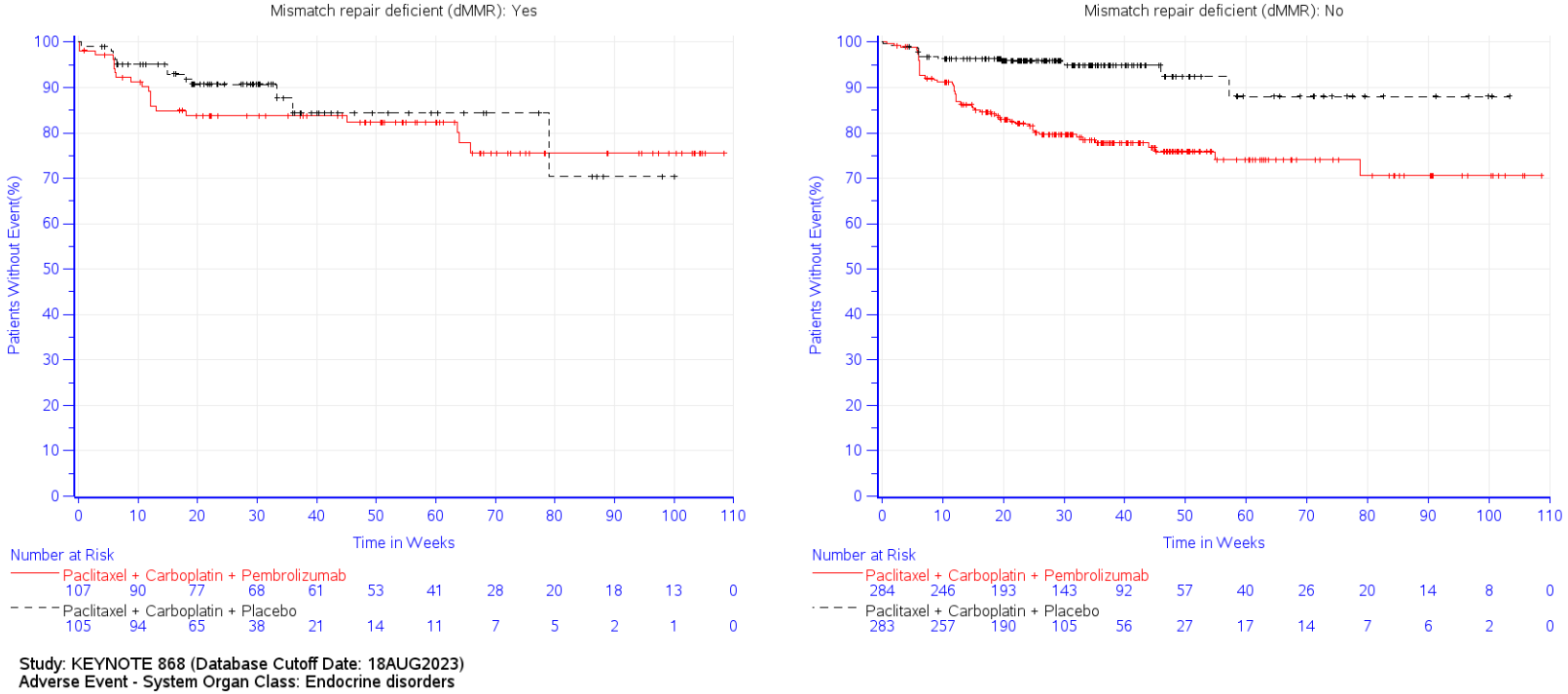


Abbildung 12: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für die SOC Endokrine Erkrankungen der Studie KEYNOTE 868

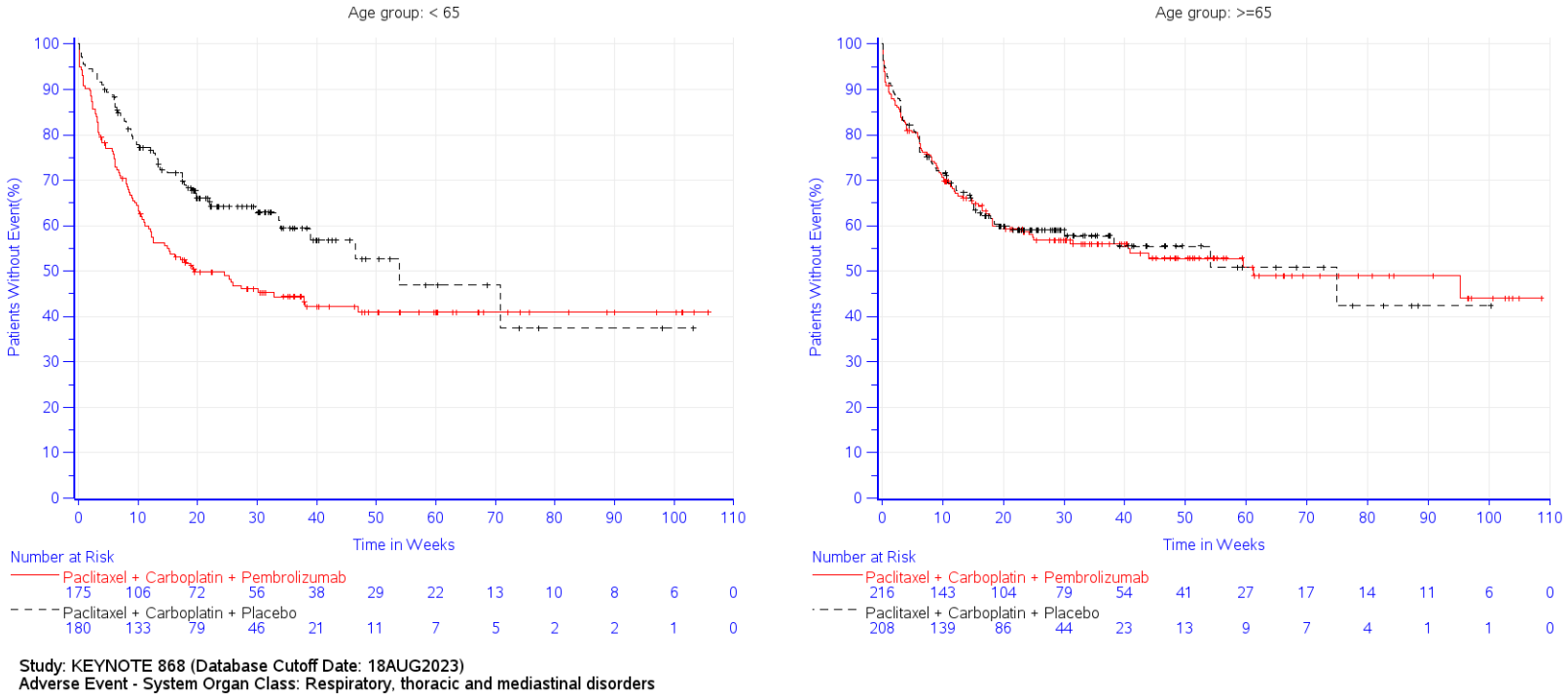


Abbildung 13: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Alter für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für die SOC Erkrankungen der Atemwege, des Brustraums und Mediastinums der Studie KEYNOTE 868

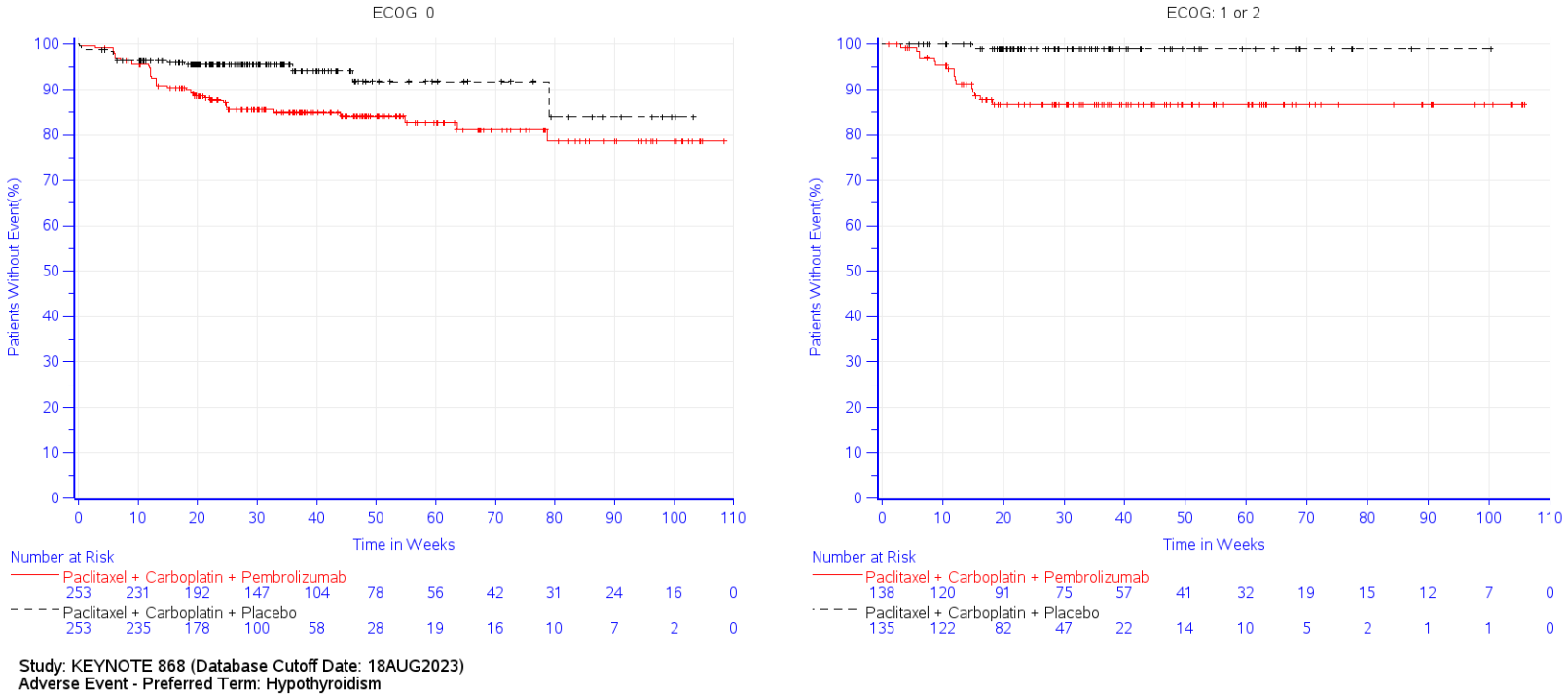


Abbildung 14: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Krankheitsschwere für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Hypothyreose der Studie KEYNOTE 868

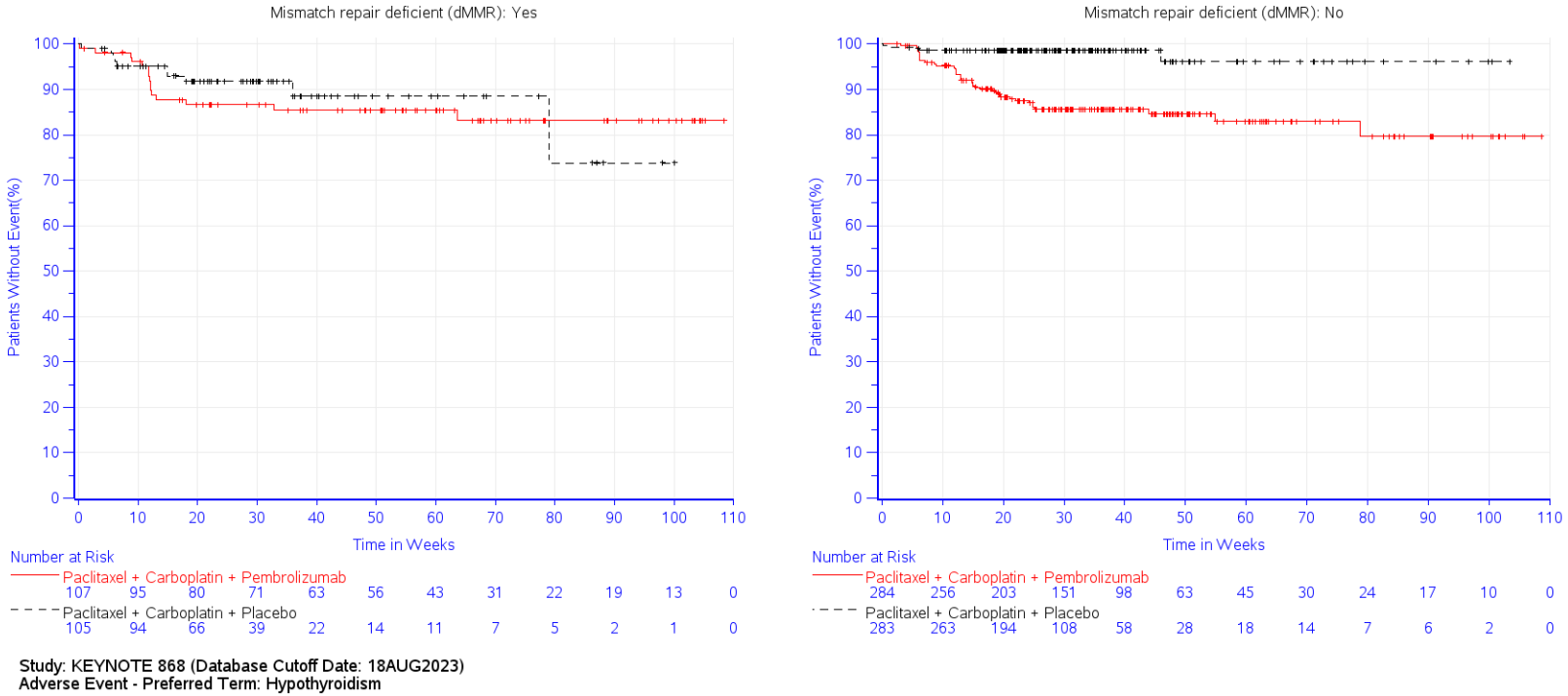


Abbildung 15: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Hypothyreose der Studie KEYNOTE 868

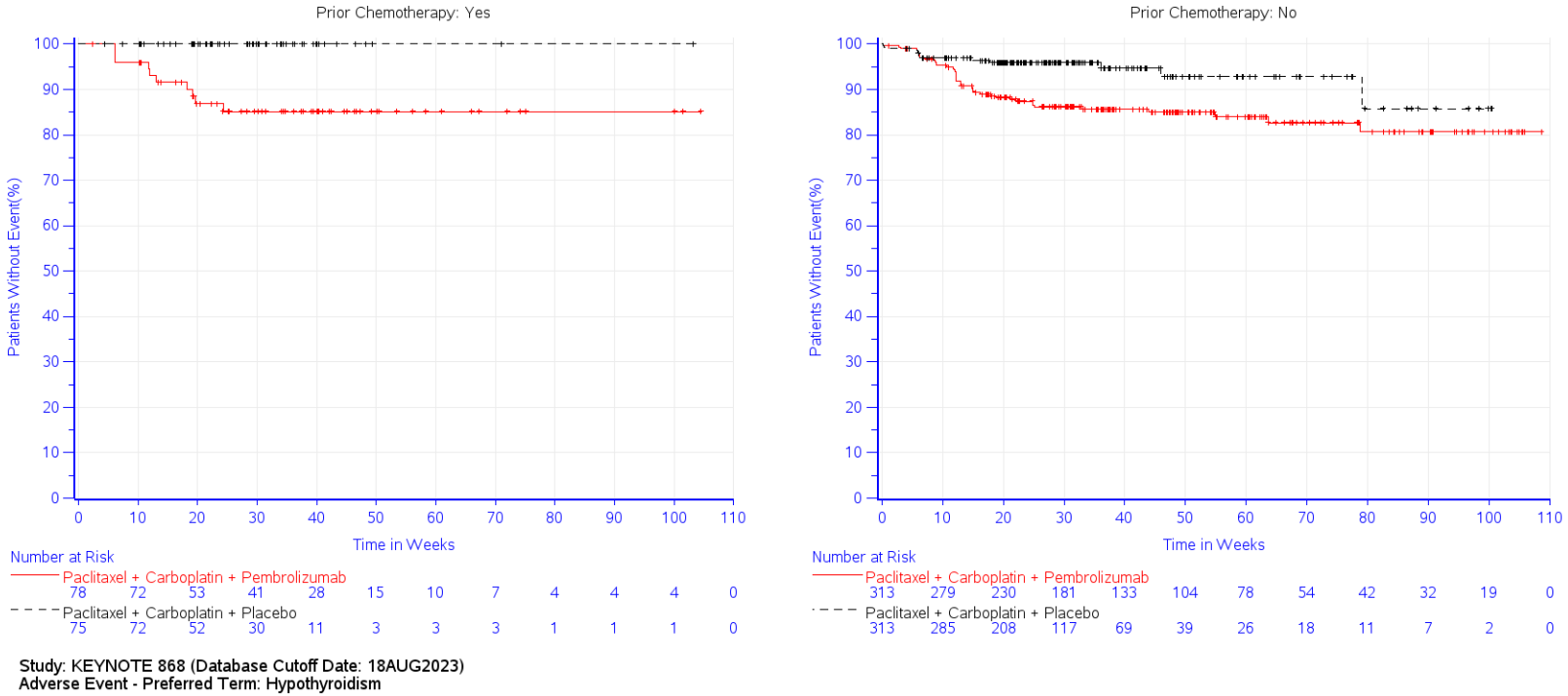


Abbildung 16: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Hypothyreose der Studie KEYNOTE 868

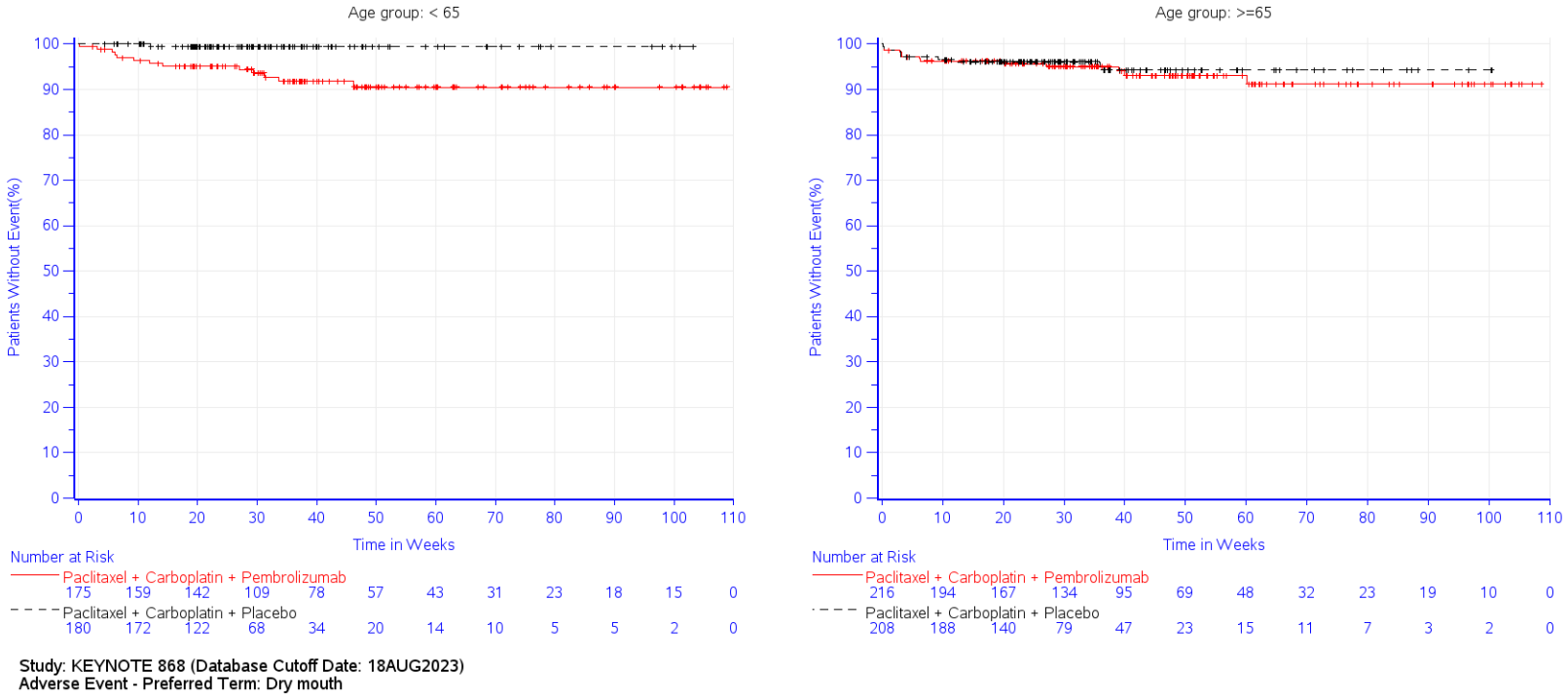


Abbildung 17: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Alter für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Mundtrockenheit der Studie KEYNOTE 868

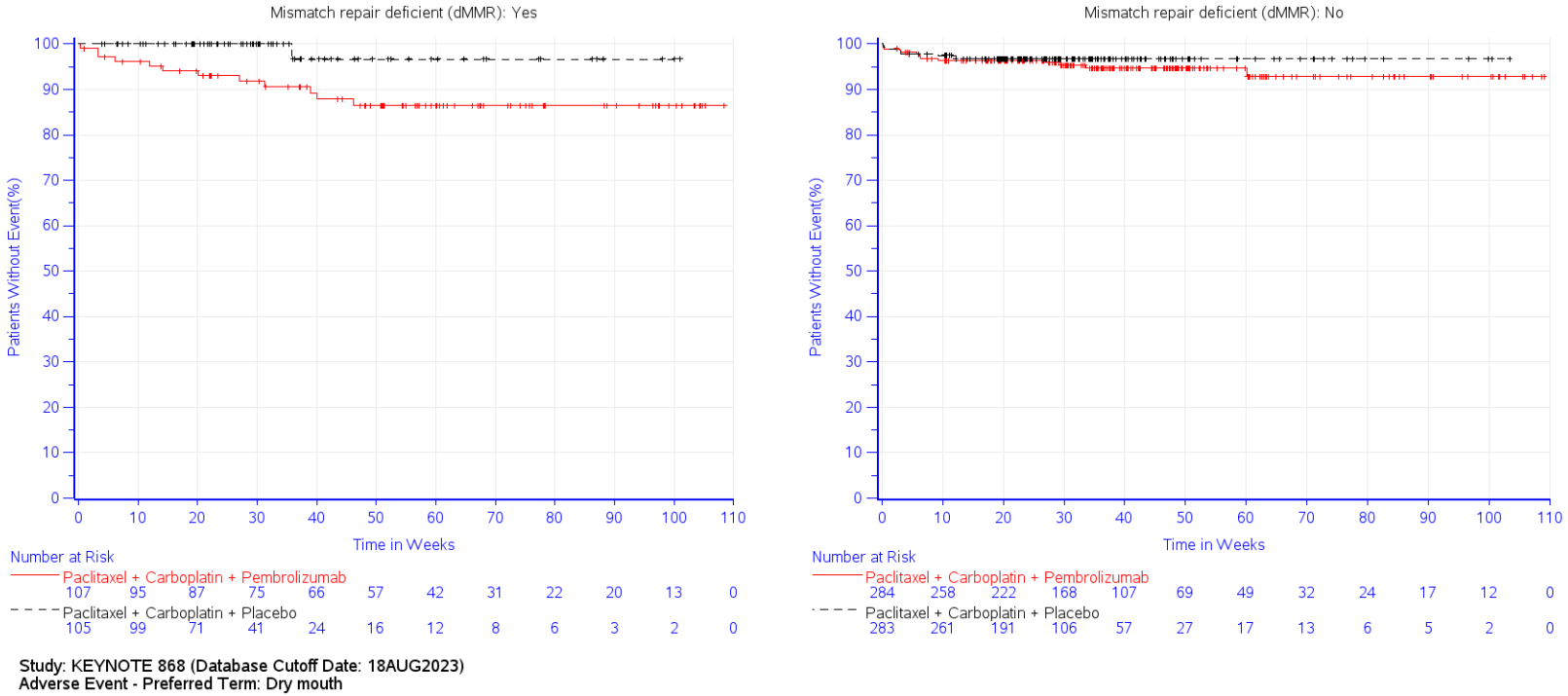


Abbildung 18: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Mundtrockenheit der Studie KEYNOTE 868

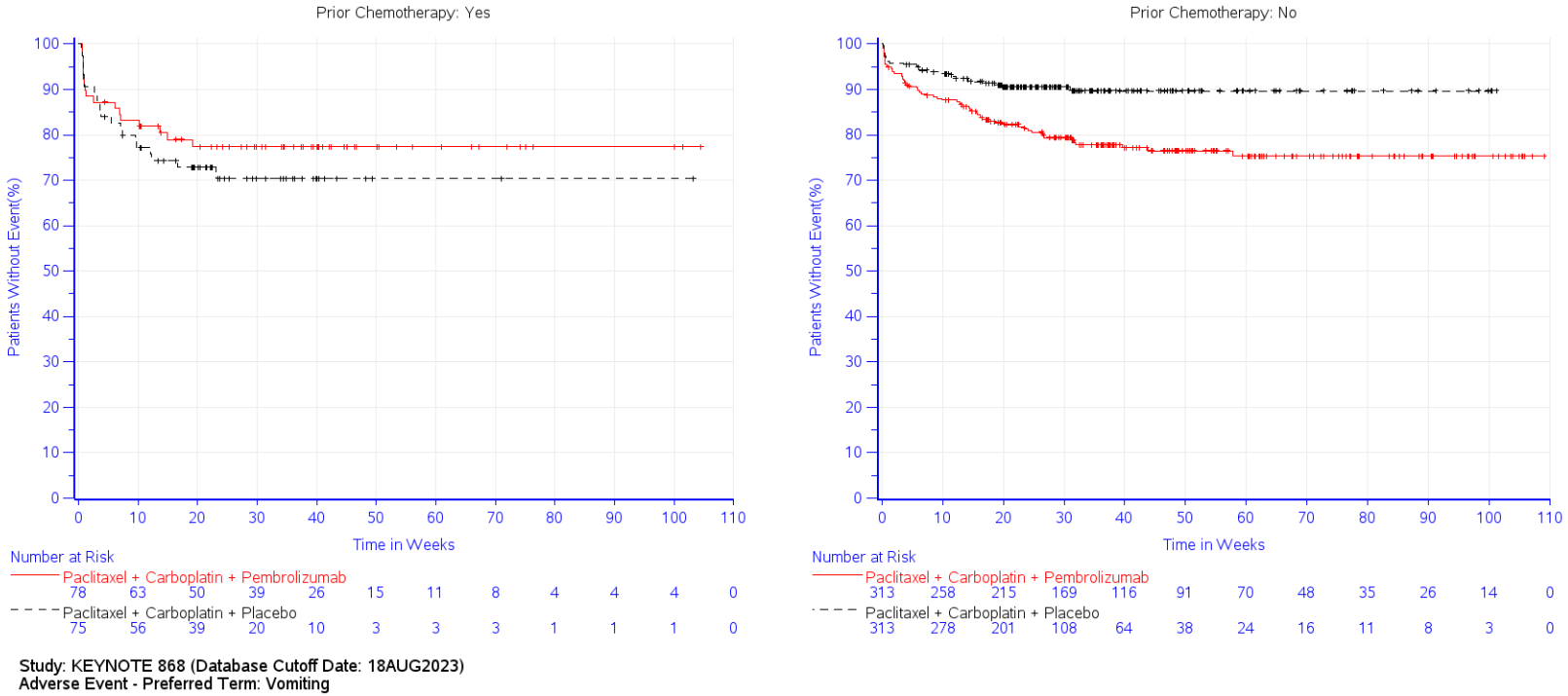


Abbildung 19: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Vorangegangener Chemotherapie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Erbrechen der Studie KEYNOTE 868

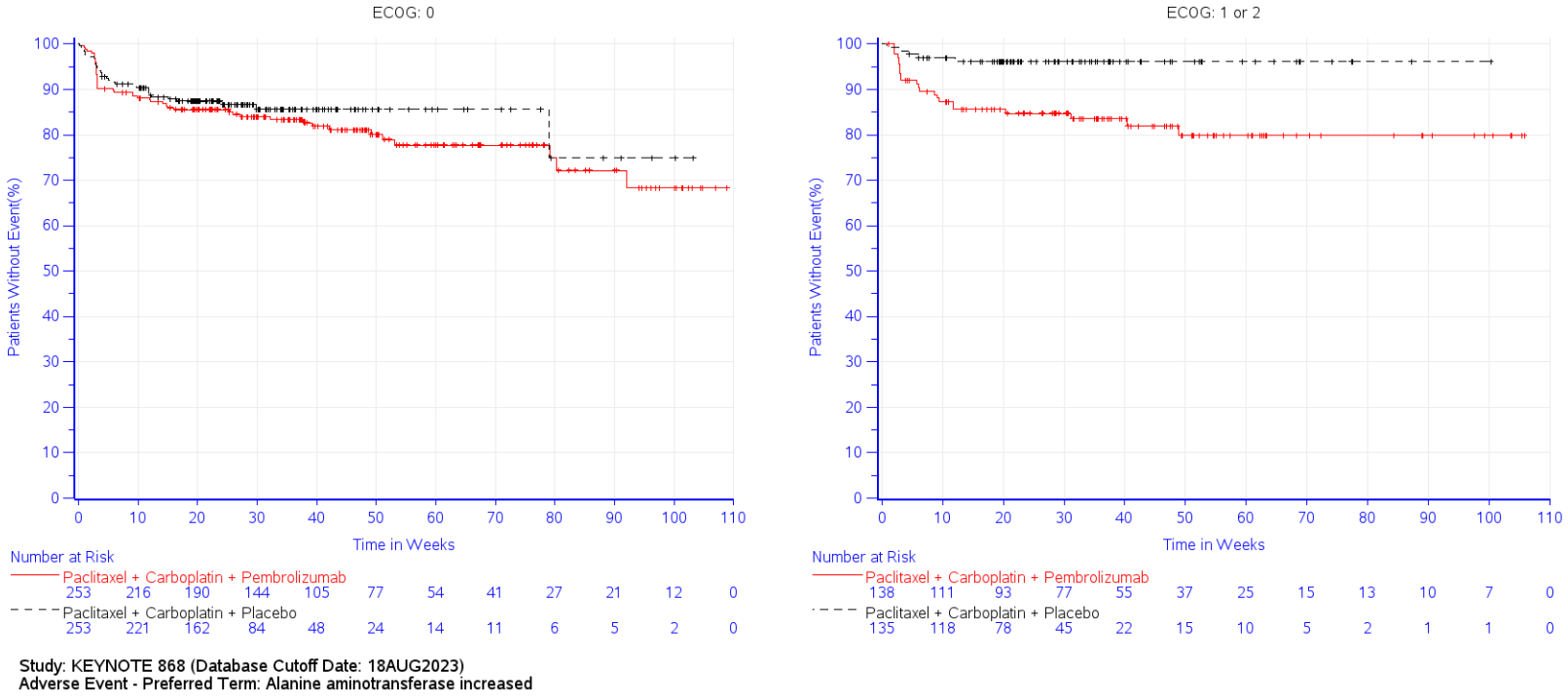


Abbildung 20: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Krankheitsschwere für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Alaninaminotransferase erhöht der Studie KEYNOTE 868

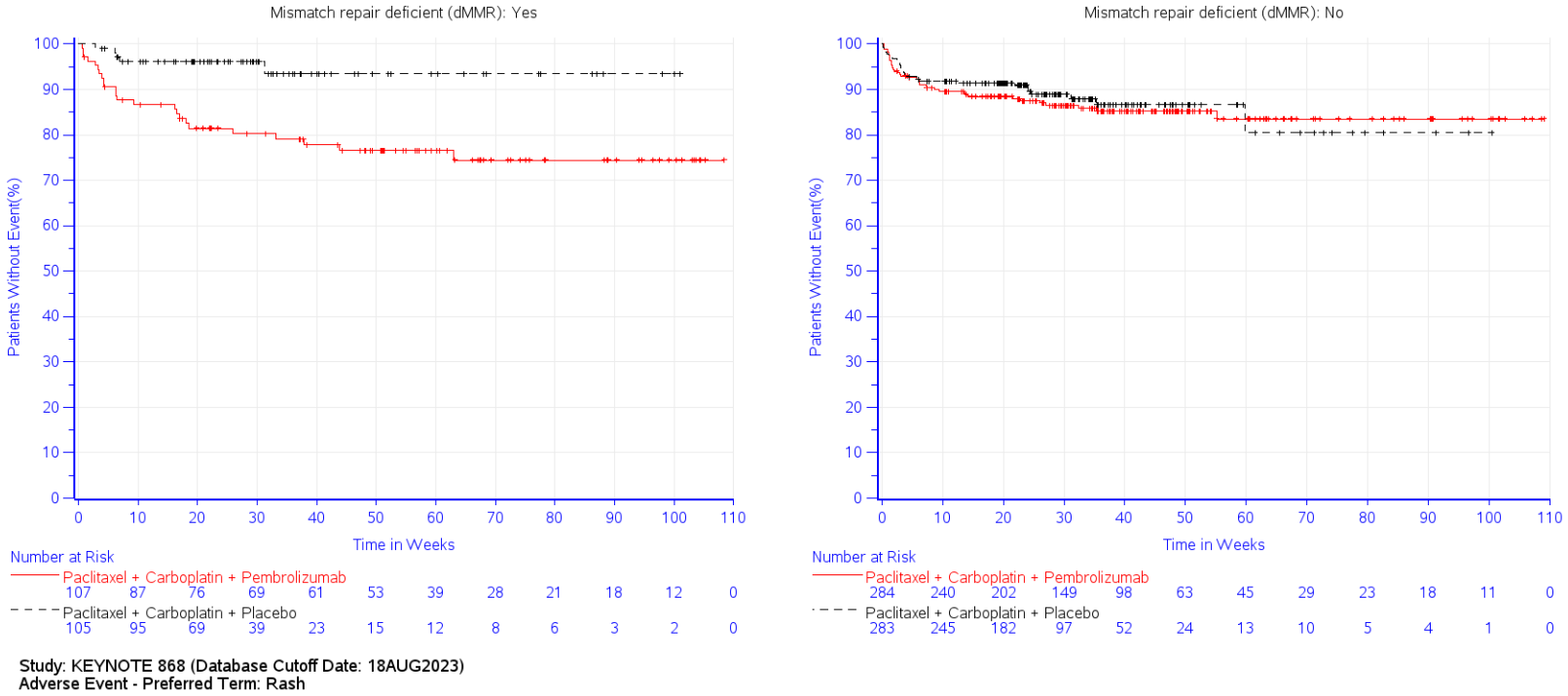


Abbildung 21: Kaplan-Meier-Kurven für die Subgruppenanalyse nach MMR-Status für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Ausschlag der Studie KEYNOTE 868

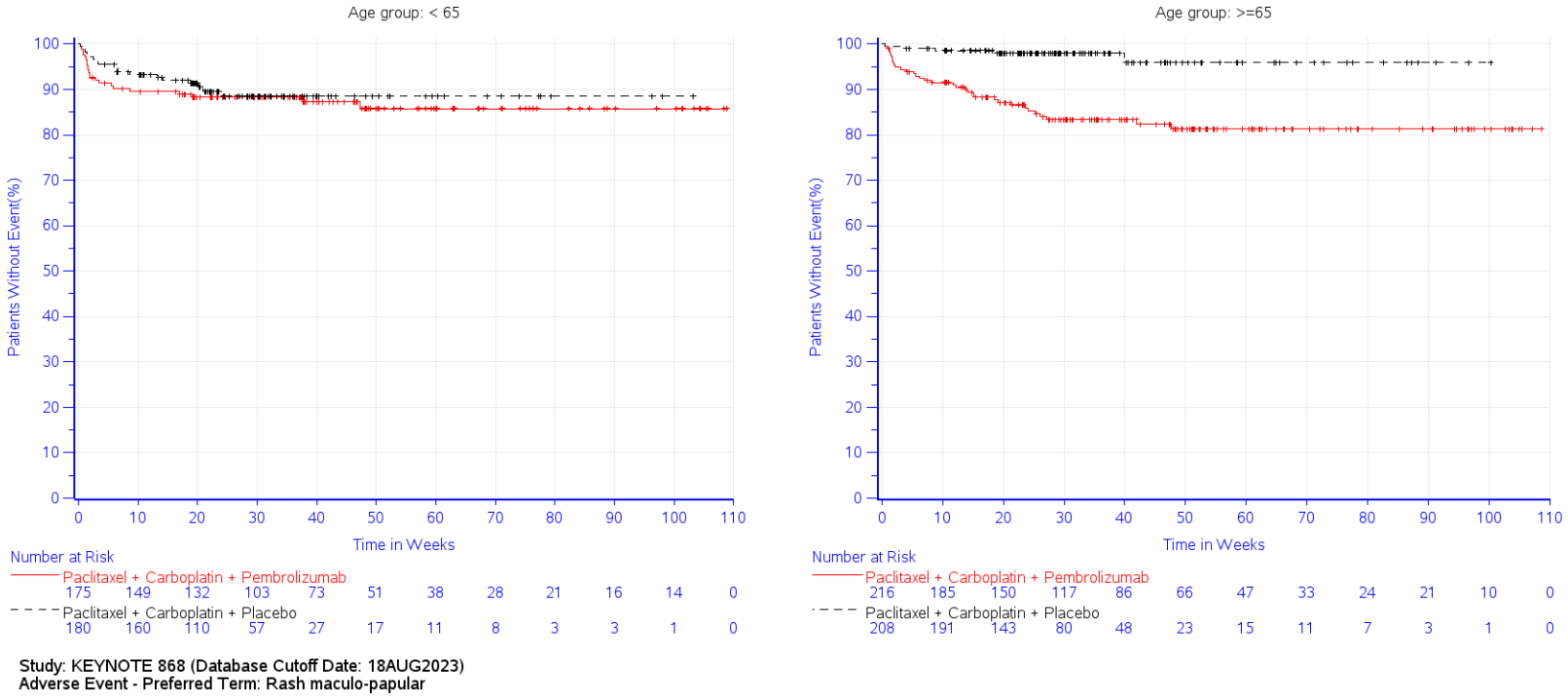


Abbildung 22: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Alter für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für den PT Ausschlag makulo-papulös der Studie KEYNOTE 868

Schwerwiegende unerwünschte Ereignisse (SOC und PT)

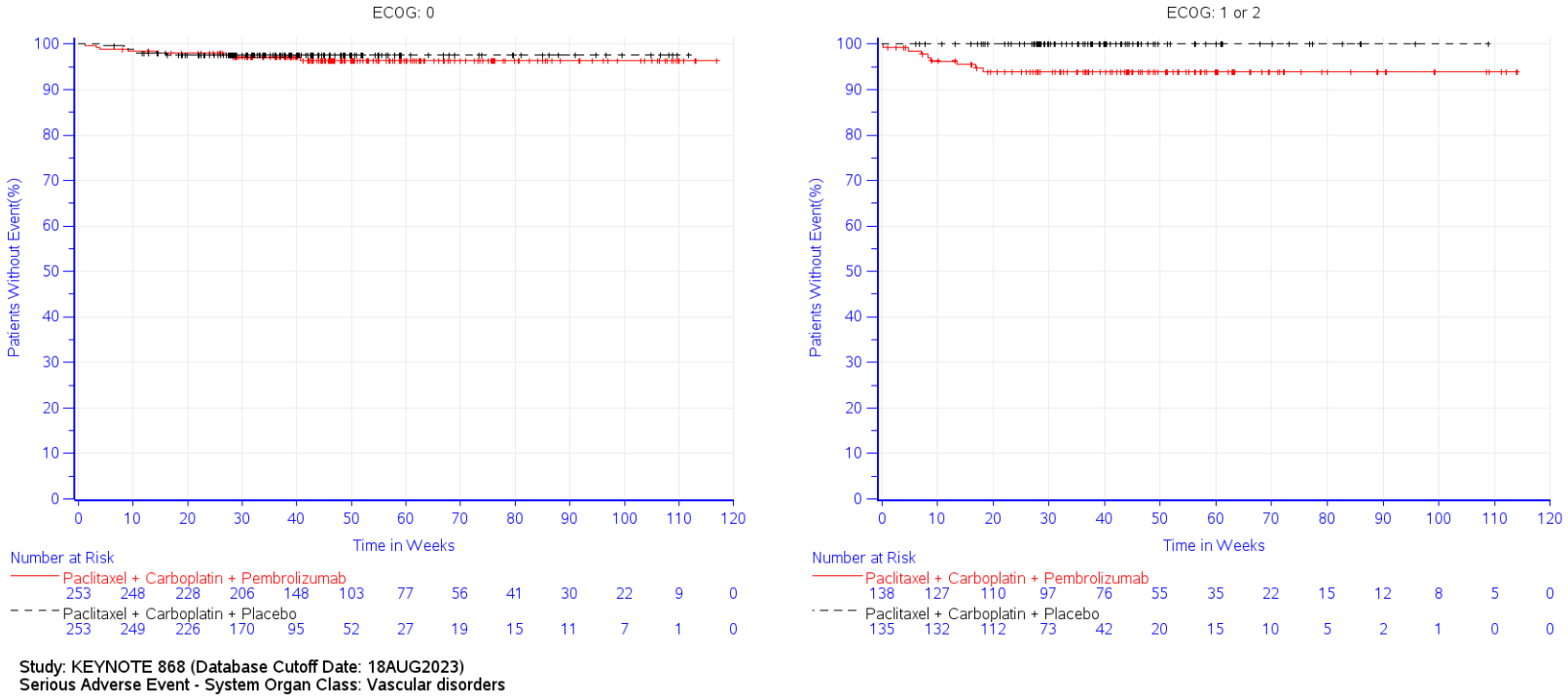


Abbildung 23: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Krankheitsschwere für den Endpunkt Schwerwiegende unerwünschte Ereignisse (SOC und PT) für die SOC Gefäßerkrankungen der Studie KEYNOTE 868

Anhang 4-G4: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest (p ≥ 0,05)

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

Aufgrund der längeren Beobachtungsdauer wird der Regulatory Update Report (18. August 2023) für alle Wirksamkeitsendpunkte (außer die patientenberichteten Endpunkte zur Krankheitssymptomatik) sowie unerwünschte Ereignisse herangezogen. Für alle patientenberichteten Endpunkte wird die Interimsanalyse (dMMR 16. Dezember 2022, pMMR 06. Dezember 2022) herangezogen, da diese die längste Beobachtungsdauer für die patientenberichteten Endpunkte darstellt und zudem eine Entblindung nach dem ersten Datenschnitt (Entblindung zum 06. Februar 2023) stattfand.

Anhang 4-G4.1: Mortalität

Gesamtüberleben

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

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		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]	
Age group									
< 65	183	34 (18.6)	Not reached [-; -]	191	48 (25.1)	41.4 [27.4; -]	0.66 [0.42; 1.02]	0.064	0.554
≥65	225	60 (26.7)	Not reached [26.8; -]	220	71 (32.3)	28.7 [23.0; 42.7]	0.77 [0.55; 1.09]	0.138	
ECOG									
0	260	50 (19.2)	Not reached [-; -]	267	63 (23.6)	41.4 [28.7; -]	0.74 [0.51; 1.07]	0.109	0.808
1 or 2	148	44 (29.7)	27.2 [21.4; -]	144	56 (38.9)	19.6 [17.2; 32.2]	0.70 [0.47; 1.04]	0.075	
Region									
WHO Stratum A	404	93 (23.0)	n.c.	406	119 (29.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	110	17 (15.5)	Not reached [-; -]	112	27 (24.1)	42.7 [42.7; -]	0.57 [0.31; 1.04]	0.068	0.277
No	298	77 (25.8)	28.9 [26.8; -]	299	92 (30.8)	28.7 [24.0; 34.6]	0.80 [0.59; 1.08]	0.138	
Age group									
< 65	183	34 (18.6)	Not reached [-; -]	191	48 (25.1)	41.4 [27.4; -]	0.66 [0.42; 1.02]	0.064	0.748
≥65 to <75	163	44 (27.0)	Not reached [26.8; -]	165	49 (29.7)	29.3 [25.3; -]	0.82 [0.55; 1.23]	0.344	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]	p-Value for Interaction Test[f]
≥75	62	16 (25.8)	Not reached [21.1; -]	55	22 (40.0)	23.0 [19.5; -]	0.75 [0.39; 1.45]	0.393	
Race									
White	307	71 (23.1)	Not reached [-; -]	300	78 (26.0)	41.4 [29.3; -]	0.84 [0.61; 1.16]	0.289	0.141
All Others	80	19 (23.8)	Not reached [24.8; -]	87	32 (36.8)	20.5 [17.4; 32.2]	0.51 [0.29; 0.91]	0.022	
Histology									
Endometrioid	248	48 (19.4)	Not reached [-; -]	243	59 (24.3)	42.7 [28.7; -]	0.71 [0.49; 1.05]	0.083	0.745
Other	160	46 (28.8)	Not reached [21.1; -]	167	59 (35.3)	26.6 [19.5; 34.6]	0.79 [0.54; 1.16]	0.229	
Status of Disease									
Primary	165	36 (21.8)	Not reached [28.9; -]	175	58 (33.1)	34.6 [19.5; -]	0.59 [0.39; 0.89]	0.012	0.139
Recurrent/Persistent	243	58 (23.9)	Not reached [27.2; -]	236	61 (25.8)	29.3 [26.6; -]	0.87 [0.61; 1.25]	0.459	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: intention-to-treat population

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

d: Based on unstratified Cox regression model with treatment as a covariate for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model with treatment as a covariate stratified by prior chemotherapy. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

f: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); WHO: World Health Organization

Anhang 4-G4.2: Morbidität

Progressionsfreies Überleben

Tabelle 4G-5: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Progressionsfreies Überleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Progression-Free Survival (INV Primary Censoring Rule)	**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]**
Age group									
< 65	183	83 (45.4)	19.5 [13.9; -]	191	112 (58.6)	10.6 [8.3; 11.9]	0.57 [0.43; 0.76]	< 0.001	0.512
≥65	225	116 (51.6)	13.6 [11.3; 17.6]	220	145 (65.9)	9.3 [8.5; 11.2]	0.62 [0.49; 0.80]	< 0.001	
ECOG									
0	260	119 (45.8)	17.2 [14.0; -]	267	160 (59.9)	11.0 [8.6; 11.5]	0.58 [0.45; 0.73]	< 0.001	0.575
1 or 2	148	80 (54.1)	12.1 [10.6; 19.3]	144	97 (67.4)	8.6 [8.0; 11.1]	0.63 [0.47; 0.85]	0.003	
Region									
WHO Stratum A	404	195 (48.3)	n.c.	406	256 (63.1)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	4 (100.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Age group									
< 65	183	83 (45.4)	19.5 [13.9; -]	191	112 (58.6)	10.6 [8.3; 11.9]	0.57 [0.43; 0.76]	< 0.001	0.806
≥65 to <75	163	84 (51.5)	14.0 [11.1; 22.4]	165	110 (66.7)	9.3 [8.5; 11.3]	0.62 [0.47; 0.83]	0.001	
≥75	62	32 (51.6)	13.1 [10.9; 20.0]	55	35 (63.6)	11.1 [6.6; 11.4]	0.63 [0.39; 1.02]	0.061	
Race									
White	307	150 (48.9)	16.9 [13.1; 25.0]	300	185 (61.7)	10.2 [8.7; 11.4]	0.62 [0.50; 0.77]	< 0.001	0.568
All Others	80	39 (48.8)	13.9 [10.6; -]	87	56 (64.4)	8.5 [6.9; 11.5]	0.55 [0.37; 0.84]	0.005	
Histology									
Endometrioid	248	115 (46.4)	19.3 [13.5; -]	243	142 (58.4)	11.2 [8.5; 11.8]	0.59 [0.46; 0.75]	< 0.001	0.719
Other	160	84 (52.5)	13.1 [10.2; 18.8]	167	114 (68.3)	8.7 [8.3; 10.9]	0.64 [0.48; 0.85]	0.002	

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Progression-Free Survival (INV Primary Censoring Rule)	**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]**
Measurable Disease at Baseline									
Yes	319	164 (51.4)	13.5 [11.3; 17.6]	334	224 (67.1)	8.5 [8.1; 9.7]	0.57 [0.46; 0.69]	< 0.001	0.136
No	89	35 (39.3)	19.8 [16.8; -]	77	33 (42.9)	16.6 [11.2; -]	0.84 [0.52; 1.35]	0.463	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: intention-to-treat population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; INV: Investigator; 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); WHO: World Health Organization

Zeit bis zur ersten Folgetherapie oder Tod

Tabelle 4G-6: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Zeit bis zur ersten Folgetherapie oder Tod aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Time to Subsequent Therapy or Death	**N[b]**	**Participants with Event n (%)**	**Median Time[c] in Months [95 %-CI]**	**N[b]**	**Participants with Event n (%)**	**Median Time[c] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][d]**	**p-Value[d,e]**	**p-Value for Interaction Test[f]**
Age group									
< 65	183	79 (43.2)	20.7 [14.6; -]	191	125 (65.4)	9.5 [8.1; 11.2]	0.47 [0.36; 0.63]	< 0.001	0.791
≥65	225	111 (49.3)	15.1 [12.2; 17.8]	220	164 (74.5)	9.0 [8.0; 9.9]	0.48 [0.38; 0.62]	< 0.001	
ECOG									
0	260	119 (45.8)	17.8 [14.0; -]	267	180 (67.4)	9.7 [8.6; 10.8]	0.50 [0.39; 0.63]	< 0.001	0.571
1 or 2	148	71 (48.0)	15.7 [12.1; 22.5]	144	109 (75.7)	8.5 [7.0; 9.5]	0.44 [0.33; 0.60]	< 0.001	
Region									
WHO Stratum A	404	186 (46.0)	n.c.	406	288 (70.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	4 (100.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: intention-to-treat population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); WHO: World Health Organization

Krankheitssymptomatik

PROMIS Erschöpfung SF 7a

Tabelle 4G-7: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt PROMIS Erschöpfung SF 7a aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
PROMIS Fatigue (7A)	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	90	50.36 (8.19)	2.24 (0.62)	0.33	-	0.459
Paclitaxel + Carboplatin + Placebo	124	103	51.52 (7.29)	1.90 (0.58)	[-1.34; 2.01]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	117	51.38 (8.14)	3.41 (0.54)	1.15	-	
Paclitaxel + Carboplatin + Placebo	142	100	50.68 (8.61)	2.25 (0.59)	[-0.43; 2.74]		
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	139	48.93 (8.00)	3.35 (0.50)	1.15	-	0.312
Paclitaxel + Carboplatin + Placebo	177	139	50.12 (7.41)	2.20 (0.50)	[-0.26; 2.56]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	68	55.03 (6.89)	1.80 (0.70)	-0.12	-	
Paclitaxel + Carboplatin + Placebo	89	64	53.25 (8.71)	1.92 (0.72)	[-2.11; 1.88]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	204	51.09 (8.01)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	202	51.14 (7.96)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	40.47 (13.22)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	43.90 (-)	n.c.			

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
PROMIS Fatigue (7A)	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	51	50.29 (7.96)	3.18 (0.76)	0.56	-	0.744
Paclitaxel + Carboplatin + Placebo	66	47	51.41 (7.14)	2.62 (0.80)	[-1.66; 2.78]		
No							
Paclitaxel + Carboplatin + Pembrolizumab	198	156	51.15 (8.24)	2.78 (0.48)	0.85	-	
Paclitaxel + Carboplatin + Placebo	200	156	51.01 (8.21)	1.93 (0.48)	[-0.48; 2.18]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); PROMIS: Patient Reported Outcomes Measurement Information System; SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

PROMIS Körperliche Funktionsfähigkeit SF 8c

Tabelle 4G-8: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt PROMIS Körperliche Funktionsfähigkeit SF 8c aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
PROMIS Physical Function (8C)	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	91	45.21 (8.41)	-0.35 (0.60)	1.00	-	0.112
Paclitaxel + Carboplatin + Placebo	124	100	46.35 (9.64)	-1.35 (0.57)	[-0.62; 2.63]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	111	45.82 (8.95)	-2.99 (0.53)	-0.96	-	
Paclitaxel + Carboplatin + Placebo	142	99	45.42 (9.19)	-2.03 (0.56)	[-2.47; 0.56]		
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	131	48.41 (7.79)	-2.70 (0.52)	-0.13	-	0.696
Paclitaxel + Carboplatin + Placebo	177	136	48.45 (8.92)	-2.57 (0.51)	[-1.57; 1.30]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	71	40.25 (7.78)	0.39 (0.62)	0.45	-	
Paclitaxel + Carboplatin + Placebo	89	63	40.37 (8.02)	-0.06 (0.66)	[-1.35; 2.24]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	200	45.51 (8.63)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	198	45.95 (9.40)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	2	48.40 (18.24)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	34.70 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	50	45.66 (8.35)	-2.02 (0.71)	0.93	-	0.302
Paclitaxel + Carboplatin + Placebo	66	45	46.44 (9.04)	-2.95 (0.76)	[-1.16; 3.02]		
No							

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
PROMIS Physical Function (8C)	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Paclitaxel + Carboplatin + Pembrolizumab	198	152	45.51 (8.83)	-1.66 (0.48)	-0.25	-	
Paclitaxel + Carboplatin + Placebo	200	154	45.73 (9.54)	-1.41 (0.48)	[-1.58; 1.08]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); PROMIS: Patient Reported Outcomes Measurement Information System; SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

FACT-En TOI

Tabelle 4G-9: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt FACT-En TOI aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT-En TOI	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	142	100.35 (13.41)	-3.68 (0.94)	-1.67	-	0.534
Paclitaxel + Carboplatin + Placebo	177	150	97.98 (16.31)	-2.01 (0.92)	[-4.27; 0.92]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	73	87.63 (17.64)	0.95 (1.46)	-2.59	-	
Paclitaxel + Carboplatin + Placebo	89	70	85.81 (20.48)	3.54 (1.50)	[-6.73; 1.54]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	212	95.99 (15.97)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	219	94.07 (18.62)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	99.09 (29.25)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	103.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	53	95.78 (13.94)	-2.65 (1.42)	0.17	-	0.227
Paclitaxel + Carboplatin + Placebo	66	49	96.61 (15.81)	-2.82 (1.48)	[-3.91; 4.25]		
No							
Paclitaxel + Carboplatin + Pembrolizumab	198	162	96.12 (16.80)	-2.11 (0.94)	-2.60	-0.19	
Paclitaxel + Carboplatin + Placebo	200	171	93.39 (19.29)	0.48 (0.91)	[-5.17; -0.03]	[-0.37; -0.00]	

a: Database Cutoff Date: 06DEC2022
b: Number of participants: full-analysis-set population
c: Number of participants with data available for analysis
d: Mean and SD at baseline are calculated based on number of participants with data available for analysis
e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT-En TOI	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]

covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT-En: Functional Assessment of Cancer Therapy-Endometrial; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; TOI: Trial Outcome Index; WHO: World Health Organization

FACT Symptomskala Körperliches Wohlbefinden

Tabelle 4G-10: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die FACT Symptomskala Körperliches Wohlbefinden aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Physical Well-Being Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	99	23.14 (5.07)	-1.30 (0.42)	0.13	-	0.106
Paclitaxel + Carboplatin + Placebo	124	111	22.54 (5.42)	-1.43 (0.40)	[-1.02; 1.28]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	124	23.54 (4.95)	-2.63 (0.35)	-1.23	-0.27	
Paclitaxel + Carboplatin + Placebo	142	113	23.32 (5.23)	-1.40 (0.36)	[-2.22; -0.25]	[-0.49; -0.05]	
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	148	24.71 (3.88)	-2.50 (0.32)	-0.65	-	0.968
Paclitaxel + Carboplatin + Placebo	177	152	24.08 (4.43)	-1.85 (0.32)	[-1.54; 0.24]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	75	20.70 (5.83)	-0.90 (0.50)	-0.49	-	
Paclitaxel + Carboplatin + Placebo	89	72	20.50 (6.21)	-0.41 (0.52)	[-1.92; 0.94]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	220	23.38 (4.93)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	223	22.92 (5.34)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	22.00 (10.39)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	26.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	56	23.41 (3.99)	-2.18 (0.51)	-0.03	-	0.328
Paclitaxel + Carboplatin + Placebo	66	51	23.38 (4.16)	-2.16 (0.54)	[-1.51; 1.46]		
No							

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Physical Well-Being Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Paclitaxel + Carboplatin + Pembrolizumab	198	167	23.35 (5.30)	-1.93 (0.32)	-0.75	-	
Paclitaxel + Carboplatin + Placebo	200	173	22.80 (5.63)	-1.19 (0.31)	[-1.62; 0.12]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT: Functional Assessment of Cancer Therapy; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

FACT Symptomskala Funktionales Wohlbefinden

Tabelle 4G-11: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die FACT Symptomskala Funktionales Wohlbefinden aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Functional Well-Being Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	99	18.60 (6.08)	0.16 (0.48)	0.19	-	0.226
Paclitaxel + Carboplatin + Placebo	124	110	17.60 (7.49)	-0.03 (0.46)	[-1.11; 1.49]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	121	18.26 (6.51)	-1.21 (0.43)	-0.92	-	
Paclitaxel + Carboplatin + Placebo	142	111	18.12 (7.21)	-0.29 (0.44)	[-2.14; 0.29]		
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	146	19.70 (5.91)	-0.91 (0.38)	-0.39	-	0.918
Paclitaxel + Carboplatin + Placebo	177	150	19.41 (6.79)	-0.52 (0.37)	[-1.44; 0.66]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	74	15.88 (6.33)	0.25 (0.57)	-0.39	-	
Paclitaxel + Carboplatin + Placebo	89	71	14.60 (7.45)	0.63 (0.59)	[-2.02; 1.24]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	217	18.36 (6.29)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	220	17.86 (7.36)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	22.33 (8.14)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	18.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	56	18.37 (6.41)	-0.56 (0.58)	0.38	-	0.325
Paclitaxel + Carboplatin + Placebo	66	49	18.43 (6.89)	-0.94 (0.62)	[-1.31; 2.07]		
No							

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Functional Well-Being Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Paclitaxel + Carboplatin + Pembrolizumab	198	164	18.43 (6.29)	-0.58 (0.38)	-0.65	-	
Paclitaxel + Carboplatin + Placebo	200	172	17.70 (7.48)	0.07 (0.37)	[-1.69; 0.39]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT: Functional Assessment of Cancer Therapy; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

FACT Endometriumkarzinomspezifische Subskala

Tabelle 4G-12: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für die FACT Endometriumkarzinomspezifische Subskala aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Endometrial Cancer Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	144	55.76 (6.58)	-0.24 (0.44)	-0.63	-	0.484
Paclitaxel + Carboplatin + Placebo	177	153	54.60 (8.49)	0.38 (0.42)	[-1.83; 0.58]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	76	50.76 (8.73)	2.16 (0.63)	-1.00	-	
Paclitaxel + Carboplatin + Placebo	89	71	51.07 (11.08)	3.15 (0.66)	[-2.79; 0.80]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	217	54.02 (7.73)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	223	53.46 (9.52)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	54.76 (10.95)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	59.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	55	53.87 (6.76)	0.34 (0.63)	-0.14	-	0.335
Paclitaxel + Carboplatin + Placebo	66	51	55.04 (7.78)	0.48 (0.66)	[-1.95; 1.67]		
No							
Paclitaxel + Carboplatin + Pembrolizumab	198	165	54.09 (8.07)	0.59 (0.42)	-0.91	-	
Paclitaxel + Carboplatin + Placebo	200	173	53.02 (9.94)	1.50 (0.41)	[-2.06; 0.25]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Endometrial Cancer Subscale	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
covariance between visits is assumed							
f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero							
g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed							
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT: Functional Assessment of Cancer Therapy; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization							

Belastung durch Nebenwirkungen der Krebstherapie

Tabelle 4G-13: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Belastung durch Nebenwirkungen der Krebstherapie aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
FACT Bother from Side Effects of Cancer Therapy	**N[b]**	**N[c]**	**Mean at Baseline (SD)[d]**	**Mean Change from Baseline (SE)[e]**	**Mean Difference[e] [95 %-CI]**	**Standardized Mean Difference[f] [95 %-CI]**	**p-Value for Interaction Test[g]**
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	93	3.61 (0.92)	-0.87 (0.09)	-0.05	-	0.149
Paclitaxel + Carboplatin + Placebo	124	98	3.55 (0.95)	-0.82 (0.09)	[-0.30; 0.21]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	119	3.63 (0.84)	-1.12 (0.08)	-0.30	-0.27	
Paclitaxel + Carboplatin + Placebo	142	105	3.72 (0.67)	-0.82 (0.09)	[-0.54; -0.07]	[-0.48; -0.06]	
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	141	3.72 (0.80)	-0.99 (0.07)	-0.14	-	0.518
Paclitaxel + Carboplatin + Placebo	177	140	3.71 (0.72)	-0.85 (0.07)	[-0.33; 0.05]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	71	3.44 (1.00)	-1.03 (0.12)	-0.27	-	
Paclitaxel + Carboplatin + Placebo	89	63	3.48 (1.00)	-0.76 (0.13)	[-0.62; 0.08]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	210	3.62 (0.88)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	202	3.64 (0.82)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	2	4.00 (0.00)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	4.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	52	3.37 (1.01)	-0.73 (0.12)	-0.03	-	0.329
Paclitaxel + Carboplatin + Placebo	66	49	3.35 (1.09)	-0.69 (0.13)	[-0.38; 0.31]		

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT Bother from Side Effects of Cancer Therapy	**N[b]**	**N[c]**	**Mean at Baseline (SD)[d]**	**Mean Change from Baseline (SE)[e]**	**Mean Difference[e] [95 %-CI]**	**Standardized Mean Difference[f] [95 %-CI]**	**p-Value for Interaction Test[g]**
No							
Paclitaxel + Carboplatin + Pembrolizumab	198	160	3.71 (0.81)	-1.10 (0.07)	-0.24	-0.21	
Paclitaxel + Carboplatin + Placebo	200	154	3.73 (0.70)	-0.86 (0.07)	[-0.43; -0.04]	[-0.39; -0.03]	

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT-En: Functional Assessment of Cancer Therapy-Endometrial; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

Neuropathie [FACT/GOG-Ntx-4]

Tabelle 4G-14: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Neuropathie (FACT/GOG-Ntx-4) aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]					Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
FACT GOG-NTX-4	N[b]	N[c]	Mean at Baseline (SD)[d]	Mean Change from Baseline (SE)[e]	Mean Difference[e] [95 %-CI]	Standardized Mean Difference[f] [95 %-CI]	p-Value for Interaction Test[g]
Age group							
< 65							
Paclitaxel + Carboplatin + Pembrolizumab	121	98	14.29 (3.08)	-3.48 (0.34)	0.01	-	0.278
Paclitaxel + Carboplatin + Placebo	124	105	14.05 (3.08)	-3.48 (0.33)	[-0.92; 0.93]		
≥65							
Paclitaxel + Carboplatin + Pembrolizumab	147	123	14.02 (3.12)	-4.27 (0.33)	-0.78	-	
Paclitaxel + Carboplatin + Placebo	142	110	14.03 (2.97)	-3.50 (0.35)	[-1.72; 0.17]		
ECOG							
0							
Paclitaxel + Carboplatin + Pembrolizumab	178	145	14.36 (2.88)	-3.76 (0.28)	-0.35	-	0.951
Paclitaxel + Carboplatin + Placebo	177	149	14.32 (2.73)	-3.40 (0.28)	[-1.14; 0.43]		
1 or 2							
Paclitaxel + Carboplatin + Pembrolizumab	90	76	13.72 (3.46)	-4.11 (0.43)	-0.39	-	
Paclitaxel + Carboplatin + Placebo	89	66	13.41 (3.51)	-3.73 (0.46)	[-1.64; 0.87]		
Region							
WHO Stratum A							
Paclitaxel + Carboplatin + Pembrolizumab	264	218	14.11 (3.11)	n.c.	n.c.	n.c.	n.c.
Paclitaxel + Carboplatin + Placebo	264	214	14.03 (3.02)	n.c.			
Rest of World							
Paclitaxel + Carboplatin + Pembrolizumab	4	3	16.00 (0.00)	n.c.	n.c.	n.c.	
Paclitaxel + Carboplatin + Placebo	2	1	16.00 (-)	n.c.			
Prior chemotherapy							
Yes							
Paclitaxel + Carboplatin + Pembrolizumab	70	55	12.39 (4.25)	-2.73 (0.38)	-0.95	-	0.444
Paclitaxel + Carboplatin + Placebo	66	50	12.23 (3.49)	-1.78 (0.41)	[-2.07; 0.17]		

No							
Paclitaxel + Carboplatin + Pembrolizumab	198	166	14.72 (2.36)	-4.33 (0.29)	-0.28	-	
Paclitaxel + Carboplatin + Placebo	200	165	14.59 (2.63)	-4.05 (0.29)	[-1.09; 0.53]		

a: Database Cutoff Date: 06DEC2022

b: Number of participants: full-analysis-set population

c: Number of participants with data available for analysis

d: Mean and SD at baseline are calculated based on number of participants with data available for analysis

e: MMRM of change from baseline with treatment, time, baseline endpoint score and age at baseline as covariates. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: MMRM of change from baseline with treatment, subgroup, time, baseline endpoint score and age at baseline as covariates and treatment-by-subgroup interaction. A continuous time assessment (relative analysis day) is used, and spatial power covariance between visits is assumed

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FACT: Functional Assessment of Cancer Therapy; GOG-NTX: Gynecologic Oncology Group-Neurotoxicity; MMRM: Mixed-effect Model Repeated Measures; n.c.: not calculated. (At least 10 participants per subgroup necessary); SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization

Anhang 4-G4.3: Nebenwirkungen

Unerwünschte Ereignisse Gesamtraten

Unerwünschte Ereignisse gesamt

Tabelle 4G-15: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Unerwünschte Ereignisse gesamt aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	175	174 (99.4)	0.3 [-; -]	180	180 (100.0)	0.3 [0.3; 0.4]	1.12 [0.91; 1.39]	0.275	0.452
≥65	216	214 (99.1)	0.3 [0.3; 0.4]	208	207 (99.5)	0.3 [-; -]	1.02 [0.84; 1.23]	0.873	
ECOG									
0	253	251 (99.2)	0.3 [0.3; 0.4]	253	253 (100.0)	0.3 [0.3; 0.4]	1.04 [0.87; 1.24]	0.664	0.595
1 or 2	138	137 (99.3)	0.3 [0.1; 0.3]	135	134 (99.3)	0.3 [0.1; 0.3]	1.13 [0.89; 1.44]	0.323	
Region									
WHO Stratum A	387	384 (99.2)	n.c.	383	382 (99.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	4 (100.0)	n.c.	5	5 (100.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	106 (99.1)	0.3 [0.1; 0.3]	105	105 (100.0)	0.3 [0.3; 0.4]	1.16 [0.88; 1.52]	0.285	0.604
No	284	282 (99.3)	0.3 [0.3; 0.4]	283	282 (99.6)	0.3 [-; -]	1.05 [0.89; 1.24]	0.585	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); WHO: World Health Organization

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-16: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	175	64 (36.6)	Not reached [80.9; -]	180	37 (20.6)	Not reached [-; -]	1.73 [1.15; 2.60]	0.008	0.589
≥65	216	91 (42.1)	73.0 [50.6; -]	208	45 (21.6)	Not reached [-; -]	1.97 [1.38; 2.82]	< 0.001	
ECOG									
0	253	91 (36.0)	Not reached [73.0; -]	253	44 (17.4)	Not reached [-; -]	1.99 [1.39; 2.86]	< 0.001	0.529
1 or 2	138	64 (46.4)	80.9 [23.3; -]	135	38 (28.1)	Not reached [-; -]	1.72 [1.15; 2.57]	0.009	
Region									
WHO Stratum A	387	154 (39.8)	n.c.	383	81 (21.1)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	40 (37.4)	Not reached [-; -]	105	21 (20.0)	Not reached [-; -]	1.87 [1.10; 3.17]	0.021	0.788
No	284	115 (40.5)	80.9 [60.6; -]	283	61 (21.6)	Not reached [-; -]	1.88 [1.37; 2.56]	< 0.001	
Prior Chemotherapy									
Yes	78	38 (48.7)	60.6 [31.4; 71.6]	75	16 (21.3)	Not reached [-; -]	2.20 [1.22; 3.97]	0.009	0.353
No	313	117 (37.4)	Not reached [80.9; -]	313	66 (21.1)	Not reached [-; -]	1.77 [1.30; 2.39]	< 0.001	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); WHO: World Health Organization

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

Tabelle 4G-17: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Severe Adverse Event (CTCAE-Grade 3-5)	**N[b]**	**Participants with Event n (%)**	**Median Time[c] in Weeks [95 %-CI]**	**N[b]**	**Participants with Event n (%)**	**Median Time[c] in Weeks [95 %-CI]**	**Hazard Ratio [95 %-CI][d]**	**p-Value[d,e]**	**p-Value for Interaction Test[f]**
Age group									
< 65	175	111 (63.4)	19.7 [14.3; 24.1]	180	89 (49.4)	24.1 [15.6; -]	1.22 [0.92; 1.61]	0.173	0.343
≥65	216	146 (67.6)	15.1 [12.0; 19.0]	208	102 (49.0)	31.7 [17.7; -]	1.44 [1.12; 1.86]	0.005	
ECOG									
0	253	159 (62.8)	20.7 [15.4; 28.7]	253	111 (43.9)	50.9 [25.7; -]	1.42 [1.11; 1.81]	0.005	0.370
1 or 2	138	98 (71.0)	12.6 [9.0; 17.9]	135	80 (59.3)	15.0 [10.7; 21.1]	1.22 [0.90; 1.64]	0.197	
Region									
WHO Stratum A	387	255 (65.9)	n.c.	383	187 (48.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	5	4 (80.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	68 (63.6)	20.3 [15.4; 52.9]	105	50 (47.6)	28.1 [17.9; -]	1.22 [0.84; 1.76]	0.300	0.504
No	284	189 (66.5)	15.1 [12.1; 19.9]	283	141 (49.8)	25.7 [16.0; -]	1.39 [1.12; 1.73]	0.003	
Prior Chemotherapy									
Yes	78	59 (75.6)	9.6 [6.1; 17.1]	75	35 (46.7)	Not reached [12.1; -]	1.90 [1.25; 2.89]	0.003	0.069
No	313	198 (63.3)	18.6 [15.1; 24.1]	313	156 (49.8)	26.0 [17.9; 74.0]	1.22 [0.99; 1.51]	0.060	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; 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); WHO: World Health Organization

Therapieabbruch wegen unerwünschter Ereignisse/ Nebenwirkungen/ Komplikationen

Tabelle 4G-18: Subgruppenanalysen mit nicht signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse/ Nebenwirkungen/ Komplikationen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Treatment Discontinuation Due to Adverse Events/Side Effects/Complications	**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									
0	253	49 (19.4)	104.1 [104.1; -]	253	15 (5.9)	Not reached [-; -]	2.01 [1.12; 3.63]	0.020	0.144
1 or 2	138	22 (15.9)	Not reached [86.1; -]	135	13 (9.6)	Not reached [-; -]	1.18 [0.58; 2.38]	0.652	
Region									
WHO Stratum A	387	70 (18.1)	n.c.	383	28 (7.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	21 (19.6)	104.1 [-; -]	105	6 (5.7)	Not reached [-; -]	1.87 [0.73; 4.81]	0.194	0.801
No	284	50 (17.6)	Not reached [-; -]	283	22 (7.8)	Not reached [-; -]	1.59 [0.95; 2.64]	0.076	
Prior Chemotherapy									
Yes	78	11 (14.1)	Not reached [-; -]	75	7 (9.3)	Not reached [66.7; -]	1.13 [0.43; 2.98]	0.809	0.351
No	313	60 (19.2)	104.1 [104.1; -]	313	21 (6.7)	Not reached [-; -]	1.79 [1.08; 2.98]	0.025	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); WHO: World Health Organization

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

Tabelle 4G-19: Subgruppenanalysen mit nicht statistisch 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 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]: Cardiac disorders									
Age group									
< 65	175	23 (13.1)	Not reached [-; -]	180	10 (5.6)	Not reached [-; -]	2.23 [1.06; 4.71]	0.035	0.387
≥65	216	37 (17.1)	Not reached [-; -]	208	23 (11.1)	Not reached [-; -]	1.46 [0.86; 2.46]	0.158	
ECOG									
0	253	37 (14.6)	Not reached [-; -]	253	19 (7.5)	Not reached [-; -]	1.81 [1.04; 3.16]	0.036	0.699
1 or 2	138	23 (16.7)	Not reached [-; -]	135	14 (10.4)	Not reached [-; -]	1.54 [0.79; 3.00]	0.207	
Region									
WHO Stratum A	387	60 (15.5)	n.c.	383	32 (8.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	21 (19.6)	Not reached [-; -]	105	6 (5.7)	Not reached [-; -]	3.30 [1.33; 8.22]	0.010	0.079
No	284	39 (13.7)	Not reached [-; -]	283	27 (9.5)	Not reached [-; -]	1.34 [0.82; 2.20]	0.243	
Prior Chemotherapy									
Yes	78	10 (12.8)	Not reached [-; -]	75	10 (13.3)	Not reached [-; -]	0.89 [0.36; 2.15]	0.788	0.118
No	313	50 (16.0)	Not reached [-; -]	313	23 (7.3)	Not reached [-; -]	2.04 [1.24; 3.36]	0.005	
SOC[g]: Endocrine disorders									
Age group									
< 65	175	40 (22.9)	Not reached [-; -]	180	11 (6.1)	Not reached [79.0; -]	3.55 [1.81; 6.94]	< 0.001	0.316
≥65	216	39 (18.1)	Not reached [-; -]	208	15 (7.2)	Not reached [-; -]	2.27 [1.25; 4.13]	0.007	
ECOG									
0	253	59 (23.3)	Not reached [-; -]	253	21 (8.3)	Not reached [-; -]	2.59 [1.57; 4.28]	< 0.001	0.567
1 or 2	138	20 (14.5)	Not reached [-; -]	135	5 (3.7)	Not reached [-; -]	3.74 [1.40; 10.01]	0.009	
Region									
WHO Stratum A	387	78 (20.2)	n.c.	383	26 (6.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1	n.c.	5	0	n.c.	n.c.	n.c.	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
		(25.0)			(0.0)				
Prior Chemotherapy									
Yes	78	17 (21.8)	Not reached [-; -]	75	3 (4.0)	Not reached [-; -]	5.71 [1.67; 19.49]	0.005	0.208
No	313	62 (19.8)	Not reached [-; -]	313	23 (7.3)	Not reached [-; -]	2.43 [1.50; 3.93]	< 0.001	
SOC[g]: General disorders and administration site conditions									
Age group									
< 65	175	140 (80.0)	4.1 [3.1; 6.1]	180	133 (73.9)	6.1 [3.1; 9.1]	1.09 [0.86; 1.39]	0.462	0.418
≥65	216	182 (84.3)	3.5 [3.1; 5.7]	208	154 (74.0)	5.3 [3.1; 7.4]	1.25 [1.01; 1.56]	0.039	
ECOG									
0	253	209 (82.6)	3.7 [3.1; 5.9]	253	181 (71.5)	5.0 [3.1; 8.0]	1.18 [0.97; 1.45]	0.097	0.923
1 or 2	138	113 (81.9)	4.1 [3.1; 6.0]	135	106 (78.5)	6.1 [3.3; 8.9]	1.18 [0.91; 1.54]	0.220	
Region									
WHO Stratum A	387	320 (82.7)	n.c.	383	285 (74.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	5	2 (40.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	90 (84.1)	3.7 [3.0; 6.1]	105	74 (70.5)	9.1 [4.3; 12.4]	1.44 [1.05; 1.96]	0.022	0.175
No	284	232 (81.7)	4.1 [3.3; 5.7]	283	213 (75.3)	4.1 [3.1; 6.1]	1.09 [0.91; 1.32]	0.346	
Prior Chemotherapy									
Yes	78	69 (88.5)	3.5 [3.0; 8.9]	75	55 (73.3)	3.4 [2.0; 9.1]	1.25 [0.87; 1.78]	0.224	0.749
No	313	253 (80.8)	4.1 [3.1; 5.9]	313	232 (74.1)	6.0 [3.4; 8.1]	1.16 [0.97; 1.38]	0.109	
SOC[g]: Infections and infestations									
Age group									
< 65	175	85 (48.6)	44.6 [27.7; 85.6]	180	63 (35.0)	57.7 [38.4; -]	1.22 [0.88; 1.70]	0.240	0.566
≥65	216	103 (47.7)	47.7 [32.0; 53.6]	208	68 (32.7)	Not reached [36.6; -]	1.33 [0.97; 1.81]	0.074	
ECOG									
0	253	122 (48.2)	46.1 [35.6; 59.9]	253	82 (32.4)	71.1 [38.4; -]	1.35 [1.02; 1.79]	0.039	0.455
1 or 2	138	66 (47.8)	47.7 [27.1; 69.1]	135	49 (36.3)	63.7 [34.6; -]	1.15 [0.79; 1.67]	0.475	
Region									
WHO Stratum A	387	186 (48.1)	n.c.	383	129 (33.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	5	2 (40.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
Mismatch repair deficient (dMMR)									
Yes	107	62 (57.9)	38.1 [27.1; 54.1]	105	37 (35.2)	44.0 [34.6; -]	1.37 [0.90; 2.08]	0.145	0.508
No	284	126 (44.4)	48.0 [35.7; 80.9]	283	94 (33.2)	Not reached [57.7; -]	1.23 [0.94; 1.60]	0.137	
Prior Chemotherapy									
Yes	78	37 (47.4)	37.3 [15.6; -]	75	28 (37.3)	Not reached [30.0; -]	1.22 [0.74; 2.00]	0.428	0.822
No	313	151 (48.2)	49.7 [34.3; 59.9]	313	103 (32.9)	71.1 [44.0; -]	1.28 [0.99; 1.65]	0.057	
SOC[g]: Injury, poisoning and procedural complications									
Age group									
< 65	175	53 (30.3)	Not reached [-; -]	180	46 (25.6)	Not reached [-; -]	1.15 [0.77; 1.70]	0.502	0.098
≥65	216	79 (36.6)	Not reached [57.1; -]	208	43 (20.7)	Not reached [-; -]	1.69 [1.16; 2.46]	0.006	
ECOG									
0	253	83 (32.8)	Not reached [-; -]	253	47 (18.6)	Not reached [-; -]	1.69 [1.18; 2.42]	0.004	0.123
1 or 2	138	49 (35.5)	83.4 [56.1; -]	135	42 (31.1)	Not reached [39.0; -]	1.08 [0.71; 1.63]	0.731	
Region									
WHO Stratum A	387	131 (33.9)	n.c.	383	88 (23.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	36 (33.6)	Not reached [-; -]	105	28 (26.7)	Not reached [-; -]	1.24 [0.76; 2.04]	0.389	0.377
No	284	96 (33.8)	Not reached [57.1; -]	283	61 (21.6)	Not reached [-; -]	1.49 [1.08; 2.06]	0.015	
Prior Chemotherapy									
Yes	78	28 (35.9)	57.1 [39.1; -]	75	18 (24.0)	Not reached [-; -]	1.40 [0.77; 2.54]	0.273	0.903
No	313	104 (33.2)	Not reached [-; -]	313	71 (22.7)	Not reached [-; -]	1.40 [1.04; 1.90]	0.028	
SOC[g]: Renal and urinary disorders									
Age group									
< 65	175	35 (20.0)	Not reached [-; -]	180	28 (15.6)	Not reached [-; -]	1.16 [0.70; 1.91]	0.570	0.467
≥65	216	72 (33.3)	Not reached [83.1; -]	208	43 (20.7)	Not reached [68.1; -]	1.52 [1.04; 2.22]	0.031	
ECOG									
0	253	65 (25.7)	Not reached [-; -]	253	37 (14.6)	Not reached [-; -]	1.62 [1.08; 2.43]	0.020	0.196
1 or 2	138	42 (30.4)	Not reached [88.3; -]	135	34 (25.2)	Not reached [-; -]	1.12 [0.71; 1.77]	0.626	
Region									

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
WHO Stratum A	387	106 (27.4)	n.c.	383	71 (18.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	29 (27.1)	Not reached [-; -]	105	17 (16.2)	Not reached [-; -]	1.58 [0.86; 2.88]	0.140	0.802
No	284	78 (27.5)	Not reached [88.3; -]	283	54 (19.1)	Not reached [-; -]	1.34 [0.95; 1.90]	0.098	
Prior Chemotherapy									
Yes	78	17 (21.8)	Not reached [-; -]	75	12 (16.0)	Not reached [-; -]	1.36 [0.65; 2.86]	0.413	0.878
No	313	90 (28.8)	Not reached [-; -]	313	59 (18.8)	Not reached [-; -]	1.39 [1.00; 1.94]	0.049	
SOC[g]: Respiratory, thoracic and mediastinal disorders									
ECOG									
0	253	122 (48.2)	40.6 [19.1; -]	253	93 (36.8)	54.1 [46.4; -]	1.33 [1.01; 1.75]	0.040	0.427
1 or 2	138	66 (47.8)	31.4 [14.9; -]	135	57 (42.2)	Not reached [16.4; -]	1.13 [0.79; 1.62]	0.486	
Region									
WHO Stratum A	387	188 (48.6)	n.c.	383	150 (39.2)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	56 (52.3)	19.1 [12.3; -]	105	41 (39.0)	39.0 [30.1; -]	1.39 [0.92; 2.08]	0.115	0.663
No	284	132 (46.5)	40.6 [24.9; -]	283	109 (38.5)	54.1 [46.4; -]	1.21 [0.94; 1.57]	0.135	
Prior Chemotherapy									
Yes	78	34 (43.6)	61.1 [15.0; -]	75	37 (49.3)	22.3 [15.1; -]	0.83 [0.52; 1.33]	0.444	0.057
No	313	154 (49.2)	31.4 [18.1; -]	313	113 (36.1)	54.1 [46.4; -]	1.40 [1.10; 1.79]	0.007	
SOC[g]: Skin and subcutaneous tissue disorders									
Age group									
< 65	175	140 (80.0)	3.1 [2.7; 3.3]	180	119 (66.1)	5.7 [3.1; 8.7]	1.43 [1.12; 1.83]	0.004	0.067
≥65	216	161 (74.5)	3.9 [3.1; 5.9]	208	141 (67.8)	3.1 [3.1; 3.9]	1.07 [0.85; 1.34]	0.574	
ECOG									
0	253	200 (79.1)	3.1 [3.0; 3.6]	253	168 (66.4)	3.1 [3.1; 5.9]	1.24 [1.01; 1.53]	0.038	0.833
1 or 2	138	101 (73.2)	3.1 [2.9; 5.9]	135	92 (68.1)	3.3 [3.1; 6.1]	1.19 [0.90; 1.58]	0.231	
Region									
WHO Stratum A	387	298 (77.0)	n.c.	383	257 (67.1)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
Rest of World	4	3 (75.0)	n.c.	5	3 (60.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	89 (83.2)	3.1 [2.7; 5.4]	105	72 (68.6)	3.1 [3.0; 6.1]	1.32 [0.97; 1.80]	0.082	0.592
No	284	212 (74.6)	3.1 [3.0; 3.9]	283	188 (66.4)	3.3 [3.1; 6.1]	1.18 [0.97; 1.44]	0.091	
Prior Chemotherapy									
Yes	78	55 (70.5)	3.9 [3.1; 6.1]	75	51 (68.0)	3.7 [3.0; 12.1]	1.01 [0.69; 1.48]	0.972	0.266
No	313	246 (78.6)	3.1 [2.9; 3.3]	313	209 (66.8)	3.1 [3.1; 5.7]	1.28 [1.06; 1.54]	0.009	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); SOC: System Organ Class; WHO: World Health Organization

Tabelle 4G-20: Subgruppenanalysen mit nicht statistisch signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für PT aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]: Hyperthyroidism									
Age group									
< 65	175	18 (10.3)	Not reached [-; -]	180	3 (1.7)	Not reached [-; -]	5.84 [1.71; 19.93]	0.005	0.108
≥65	216	14 (6.5)	Not reached [-; -]	208	7 (3.4)	Not reached [-; -]	1.61 [0.64; 4.03]	0.310	
ECOG									
0	253	25 (9.9)	Not reached [-; -]	253	7 (2.8)	Not reached [-; -]	3.26 [1.40; 7.57]	0.006	0.577
1 or 2	138	7 (5.1)	Not reached [-; -]	135	3 (2.2)	Not reached [-; -]	1.85 [0.47; 7.28]	0.382	
Region									
WHO Stratum A	387	31 (8.0)	n.c.	383	10 (2.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	10 (9.3)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	3.90 [0.83; 18.18]	0.084	0.548
No	284	22 (7.7)	Not reached [-; -]	283	8 (2.8)	Not reached [-; -]	2.52 [1.12; 5.68]	0.026	
Prior Chemotherapy									
Yes	78	4 (5.1)	Not reached [-; -]	75	2 (2.7)	Not reached [-; -]	1.91 [0.35; 10.42]	0.456	0.546
No	313	28 (8.9)	Not reached [-; -]	313	8 (2.6)	Not reached [-; -]	3.06 [1.39; 6.76]	0.006	
SOC: Endocrine disorders - PT[g]: Hypothyroidism									
Age group									
< 65	175	26 (14.9)	Not reached [-; -]	180	8 (4.4)	Not reached [79.0; -]	3.02 [1.36; 6.70]	0.007	0.785
≥65	216	28 (13.0)	Not reached [-; -]	208	7 (3.4)	Not reached [-; -]	3.68 [1.60; 8.45]	0.002	
Region									
WHO Stratum A	387	54 (14.0)	n.c.	383	15 (3.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Gastrointestinal disorders - PT[g]: Dry mouth									
ECOG									
0	253	20 (7.9)	Not reached [-; -]	253	6 (2.4)	Not reached [-; -]	2.95 [1.18; 7.39]	0.021	0.293
1 or 2	138	6 (4.3)	Not reached [-; -]	135	4 (3.0)	Not reached [-; -]	1.13 [0.31; 4.07]	0.856	
Region									

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
WHO Stratum A	387	26 (6.7)	n.c.	383	10 (2.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Prior Chemotherapy									
Yes	78	4 (5.1)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	3.61 [0.40; 32.45]	0.252	0.666
No	313	22 (7.0)	Not reached [-; -]	313	9 (2.9)	Not reached [-; -]	2.06 [0.94; 4.50]	0.071	
SOC: Gastrointestinal disorders - PT[g]: Stomatitis									
Age group									
< 65	175	16 (9.1)	Not reached [-; -]	180	7 (3.9)	Not reached [-; -]	2.17 [0.89; 5.29]	0.090	0.679
≥65	216	26 (12.0)	Not reached [-; -]	208	14 (6.7)	Not reached [-; -]	1.69 [0.88; 3.25]	0.114	
ECOG									
0	253	27 (10.7)	Not reached [-; -]	253	15 (5.9)	Not reached [-; -]	1.64 [0.87; 3.10]	0.127	0.572
1 or 2	138	15 (10.9)	Not reached [-; -]	135	6 (4.4)	Not reached [-; -]	2.40 [0.93; 6.20]	0.070	
Region									
WHO Stratum A	387	42 (10.9)	n.c.	383	21 (5.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	13 (12.1)	Not reached [-; -]	105	9 (8.6)	Not reached [-; -]	1.14 [0.48; 2.73]	0.760	0.265
No	284	29 (10.2)	Not reached [-; -]	283	12 (4.2)	Not reached [-; -]	2.38 [1.21; 4.67]	0.012	
Prior Chemotherapy									
Yes	78	12 (15.4)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	2.83 [0.91; 8.78]	0.072	0.394
No	313	30 (9.6)	Not reached [-; -]	313	17 (5.4)	Not reached [-; -]	1.63 [0.89; 2.97]	0.110	
SOC: Gastrointestinal disorders - PT[g]: Vomiting									
Age group									
< 65	175	43 (24.6)	Not reached [-; -]	180	25 (13.9)	Not reached [-; -]	1.72 [1.05; 2.82]	0.032	0.751
≥65	216	40 (18.5)	Not reached [-; -]	208	25 (12.0)	Not reached [-; -]	1.52 [0.92; 2.51]	0.101	
ECOG									
0	253	56 (22.1)	Not reached [-; -]	253	32 (12.6)	Not reached [-; -]	1.72 [1.11; 2.66]	0.015	0.648
1 or 2	138	27 (19.6)	Not reached [-; -]	135	18 (13.3)	Not reached [-; -]	1.43 [0.78; 2.59]	0.246	
Region									
WHO Stratum A	387	82 (21.2)	n.c.	383	48 (12.5)	n.c.	n.c.	n.c.	n.c.

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]**
Rest of World	4	1 (25.0)	n.c.	5	2 (40.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	23 (21.5)	Not reached [-; -]	105	9 (8.6)	Not reached [-; -]	2.54 [1.17; 5.51]	0.018	0.181
No	284	60 (21.1)	Not reached [-; -]	283	41 (14.5)	Not reached [-; -]	1.41 [0.95; 2.10]	0.090	
SOC: General disorders and administration site conditions - PT[g]: Chills									
Age group									
< 65	175	7 (4.0)	Not reached [-; -]	180	4 (2.2)	Not reached [-; -]	1.71 [0.50; 5.86]	0.391	0.523
≥65	216	15 (6.9)	Not reached [-; -]	208	5 (2.4)	Not reached [-; -]	2.69 [0.97; 7.43]	0.056	
ECOG									
0	253	12 (4.7)	Not reached [-; -]	253	5 (2.0)	Not reached [-; -]	2.26 [0.79; 6.42]	0.127	0.950
1 or 2	138	10 (7.2)	Not reached [-; -]	135	4 (3.0)	Not reached [-; -]	2.33 [0.73; 7.48]	0.154	
Region									
WHO Stratum A	387	22 (5.7)	n.c.	383	9 (2.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	6 (5.6)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	2.50 [0.50; 12.57]	0.268	0.829
No	284	16 (5.6)	Not reached [-; -]	283	7 (2.5)	Not reached [-; -]	2.20 [0.90; 5.35]	0.083	
Prior Chemotherapy									
Yes	78	4 (5.1)	Not reached [-; -]	75	3 (4.0)	Not reached [-; -]	1.27 [0.28; 5.69]	0.755	0.382
No	313	18 (5.8)	Not reached [-; -]	313	6 (1.9)	Not reached [-; -]	2.79 [1.10; 7.05]	0.030	
SOC: General disorders and administration site conditions - PT[g]: Pyrexia									
Age group									
< 65	175	19 (10.9)	Not reached [-; -]	180	7 (3.9)	Not reached [-; -]	2.28 [0.95; 5.49]	0.065	0.785
≥65	216	14 (6.5)	Not reached [-; -]	208	6 (2.9)	Not reached [-; -]	2.10 [0.81; 5.49]	0.129	
ECOG									
0	253	23 (9.1)	Not reached [-; -]	253	7 (2.8)	Not reached [-; -]	2.75 [1.17; 6.45]	0.020	0.306
1 or 2	138	10 (7.2)	Not reached [-; -]	135	6 (4.4)	Not reached [-; -]	1.55 [0.56; 4.28]	0.401	
Region									
WHO Stratum A	387	33 (8.5)	n.c.	383	13 (3.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0	n.c.	5	0	n.c.	n.c.	n.c.	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]**
		(0.0)			(0.0)				
Mismatch repair deficient (dMMR)									
Yes	107	12 (11.2)	Not reached [-; -]	105	3 (2.9)	Not reached [-; -]	3.51 [0.98; 12.53]	0.053	0.445
No	284	21 (7.4)	Not reached [-; -]	283	10 (3.5)	Not reached [-; -]	1.82 [0.85; 3.88]	0.124	
Prior Chemotherapy									
Yes	78	5 (6.4)	Not reached [-; -]	75	2 (2.7)	Not reached [-; -]	2.34 [0.45; 12.11]	0.311	0.976
No	313	28 (8.9)	Not reached [-; -]	313	11 (3.5)	Not reached [-; -]	2.19 [1.08; 4.42]	0.029	
SOC: Investigations - PT[g]: Alanine aminotransferase increased									
Age group									
< 65	175	40 (22.9)	Not reached [-; -]	180	25 (13.9)	Not reached [79.0; -]	1.47 [0.88; 2.43]	0.138	0.492
≥65	216	32 (14.8)	Not reached [-; -]	208	14 (6.7)	Not reached [-; -]	1.99 [1.06; 3.76]	0.033	
Region									
WHO Stratum A	387	71 (18.3)	n.c.	383	38 (9.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	20 (18.7)	Not reached [-; -]	105	13 (12.4)	Not reached [79.0; -]	1.29 [0.63; 2.64]	0.483	0.354
No	284	52 (18.3)	Not reached [92.0; -]	283	26 (9.2)	Not reached [-; -]	1.84 [1.14; 2.95]	0.012	
Prior Chemotherapy									
Yes	78	7 (9.0)	Not reached [-; -]	75	6 (8.0)	Not reached [-; -]	1.00 [0.33; 3.04]	0.994	0.365
No	313	65 (20.8)	Not reached [-; -]	313	33 (10.5)	Not reached [-; -]	1.77 [1.16; 2.71]	0.008	
SOC: Investigations - PT[g]: Aspartate aminotransferase increased									
Age group									
< 65	175	29 (16.6)	Not reached [-; -]	180	17 (9.4)	Not reached [-; -]	1.57 [0.86; 2.86]	0.145	0.215
≥65	216	32 (14.8)	Not reached [-; -]	208	10 (4.8)	Not reached [-; -]	2.80 [1.37; 5.73]	0.005	
ECOG									
0	253	42 (16.6)	Not reached [-; -]	253	21 (8.3)	Not reached [-; -]	1.76 [1.04; 2.99]	0.036	0.380
1 or 2	138	19 (13.8)	Not reached [-; -]	135	6 (4.4)	Not reached [-; -]	2.96 [1.18; 7.43]	0.021	
Region									
WHO Stratum A	387	61 (15.8)	n.c.	383	27 (7.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]**
Mismatch repair deficient (dMMR)									
Yes	107	16 (15.0)	Not reached [-; -]	105	5 (4.8)	Not reached [-; -]	2.59 [0.94; 7.16]	0.067	0.565
No	284	45 (15.8)	Not reached [-; -]	283	22 (7.8)	Not reached [-; -]	1.89 [1.13; 3.16]	0.015	
Prior Chemotherapy									
Yes	78	7 (9.0)	Not reached [-; -]	75	6 (8.0)	Not reached [-; -]	0.96 [0.31; 2.92]	0.941	0.173
No	313	54 (17.3)	Not reached [-; -]	313	21 (6.7)	Not reached [-; -]	2.34 [1.41; 3.89]	0.001	
SOC: Investigations - PT[g]: Blood creatinine increased									
Age group									
< 65	175	32 (18.3)	Not reached [-; -]	180	12 (6.7)	Not reached [-; -]	2.40 [1.23; 4.70]	0.010	0.311
≥65	216	44 (20.4)	Not reached [-; -]	208	24 (11.5)	Not reached [76.7; -]	1.57 [0.95; 2.60]	0.078	
ECOG									
0	253	43 (17.0)	Not reached [-; -]	253	20 (7.9)	Not reached [-; -]	1.95 [1.14; 3.33]	0.014	0.913
1 or 2	138	33 (23.9)	Not reached [72.9; -]	135	16 (11.9)	Not reached [76.7; -]	1.74 [0.95; 3.17]	0.073	
Region									
WHO Stratum A	387	74 (19.1)	n.c.	383	36 (9.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	22 (20.6)	Not reached [-; -]	105	10 (9.5)	Not reached [76.7; -]	1.76 [0.82; 3.78]	0.144	0.870
No	284	54 (19.0)	Not reached [-; -]	283	26 (9.2)	Not reached [-; -]	1.90 [1.18; 3.04]	0.008	
Prior Chemotherapy									
Yes	78	20 (25.6)	Not reached [-; -]	75	8 (10.7)	Not reached [-; -]	2.46 [1.08; 5.60]	0.032	0.470
No	313	56 (17.9)	Not reached [-; -]	313	28 (8.9)	Not reached [-; -]	1.69 [1.07; 2.67]	0.025	
SOC: Metabolism and nutrition disorders - PT[g]: Hypoglycaemia									
Age group									
< 65	175	2 (1.1)	Not reached [-; -]	180	8 (4.4)	Not reached [-; -]	0.20 [0.04; 0.97]	0.046	0.260
≥65	216	4 (1.9)	Not reached [-; -]	208	5 (2.4)	Not reached [-; -]	0.55 [0.14; 2.15]	0.393	
ECOG									
0	253	3 (1.2)	Not reached [-; -]	253	10 (4.0)	Not reached [-; -]	0.21 [0.06; 0.77]	0.019	0.251
1 or 2	138	3 (2.2)	Not reached [-; -]	135	3 (2.2)	Not reached [-; -]	0.88 [0.18; 4.44]	0.882	
Region									

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]**
WHO Stratum A	387	6 (1.6)	n.c.	383	13 (3.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	4 (3.8)	Not reached [-; -]	0.56 [0.13; 2.43]	0.442	0.199
No	284	2 (0.7)	Not reached [-; -]	283	9 (3.2)	Not reached [-; -]	0.20 [0.04; 0.94]	0.041	
Prior Chemotherapy									
Yes	78	0 (0.0)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.036	0.062
No	313	6 (1.9)	Not reached [-; -]	313	9 (2.9)	Not reached [-; -]	0.49 [0.17; 1.41]	0.187	
SOC: Metabolism and nutrition disorders - PT[g]: Hypokalaemia									
Age group									
< 65	175	22 (12.6)	Not reached [-; -]	180	32 (17.8)	Not reached [-; -]	0.64 [0.37; 1.10]	0.103	0.428
≥65	216	40 (18.5)	Not reached [98.9; -]	208	44 (21.2)	Not reached [-; -]	0.76 [0.50; 1.18]	0.225	
ECOG									
0	253	41 (16.2)	Not reached [-; -]	253	42 (16.6)	Not reached [-; -]	0.89 [0.57; 1.37]	0.584	0.121
1 or 2	138	21 (15.2)	Not reached [98.9; -]	135	34 (25.2)	Not reached [-; -]	0.49 [0.28; 0.86]	0.012	
Region									
WHO Stratum A	387	62 (16.0)	n.c.	383	76 (19.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	20 (18.7)	Not reached [-; -]	105	22 (21.0)	Not reached [-; -]	0.70 [0.37; 1.30]	0.257	0.869
No	284	42 (14.8)	Not reached [-; -]	283	54 (19.1)	Not reached [-; -]	0.71 [0.47; 1.06]	0.093	
Prior Chemotherapy									
Yes	78	13 (16.7)	Not reached [-; -]	75	19 (25.3)	Not reached [-; -]	0.63 [0.31; 1.29]	0.206	0.575
No	313	49 (15.7)	Not reached [-; -]	313	57 (18.2)	Not reached [-; -]	0.74 [0.50; 1.09]	0.124	
SOC: Skin and subcutaneous tissue disorders - PT[g]: Pruritus									
Age group									
< 65	175	33 (18.9)	Not reached [-; -]	180	22 (12.2)	Not reached [-; -]	1.44 [0.84; 2.47]	0.190	0.925
≥65	216	39 (18.1)	Not reached [-; -]	208	24 (11.5)	Not reached [-; -]	1.47 [0.88; 2.46]	0.136	
ECOG									
0	253	53 (20.9)	Not reached [-; -]	253	27 (10.7)	Not reached [-; -]	1.89 [1.19; 3.01]	0.007	0.061

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
1 or 2	138	19 (13.8)	Not reached [-; -]	135	19 (14.1)	Not reached [-; -]	0.88 [0.46; 1.66]	0.685	
Region									
WHO Stratum A	387	72 (18.6)	n.c.	383	45 (11.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	1 (20.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	21 (19.6)	Not reached [-; -]	105	15 (14.3)	Not reached [-; -]	1.20 [0.62; 2.34]	0.590	0.526
No	284	51 (18.0)	Not reached [-; -]	283	31 (11.0)	Not reached [-; -]	1.58 [1.01; 2.47]	0.045	
Prior Chemotherapy									
Yes	78	18 (23.1)	Not reached [-; -]	75	8 (10.7)	Not reached [-; -]	2.32 [1.01; 5.33]	0.048	0.253
No	313	54 (17.3)	Not reached [-; -]	313	38 (12.1)	Not reached [-; -]	1.28 [0.84; 1.94]	0.250	
SOC: Skin and subcutaneous tissue disorders - PT[g]: Rash									
Age group									
< 65	175	27 (15.4)	Not reached [-; -]	180	13 (7.2)	Not reached [-; -]	1.94 [1.00; 3.79]	0.051	0.417
≥65	216	36 (16.7)	Not reached [-; -]	208	23 (11.1)	Not reached [-; -]	1.42 [0.84; 2.40]	0.194	
ECOG									
0	253	39 (15.4)	Not reached [-; -]	253	25 (9.9)	Not reached [-; -]	1.43 [0.86; 2.37]	0.168	0.435
1 or 2	138	24 (17.4)	Not reached [-; -]	135	11 (8.1)	Not reached [-; -]	2.01 [0.98; 4.12]	0.056	
Region									
WHO Stratum A	387	63 (16.3)	n.c.	383	36 (9.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Prior Chemotherapy									
Yes	78	11 (14.1)	Not reached [-; -]	75	10 (13.3)	59.7 [59.7; -]	0.96 [0.41; 2.29]	0.934	0.205
No	313	52 (16.6)	Not reached [-; -]	313	26 (8.3)	Not reached [-; -]	1.86 [1.16; 2.99]	0.010	
SOC: Skin and subcutaneous tissue disorders - PT[g]: Rash maculo-papular									
ECOG									
0	253	38 (15.0)	Not reached [-; -]	253	16 (6.3)	Not reached [-; -]	2.23 [1.24; 4.02]	0.007	0.895
1 or 2	138	18 (13.0)	Not reached [-; -]	135	7 (5.2)	Not reached [-; -]	2.56 [1.07; 6.13]	0.035	
Region									
WHO Stratum A	387	56 (14.5)	n.c.	383	23 (6.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0	n.c.	5	0	n.c.	n.c.	n.c.	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
		(0.0)			(0.0)				
Mismatch repair deficient (dMMR)									
Yes	107	18 (16.8)	Not reached [-; -]	105	9 (8.6)	Not reached [-; -]	1.83 [0.82; 4.11]	0.141	0.446
No	284	38 (13.4)	Not reached [-; -]	283	14 (4.9)	Not reached [-; -]	2.63 [1.42; 4.87]	0.002	
Prior Chemotherapy									
Yes	78	4 (5.1)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	0.98 [0.25; 3.94]	0.982	0.162
No	313	52 (16.6)	Not reached [-; -]	313	19 (6.1)	Not reached [-; -]	2.64 [1.56; 4.47]	< 0.001	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PT: Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-21: Subgruppenanalysen mit nicht statistisch signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT für SOC mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
SOC[g]: General disorders and administration site conditions									
Age group									
< 65	175	8 (4.6)	Not reached [-; -]	180	3 (1.7)	Not reached [-; -]	2.44 [0.64; 9.29]	0.190	0.529
≥65	216	6 (2.8)	Not reached [-; -]	208	1 (0.5)	Not reached [-; -]	5.69 [0.69; 47.27]	0.107	
ECOG									
0	253	8 (3.2)	Not reached [-; -]	253	2 (0.8)	Not reached [-; -]	3.72 [0.79; 17.57]	0.098	0.790
1 or 2	138	6 (4.3)	Not reached [-; -]	135	2 (1.5)	Not reached [-; -]	2.76 [0.55; 13.75]	0.216	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
Region									
WHO Stratum A	387	14 (3.6)	n.c.	383	4 (1.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.047	0.139
No	284	10 (3.5)	Not reached [-; -]	283	4 (1.4)	Not reached [-; -]	2.31 [0.72; 7.38]	0.159	
Prior Chemotherapy									
Yes	78	2 (2.6)	Not reached [-; -]	75	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.161	0.303
No	313	12 (3.8)	Not reached [-; -]	313	4 (1.3)	Not reached [-; -]	2.77 [0.89; 8.62]	0.079	
SOC[g]: Infections and infestations									
Age group									
< 65	175	15 (8.6)	Not reached [-; -]	180	9 (5.0)	Not reached [-; -]	1.45 [0.63; 3.35]	0.382	0.533
≥65	216	24 (11.1)	Not reached [-; -]	208	10 (4.8)	Not reached [-; -]	2.27 [1.08; 4.74]	0.030	
ECOG									
0	253	20 (7.9)	Not reached [-; -]	253	8 (3.2)	Not reached [-; -]	2.22 [0.97; 5.07]	0.058	0.506
1 or 2	138	19 (13.8)	Not reached [-; -]	135	11 (8.1)	Not reached [-; -]	1.63 [0.77; 3.44]	0.198	
Region									
WHO Stratum A	387	39 (10.1)	n.c.	383	19 (5.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	13 (12.1)	Not reached [-; -]	105	7 (6.7)	Not reached [-; -]	1.66 [0.66; 4.19]	0.285	0.689
No	284	26 (9.2)	Not reached [-; -]	283	12 (4.2)	Not reached [-; -]	2.01 [1.01; 4.00]	0.046	
Prior Chemotherapy									
Yes	78	8 (10.3)	Not reached [-; -]	75	5 (6.7)	Not reached [-; -]	1.32 [0.43; 4.10]	0.626	0.572
No	313	31 (9.9)	Not reached [-; -]	313	14 (4.5)	Not reached [-; -]	2.08 [1.10; 3.92]	0.024	
SOC[g]: Investigations									
Age group									
< 65	175	10 (5.7)	Not reached [-; -]	180	3 (1.7)	Not reached [-; -]	3.17 [0.87; 11.56]	0.080	0.727
≥65	216	21 (9.7)	Not reached [-; -]	208	8 (3.8)	Not reached [-; -]	2.40 [1.06; 5.44]	0.036	
ECOG									

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
0	253	15 (5.9)	Not reached [-; -]	253	8 (3.2)	Not reached [-; -]	1.85 [0.79; 4.37]	0.159	0.151
1 or 2	138	16 (11.6)	Not reached [-; -]	135	3 (2.2)	Not reached [-; -]	4.62 [1.34; 15.96]	0.015	
Region									
WHO Stratum A	387	31 (8.0)	n.c.	383	11 (2.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	11 (10.3)	Not reached [-; -]	105	6 (5.7)	Not reached [-; -]	1.57 [0.57; 4.29]	0.381	0.224
No	284	20 (7.0)	Not reached [-; -]	283	5 (1.8)	Not reached [-; -]	3.88 [1.45; 10.34]	0.007	
Prior Chemotherapy									
Yes	78	5 (6.4)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	1.10 [0.29; 4.12]	0.887	0.162
No	313	26 (8.3)	Not reached [-; -]	313	7 (2.2)	Not reached [-; -]	3.51 [1.52; 8.10]	0.003	
SOC[g]: Nervous system disorders									
Age group									
< 65	175	4 (2.3)	Not reached [-; -]	180	4 (2.2)	Not reached [-; -]	0.99 [0.25; 3.97]	0.989	0.177
≥65	216	22 (10.2)	Not reached [-; -]	208	7 (3.4)	Not reached [-; -]	3.02 [1.29; 7.08]	0.011	
ECOG									
0	253	14 (5.5)	Not reached [-; -]	253	4 (1.6)	Not reached [-; -]	3.44 [1.13; 10.44]	0.030	0.329
1 or 2	138	12 (8.7)	Not reached [-; -]	135	7 (5.2)	Not reached [-; -]	1.64 [0.64; 4.17]	0.302	
Region									
WHO Stratum A	387	26 (6.7)	n.c.	383	11 (2.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	10 (9.3)	Not reached [-; -]	105	4 (3.8)	Not reached [-; -]	2.33 [0.73; 7.48]	0.154	0.941
No	284	16 (5.6)	Not reached [-; -]	283	7 (2.5)	Not reached [-; -]	2.25 [0.92; 5.46]	0.074	
Prior Chemotherapy									
Yes	78	3 (3.8)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	3.01 [0.31; 28.89]	0.341	0.838
No	313	23 (7.3)	Not reached [-; -]	313	10 (3.2)	Not reached [-; -]	2.24 [1.06; 4.70]	0.034	
SOC[g]: Respiratory, thoracic and mediastinal disorders									
Age group									
< 65	175	12 (6.9)	Not reached [-; -]	180	4 (2.2)	Not reached [-; -]	3.07 [0.99; 9.51]	0.052	0.814

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
≥65	216	16 (7.4)	Not reached [-; -]	208	6 (2.9)	Not reached [-; -]	2.22 [0.86; 5.72]	0.097	
ECOG									
0	253	13 (5.1)	Not reached [-; -]	253	5 (2.0)	Not reached [-; -]	2.21 [0.78; 6.26]	0.135	0.837
1 or 2	138	15 (10.9)	Not reached [-; -]	135	5 (3.7)	Not reached [-; -]	2.85 [1.03; 7.85]	0.043	
Region									
WHO Stratum A	387	28 (7.2)	n.c.	383	10 (2.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	8 (7.5)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	3.65 [0.77; 17.28]	0.103	0.681
No	284	20 (7.0)	Not reached [-; -]	283	8 (2.8)	Not reached [-; -]	2.28 [1.00; 5.19]	0.050[h]	
Prior Chemotherapy									
Yes	78	10 (12.8)	Not reached [71.6; -]	75	3 (4.0)	Not reached [-; -]	2.71 [0.73; 10.01]	0.135	0.730
No	313	18 (5.8)	Not reached [-; -]	313	7 (2.2)	Not reached [-; -]	2.44 [1.02; 5.85]	0.046	
SOC[g]: Vascular disorders									
Age group									
< 65	175	4 (2.3)	Not reached [-; -]	180	4 (2.2)	Not reached [-; -]	1.03 [0.26; 4.10]	0.972	0.080
≥65	216	12 (5.6)	Not reached [-; -]	208	2 (1.0)	Not reached [-; -]	5.65 [1.26; 25.27]	0.023	
Region									
WHO Stratum A	387	16 (4.1)	n.c.	383	6 (1.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	1.96 [0.36; 10.70]	0.437	0.667
No	284	12 (4.2)	Not reached [-; -]	283	4 (1.4)	Not reached [-; -]	2.93 [0.94; 9.10]	0.063	
Prior Chemotherapy									
Yes	78	5 (6.4)	Not reached [-; -]	75	2 (2.7)	Not reached [-; -]	2.32 [0.45; 12.02]	0.316	0.922
No	313	11 (3.5)	Not reached [-; -]	313	4 (1.3)	Not reached [-; -]	2.74 [0.87; 8.60]	0.085	

a: Database Cutoff Date: 18AUG2023
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
interaction term)									
g: A system organ class appears on this report only if its incidence ≥5% 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									
h: Unrounded p-value > 0.050									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); SOC: System Organ Class; WHO: World Health Organization									

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

Tabelle 4G-22: Subgruppenanalysen mit nicht statistisch signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Event (CTCAE-Grade 3-5)	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
SOC[g]: Blood and lymphatic system disorders									
Age group									
< 65	175	38 (21.7)	Not reached [-; -]	180	26 (14.4)	Not reached [-; -]	1.48 [0.90; 2.44]	0.126	0.778
≥65	216	49 (22.7)	Not reached [-; -]	208	29 (13.9)	Not reached [-; -]	1.66 [1.05; 2.63]	0.031	
ECOG									
0	253	50 (19.8)	Not reached [-; -]	253	29 (11.5)	Not reached [-; -]	1.67 [1.06; 2.65]	0.028	0.607
1 or 2	138	37 (26.8)	Not reached [-; -]	135	26 (19.3)	Not reached [-; -]	1.49 [0.90; 2.47]	0.117	
Region									
WHO Stratum A	387	87 (22.5)	n.c.	383	53 (13.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	2 (40.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	23 (21.5)	Not reached [-; -]	105	15 (14.3)	Not reached [-; -]	1.51 [0.79; 2.89]	0.218	0.810
No	284	64 (22.5)	Not reached [-; -]	283	40 (14.1)	Not reached [-; -]	1.61 [1.08; 2.39]	0.018	
Prior Chemotherapy									
Yes	78	19 (24.4)	Not reached [-; -]	75	8 (10.7)	Not reached [-; -]	2.31 [1.01; 5.30]	0.048	0.262
No	313	68 (21.7)	Not reached [-; -]	313	47 (15.0)	Not reached [-; -]	1.45 [1.00; 2.11]	0.050[h]	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Event (CTCAE-Grade 3-5)	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
SOC[g]: Infections and infestations									
Age group									
< 65	175	19 (10.9)	Not reached [-; -]	180	11 (6.1)	Not reached [-; -]	1.49 [0.70; 3.16]	0.301	0.346
≥65	216	33 (15.3)	Not reached [-; -]	208	12 (5.8)	Not reached [-; -]	2.26 [1.16; 4.39]	0.017	
ECOG									
0	253	24 (9.5)	Not reached [-; -]	253	10 (4.0)	Not reached [-; -]	1.98 [0.94; 4.17]	0.072	0.841
1 or 2	138	28 (20.3)	Not reached [80.9; -]	135	13 (9.6)	Not reached [-; -]	1.81 [0.93; 3.52]	0.082	
Region									
WHO Stratum A	387	51 (13.2)	n.c.	383	23 (6.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	19 (17.8)	Not reached [-; -]	105	7 (6.7)	Not reached [-; -]	2.12 [0.88; 5.12]	0.094	0.755
No	284	33 (11.6)	Not reached [-; -]	283	16 (5.7)	Not reached [-; -]	1.78 [0.98; 3.25]	0.060	
Prior Chemotherapy									
Yes	78	9 (11.5)	Not reached [-; -]	75	6 (8.0)	Not reached [-; -]	1.12 [0.39; 3.23]	0.829	0.372
No	313	43 (13.7)	Not reached [-; -]	313	17 (5.4)	Not reached [-; -]	2.15 [1.22; 3.78]	0.008	
SOC[g]: Skin and subcutaneous tissue disorders									
Age group									
< 65	175	6 (3.4)	Not reached [-; -]	180	2 (1.1)	Not reached [-; -]	2.77 [0.55; 13.88]	0.216	0.951
≥65	216	10 (4.6)	Not reached [-; -]	208	3 (1.4)	Not reached [-; -]	2.97 [0.81; 10.83]	0.100	
ECOG									
0	253	12 (4.7)	Not reached [-; -]	253	3 (1.2)	Not reached [-; -]	3.53 [0.99; 12.61]	0.052	0.512
1 or 2	138	4 (2.9)	Not reached [-; -]	135	2 (1.5)	Not reached [-; -]	1.96 [0.36; 10.69]	0.438	
Region									
WHO Stratum A	387	16 (4.1)	n.c.	383	5 (1.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	1 (1.0)	Not reached [-; -]	2.91 [0.31; 26.88]	0.347	0.879
No	284	12 (4.2)	Not reached [-; -]	283	4 (1.4)	Not reached [-; -]	2.88 [0.93; 8.95]	0.068	

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Event (CTCAE-Grade 3-5)	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
Prior Chemotherapy									
Yes	78	2 (2.6)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	1.91 [0.17; 21.10]	0.596	0.668
No	313	14 (4.5)	Not reached [-; -]	313	4 (1.3)	Not reached [-; -]	3.16 [1.03; 9.66]	0.044	

a: Database Cutoff Date: 18AUG2023
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
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 ≥5% 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
h: Unrounded p-value > 0.050
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); SOC: System Organ Class; WHO: World Health Organization

Tabelle 4G-23: Subgruppenanalysen mit nicht statistisch signifikantem Interaktionstest (p ≥ 0,05) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Event (CTCAE-Grade 3-5)	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
SOC: Metabolism and nutrition disorders - PT[g]: Hyperglycaemia									
Age group									
< 65	175	10 (5.7)	Not reached [-; -]	180	1 (0.6)	Not reached [-; -]	8.27 [1.05; 65.34]	0.045	0.440
≥65	216	3 (1.4)	Not reached [-; -]	208	1 (0.5)	Not reached [-; -]	1.83 [0.18; 18.22]	0.607	
ECOG									
0	253	8 (3.2)	Not reached [-; -]	253	2 (0.8)	Not reached [-; -]	2.97 [0.62; 14.29]	0.174	0.183
1 or 2	138	5 (3.6)	Not reached [-; -]	135	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.053	
Region									
WHO Stratum A	387	13 (3.4)	n.c.	383	2 (0.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4	Not reached	105	0	Not reached	n.a.	0.046	0.283

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Event (CTCAE-Grade 3-5)	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
		(3.7)	[-; -]		(0.0)	[-; -]	[n.a.; n.a.]		
No	284	9 (3.2)	Not reached [-; -]	283	2 (0.7)	Not reached [-; -]	3.07 [0.65; 14.47]	0.155	
Prior Chemotherapy									
Yes	78	2 (2.6)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	1.36 [0.11; 16.17]	0.810	0.307
No	313	11 (3.5)	Not reached [-; -]	313	1 (0.3)	Not reached [-; -]	8.37 [1.07; 65.44]	0.043	
SOC: Respiratory, thoracic and mediastinal disorders - PT[g]: Dyspnoea									
Age group									
< 65	175	5 (2.9)	n.c.	180	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥65	216	6 (2.8)	n.c.	208	1 (0.5)	n.c.	n.c.	n.c.	
ECOG									
0	253	4 (1.6)	n.c.	253	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1 or 2	138	7 (5.1)	n.c.	135	1 (0.7)	n.c.	n.c.	n.c.	
Region									
WHO Stratum A	387	11 (2.8)	n.c.	383	1 (0.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	5	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	n.c.	105	0 (0.0)	n.c.	n.c.	n.c.	n.c.
No	284	7 (2.5)	n.c.	283	1 (0.4)	n.c.	n.c.	n.c.	
Prior Chemotherapy									
Yes	78	2 (2.6)	Not reached [-; -]	75	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.190	0.539
No	313	9 (2.9)	Not reached [-; -]	313	1 (0.3)	Not reached [-; -]	8.52 [1.07; 67.50]	0.043	

a: Database Cutoff Date: 18AUG2023

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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 ≥5% 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

CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PT: Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Anhang 4-G5: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT

Tabelle 4G-24: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) basierend auf der MedDRA Version 26.1 (Version 25.1, 06. November 2023) anhand der zugeordneten PT in der Studie KEYNOTE 868

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, Immune-complex membranoproliferative glomerulonephritis	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, Thyrotoxic crisis, Immune-mediated hyperthyroidism, Graves' disease	Yes
Hypothyroidism	Hypothyroidism, Hypothyroidic goitre, Myxoedema, Myxoedema coma, Decompensated hypothyroidism, 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

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
Severe Skin Reactions Including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN): or	Dermatitis bullous, Dermatitis exfoliative, Dermatitis exfoliative generalised, Epidermal necrosis, Erythema multiforme, Exfoliative rash, Pemphigoid, Mucous membrane pemphigoid, Pemphigus, Skin necrosis, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Toxic skin eruption, SJS-TEN overlap, Lichen planus pemphigoides	Yes
Severe Skin (continued): If Grade 3 or higher:	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, Immune-mediated myasthenia gravis	Yes
Myelitis	Myelitis, Myelitis transverse, Acute necrotising myelitis, Immune-mediated myelitis	Yes

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
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 necrotizing, Immune-mediated vasculitis	Yes
Cholangitis Sclerosing	Cholangitis sclerosing, Autoimmune cholangitis, Immune-mediated cholangitis	Yes
Hypoparathyroidism	Hypoparathyroidism, Primary hypoparathyroidism	Yes
Arthritis	Autoimmune arthritis, Immune-mediated arthritis	Yes
HLH	Haemophagocytic lymphohistiocytosis	Yes
Optic Neuritis	Optic neuritis, Immune-mediated optic neuritis	Yes
Gastritis	Gastritis, Gastritis erosive, Gastritis haemorrhagic, Haemorrhagic erosive gastritis, Immune-mediated gastritis, Ulcerative gastritis	Yes
Haemolytic Anaemia	Autoimmune haemolytic anaemia, Cold type haemolytic anaemia, Coombs negative haemolytic anaemia, Coombs positive haemolytic anaemia, Haemolytic anaemia, Warm autoimmune haemolytic anaemia	Yes
Exocrine Pancreatic Insufficiency	Pancreatic failure	Yes

Anhang 4-G6: Ergebnisse der Interimsanalyse

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1 die Ergebnisse der Interimsanalyse (dMMR 16. Dezember 2022, pMMR 06. Dezember 2022) der Studie KEYNOTE 868 dargestellt.

Table 4.1-1
Participant Characteristics
in All-comers Participants
(Intention-to-Treat Population)

Characteristic	Study: KEYNOTE 868[a]	
	Paclitaxel + Carboplatin + Pembrolizumab N[b]=404	Paclitaxel + Carboplatin + Placebo N[b]=406
Sex, n (%)		
Female	404 (100.0)	406 (100.0)
Age (Years), n (%)		
< 65	182 (45.0)	187 (46.1)
≥65	222 (55.0)	219 (53.9)
Age (Years)		
Mean (SD)	65.6 (9.2)	65.4 (9.6)
Median (Q1; Q3)	66.3 (60.6; 71.7)	66.1 (60.1; 72.2)
Min; Max	31.2; 94.0	29.2; 90.7
Race, n (%)		
American Indian or Alaska Native	2 (0.5)	4 (1.0)
Asian	20 (5.0)	18 (4.4)
Black or African American	56 (13.9)	59 (14.5)
Multiple	1 (0.2)	1 (0.2)
Native Hawaiian or other Pacific Islander	1 (0.2)	3 (0.7)
White	303 (75.0)	297 (73.2)
Missing	21 (5.2)	24 (5.9)
Ethnicity, n (%)		
Hispanic or Latino	25 (6.2)	21 (5.2)
Not Hispanic or Latino	369 (91.3)	371 (91.4)
Not reported	5 (1.2)	7 (1.7)
Unknown	5 (1.2)	7 (1.7)
Age (Years), n (%)		
< 65	182 (45.0)	187 (46.1)
≥65 to <75	162 (40.1)	164 (40.4)
≥75	60 (14.9)	55 (13.5)
Age (Years at Initial Diagnosis), n (%)		
<65	214 (53.0)	228 (56.2)
≥65	190 (47.0)	178 (43.8)
Age (Years) at Initial Diagnosis		
Mean (SD)	63.7 (9.4)	63.6 (9.6)
Median (Q1; Q3)	64.3 (58.1; 69.9)	64.0 (58.8; 70.4)
Min; Max	30.0; 92.6	27.5; 90.6
Region, n (%)		
North America	397 (98.3)	398 (98.0)
Rest of the World	7 (1.7)	8 (2.0)

Characteristic	Study: KEYNOTE 868[a]	
	Paclitaxel + Carboplatin + Pembrolizumab N[b]=404	Paclitaxel + Carboplatin + Placebo N[b]=406
Central MMR Status, n (%)		

Participant Characteristics
in All-comers Participants
(Intention-to-Treat Population)

Characteristic	Study: KEYNOTE 868[a]	
	Paclitaxel + Carboplatin + Pembrolizumab N[b]=404	Paclitaxel + Carboplatin + Placebo N[b]=406
Indeterminate	2 (0.5)	1 (0.2)
dMMR	111 (27.5)	112 (27.6)
pMMR	288 (71.3)	290 (71.4)
Missing	3 (0.7)	3 (0.7)
ECOG (Randomization), n (%)		
0	268 (66.3)	269 (66.3)
1	126 (31.2)	123 (30.3)
2	10 (2.5)	14 (3.4)
ECOG (CRF), n (%)		
0	262 (64.9)	264 (65.0)
1	131 (32.4)	124 (30.5)
2	11 (2.7)	18 (4.4)
Measurable Disease at Baseline, n (%)		
Yes	315 (78.0)	330 (81.3)
No	89 (22.0)	76 (18.7)
Prior Chemotherapy (Randomization), n (%)		
Yes	78 (19.3)	84 (20.7)
No	326 (80.7)	322 (79.3)
Prior Chemotherapy (CRF), n (%)		
Yes	80 (19.8)	81 (20.0)
No	324 (80.2)	325 (80.0)
Prior Radiation Therapy, n (%)		
Yes	160 (39.6)	178 (43.8)
No	244 (60.4)	228 (56.2)
Elapsed Time (Years) from Initial Diagnosis		
Mean (SD)	1.8 (2.5)	1.8 (2.3)
Median (Q1; Q3)	0.8 (0.1; 2.6)	1.0 (0.1; 2.7)
Min; Max	0.0; 18.3	0.0; 14.4
Histology, n (%)		
Adenocarcinoma, NOS	36 (8.9)	47 (11.6)
Clear cell	19 (4.7)	20 (4.9)
Dedifferentiated/undifferentiated	11 (2.7)	10 (2.5)
Endometrioid, grade 1	75 (18.6)	79 (19.5)
Endometrioid, grade 2	103 (25.5)	102 (25.1)
Endometrioid, grade 3	68 (16.8)	58 (14.3)
Mixed epithelial	9 (2.2)	12 (3.0)
Serous	83 (20.5)	77 (19.0)

Participant Characteristics
in All-comers Participants
(Intention-to-Treat Population)

Characteristic	Study: KEYNOTE 868[a]	
	Paclitaxel + Carboplatin + Pembrolizumab N[b]=404	Paclitaxel + Carboplatin + Placebo N[b]=406
Missing	0 (0.0)	1 (0.2)
FIGO Stage at Initial Diagnosis, n (%)		
IA	95 (23.5)	101 (24.9)
IB	51 (12.6)	59 (14.5)
II	39 (9.7)	38 (9.4)
IIIA	16 (4.0)	16 (3.9)
IIIB	9 (2.2)	7 (1.7)
IIIC1	27 (6.7)	21 (5.2)
IIIC2	22 (5.4)	13 (3.2)
IVA	13 (3.2)	9 (2.2)
IVB	132 (32.7)	142 (35.0)
Status of Disease, n (%)		
Persistant	4 (1.0)	3 (0.7)
Primary	164 (40.6)	173 (42.6)
Recurrent	236 (58.4)	230 (56.7)
Prior Brachytherapy, n (%)		
Y	98 (24.3)	121 (29.8)
N	306 (75.7)	285 (70.2)
Prior Hormonal Therapy, n (%)		
Y	23 (5.7)	20 (4.9)
N	381 (94.3)	386 (95.1)

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

CRF: Case Report Form; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Max: Maximum; Min: Minimum; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Table 4.1-2
Summary of Participants who Discontinued Trial and Study Medication
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab n (%)**	**Paclitaxel + Carboplatin + Placebo n (%)**
Participants in population[b]	404	406
Status For Trial		
Discontinued	76 (18.8)	92 (22.7)
Death	55 (13.6)	71 (17.5)
Lost To Follow-Up	1 (0.2)	0 (0.0)
Subject Decision To Withdraw From Study	19 (4.7)	21 (5.2)
Other	1 (0.2)	0 (0.0)
Ongoing	328 (81.2)	314 (77.3)
Status For Study Medication In Trial		
Started[c]	382	377
Completed	11 (2.9)	2 (0.5)
Discontinued	192 (50.3)	246 (65.3)
Adverse Event/Side Effects/Complications	53 (13.9)	23 (6.1)
Alternative Therapy (In Absence Of Progression)	2 (0.5)	3 (0.8)
Death On Study	7 (1.8)	4 (1.1)
Disease Progression, Relapse During Active Treatment	98 (25.7)	147 (39.0)
Patient Off-Treatment For Other Complicating Disease	5 (1.3)	2 (0.5)
Patient Withdrawal/Refusal After Beginning Protocol Therapy	17 (4.5)	15 (4.0)
Symptomatic Deterioration	2 (0.5)	5 (1.3)
Other	8 (2.1)	47 (12.5)
Ongoing	179 (46.9)	129 (34.2)

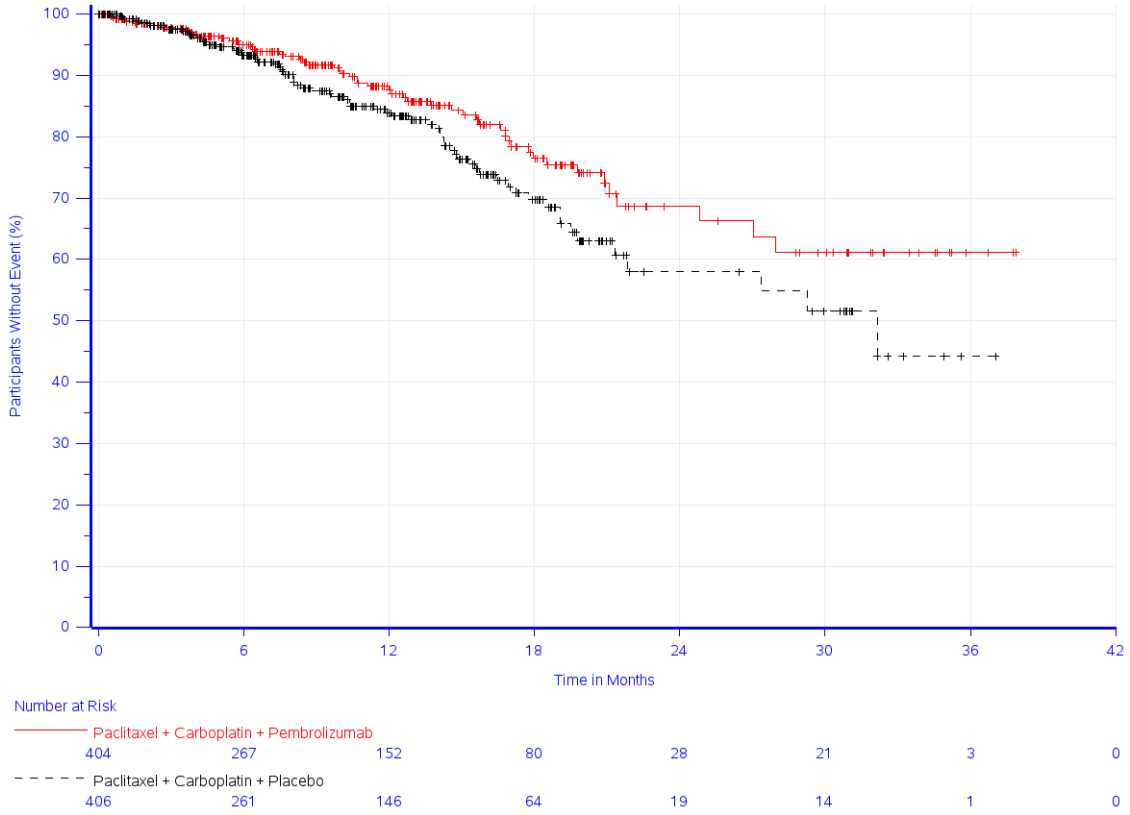
a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: Number of participants: all-participants-as-treated population
dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Table 4.2-3
Analysis of Overall Survival
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Overall Survival	404	55 (13.6)	Not reached [28.0; -]	406	71 (17.5)	32.2 [21.8; -]	0.72 [0.51; 1.03]	0.072

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.2-1
Kaplan-Meier Curves of Overall Survival
in All-comers Participants
(Intention-to-Treat Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Overall Survival

Table 4.2-4
Sensitivity Analyses of Overall Survival
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Overall Survival - Two stage[f]	404	55 (13.6)	Not reached [28.0; -]	406	71 (17.5)	27.4 [19.5; -]	0.62 [0.41; 0.93]	0.014
Overall Survival - IPCW[g]	404	45 (11.1)	Not reached [21.4; -]	406	43 (10.6)	19.1 [19.1; 19.1]	0.52 [0.30; 0.93]	0.016

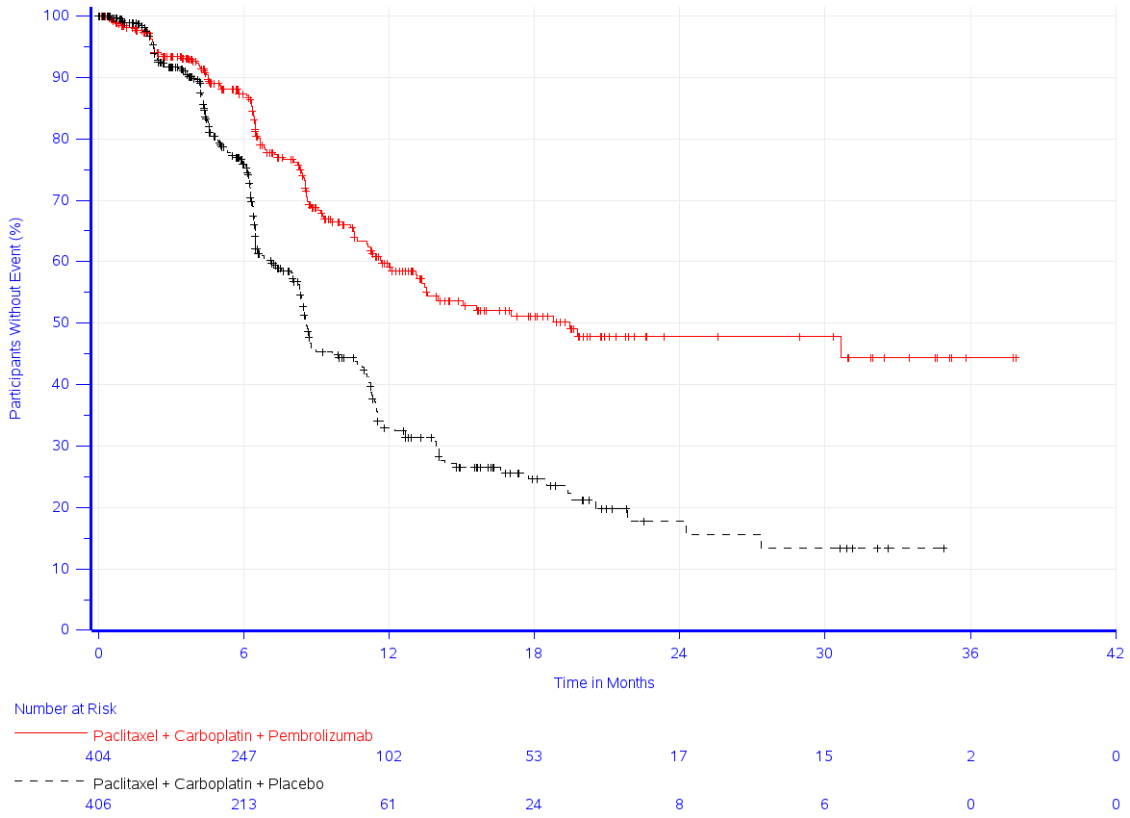
a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value based on bootstrap percentiles
f: Two-stage model is used to adjust for the effect of treatment switchover to subsequent anti-PD1/PD-L1 or lenvatinib therapies in both arms. No re-censoring was performed. Confidence interval of hazard ratio is obtained based on 1000 bootstraps
g: IPCW model is used to adjust for the effect of treatment switchover to subsequent anti-PD1/PD-L1 or lenvatinib therapies in both arms. Confidence interval of hazard ratio and p-value are obtained by fitting the Cox regression model to the bootstrap samples corrected by the IPCW approach
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; IPCW: Inverse-probability-of-censoring weighting; MMR: Mismatch Repair; PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death - Ligand 1; pMMR: Proficient Mismatch Repair

Table 4.3-5
Analysis of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1
(Protocol Censoring Rule)
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Progression-Free Survival (INV Primary Censoring Rule)	404	124 (30.7)	19.5 [13.4; -]	406	198 (48.8)	8.5 [8.3; 10.6]	0.49 [0.39; 0.62]	< 0.001

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; INV: Investigator; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.3-2
Kaplan-Meier Curves of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule)
in All-comers Participants
(Intention-to-Treat Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule)

Table 4.3-6
Analysis of Progression-Free Survival Based on BICR Assessment per RECIST 1.1
(Protocol Censoring Rule)
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Progression-Free Survival (IRC Primary Censoring Rule)	404	110 (27.2)	24.8 [17.4; -]	406	167 (41.1)	11.2 [9.4; 13.9]	0.58 [0.46; 0.74]	< 0.001

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

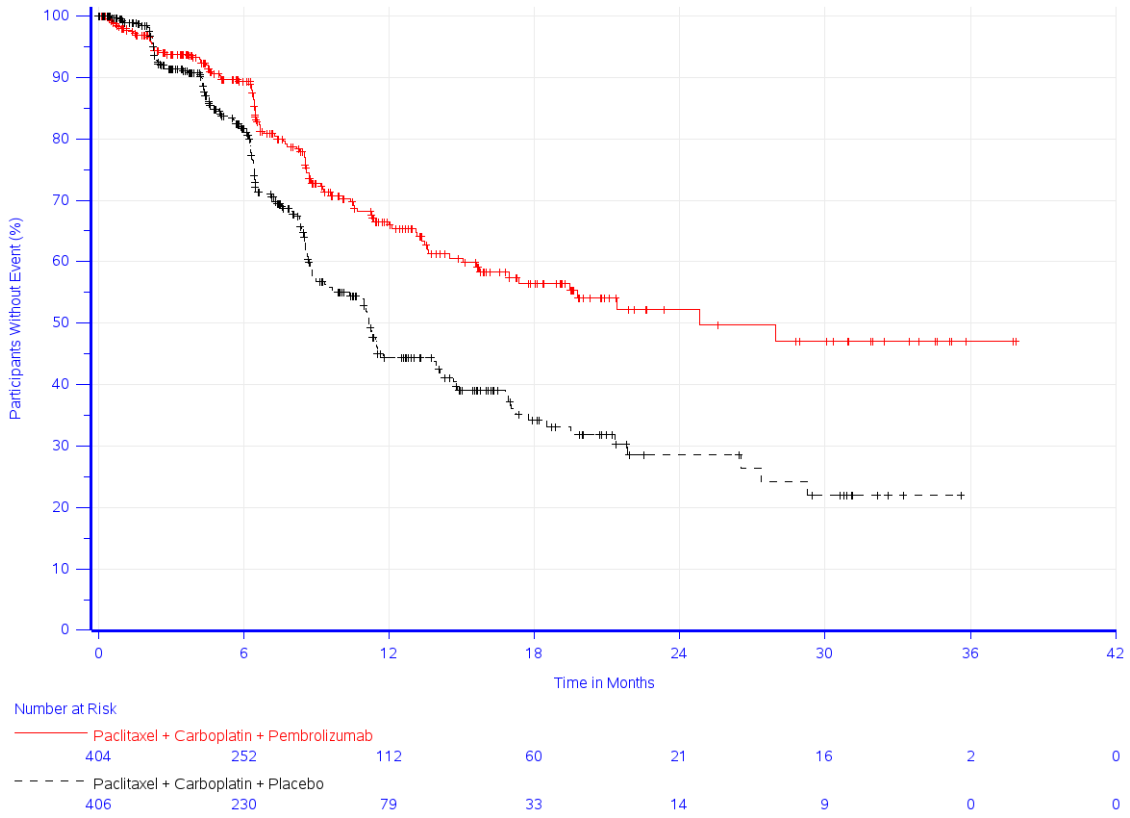
c: From product-limit (Kaplan-Meier) method for censored data

d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

CI: Confidence Interval; dMMR: Deficient Mismatch Repair; IRC: Independent Review Committee; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.3-3
Kaplan-Meier Curves of Progression-Free Survival Based on BICR Assessment per RECIST 1.1 (Protocol Censoring Rule)
in All-comers Participants
(Intention-to-Treat Population)



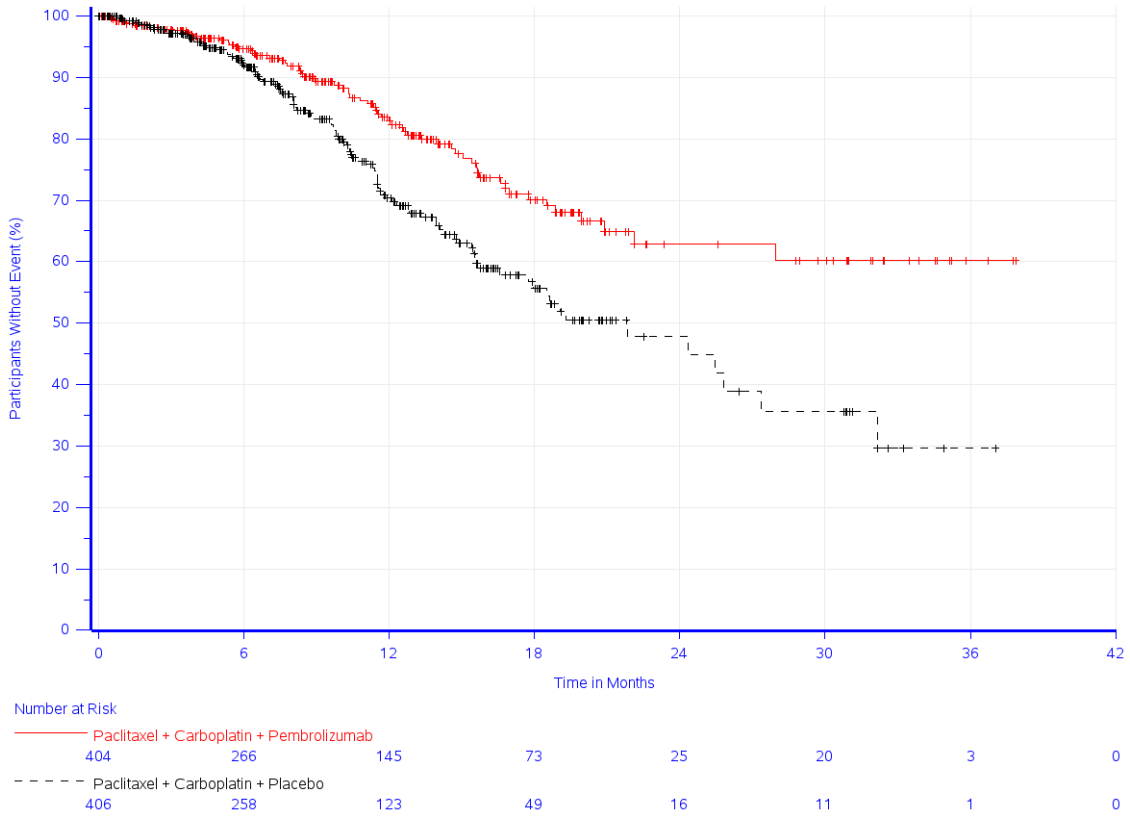
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival Based on BICR Assessment per RECIST 1.1 (Protocol Censoring Rule)

Table 4.4-7
Analysis of Progression-Free Survival On Next Line Therapy (PFS2) Based on Investigator Assessment
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Progression-Free Survival On Next Line Therapy	404	66 (16.3)	Not reached [28.0; -]	406	101 (24.9)	21.8 [17.8; 27.4]	0.56 [0.41; 0.77]	< 0.001

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.4-4
Kaplan-Meier Curves of Progression-Free Survival On Next Line Therapy (PFS2) Based on Investigator Assessment
in All-comers Participants
(Intention-to-Treat Population)



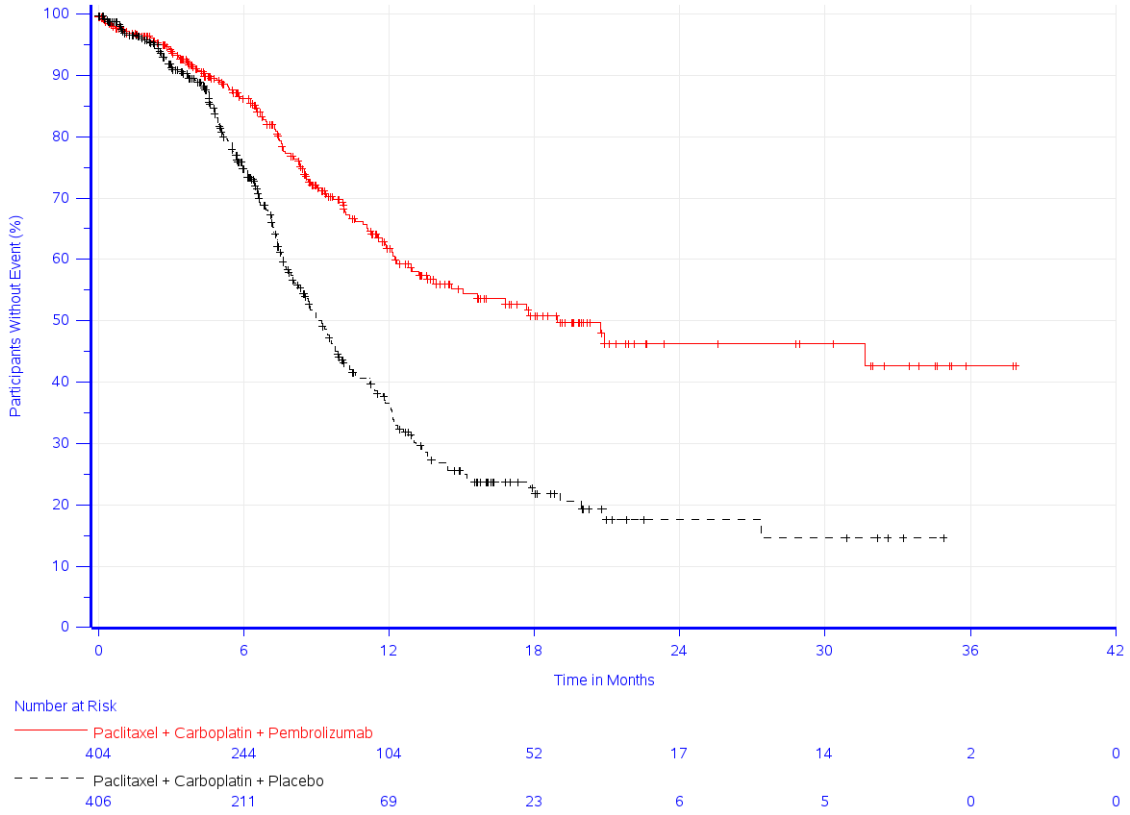
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival On Next Line Therapy (PFS2) Based on Investigator Assessment

Table 4.6-8
Analysis of Time to Subsequent Systemic Therapy or Death
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Time to Subsequent Oncologic Therapy or Death	404	121 (30.0)	19.0 [13.6; -]	406	200 (49.3)	9.1 [8.2; 10.1]	0.47 [0.37; 0.59]	< 0.001

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.6-5
Kaplan-Meier Curves of Time to Subsequent Systemic Therapy or Death
in All-comers Participants
(Intention-to-Treat Population)



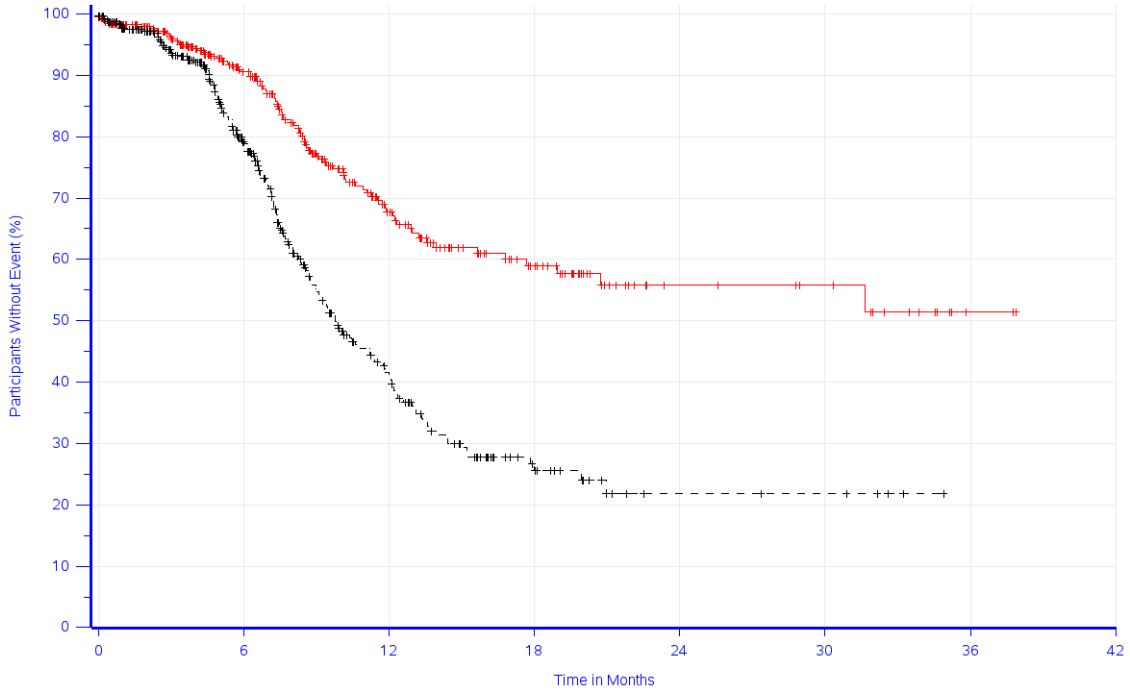
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Time to Subsequent Systemic Therapy or Death

Table 4.6-9
Analysis of Time to Subsequent Systemic Therapy
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Time to Subsequent Oncologic Therapy	404	93 (23.0)	Not reached [19.0; -]	406	171 (42.1)	9.8 [8.7; 11.4]	0.42 [0.32; 0.54]	< 0.001

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate stratified by MMR status and prior chemotherapy. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; MMR: Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.6-6
Kaplan-Meier Curves of Time to Subsequent Systemic Therapy
in All-comers Participants
(Intention-to-Treat Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Time to Subsequent Systemic Therapy

Table 4.6-10
Participants with Subsequent Systemic Oncologic Therapy
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Category[b] **Sub-category[c]**	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=404)**	**Paclitaxel + Carboplatin + Placebo (N[d]=406)**
Participants who received subsequent systemic oncologic therapy	93 (23.02)	171 (42.12)
Anti-PD-1/PD-L1	41 (10.15)	121 (29.80)
PEMBROLIZUMAB	39 (9.65)	115 (28.33)
DURVALUMAB	2 (0.50)	3 (0.74)
NIVOLUMAB	0 (0.00)	2 (0.49)
ATEZOLIZUMAB	0 (0.00)	1 (0.25)
RETIFANLIMAB	0 (0.00)	1 (0.25)
Anti-angiogenic	39 (9.65)	82 (20.20)

Study: KEYNOTE 868[a]	Participants with Event n (%)	
Category[b] Sub-category[c]	Paclitaxel + Carboplatin + Pembrolizumab (N[d]=404)	Paclitaxel + Carboplatin + Placebo (N[d]=406)
LENVATINIB	25 (6.19)	69 (17.00)
BEVACIZUMAB	12 (2.97)	11 (2.71)
CEDIRANIB	2 (0.50)	2 (0.49)
BEVACIZUMAB AWWB	2 (0.50)	1 (0.25)
BEVACIZUMAB BVZR	0 (0.00)	1 (0.25)
Chemotherapy	44 (10.89)	47 (11.58)
CARBOPLATIN	16 (3.96)	22 (5.42)
PACLITAXEL	15 (3.71)	22 (5.42)
DOXORUBICIN	10 (2.48)	9 (2.22)
LIPOSOMAL DOXORUBICIN	9 (2.23)	6 (1.48)
PEGYLATED LIPOSOMAL DOXORUBICIN HYDROCHLORIDE	6 (1.49)	3 (0.74)
CISPLATIN	3 (0.74)	3 (0.74)
LIPOSOMAL DOXORUBICIN HYDROCHLORIDE	3 (0.74)	1 (0.25)
GEMCITABINE	2 (0.50)	1 (0.25)
DOCETAXEL	0 (0.00)	3 (0.74)
TOPOTECAN	3 (0.74)	0 (0.00)
PEGYLATED LIPOSOMAL DOXORUBICIN	0 (0.00)	2 (0.49)
OTHER THERAPEUTIC PRODUCTS	0 (0.00)	1 (0.25)
Hormonal agents	17 (4.21)	20 (4.93)
LETROZOLE	10 (2.48)	10 (2.46)
MEGESTROL	5 (1.24)	6 (1.48)
TAMOXIFEN	5 (1.24)	6 (1.48)
ANASTROZOLE	1 (0.25)	2 (0.49)
MEGESTROL ACETATE	1 (0.25)	1 (0.25)
ENDOCRINE THERAPY	1 (0.25)	0 (0.00)
Other Investigational or Approved Agents	10 (2.48)	23 (5.67)
EVEROLIMUS	3 (0.74)	7 (1.72)
OLAPARIB	1 (0.25)	5 (1.23)
TRASTUZUMAB	3 (0.74)	2 (0.49)
CAPIVASERTIB	0 (0.00)	3 (0.74)
ONAPRISTONE	1 (0.25)	1 (0.25)
ETIGILIMAB	0 (0.00)	2 (0.49)
VIBOSTOLIMAB	0 (0.00)	2 (0.49)
ABEMACICLIB	1 (0.25)	0 (0.00)
AFATINIB	1 (0.25)	0 (0.00)
ALPELISIB	0 (0.00)	1 (0.25)
ANTINEOPLASTIC AGENTS	0 (0.00)	1 (0.25)
MARGETUXIMAB	0 (0.00)	1 (0.25)
METHOTREXATE	0 (0.00)	1 (0.25)
REBASTINIB	0 (0.00)	1 (0.25)
TEBOTELIMAB	0 (0.00)	1 (0.25)
TRASTUZUMAB DERUXTECAN NXKI	1 (0.25)	0 (0.00)
PROCEDURES, OTHER NON-THERAPEUTIC PRODUCTS OR AGENTS	1 (0.25)	5 (1.23)
ALL OTHER NON-THERAPEUTIC PRODUCTS	0 (0.00)	3 (0.74)
DENOSUMAB	0 (0.00)	2 (0.49)
APIXABAN	1 (0.25)	0 (0.00)
RADIOTHERAPY	15 (3.71)	25 (6.16)
RADIOTHERAPY	15 (3.71)	25 (6.16)

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: A specific medication class appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding. A participant with multiple first subsequent systemic therapies within a medication class is counted a single time for that medication class

c: Every participant is counted a single time for each applicable systemic therapy

d: Number of participants: intention-to-treat population

dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Table 4.6-11
Participants with Subsequent Systemic Oncologic Therapy
who Progressed Based on Investigator Assessment per RECIST 1.1
(Protocol Censoring Rule)
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Category[b] **Sub-category[c]**	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=106)**	**Paclitaxel + Carboplatin + Placebo (N[d]=178)**
Participants who received subsequent systemic oncologic therapy	71 (66.98)	143 (80.34)
Anti-PD-1/PD-L1	33 (31.13)	112 (62.92)
PEMBROLIZUMAB	31 (29.25)	106 (59.55)
DURVALUMAB	2 (1.89)	3 (1.69)
NIVOLUMAB	0 (0.00)	2 (1.12)
ATEZOLIZUMAB	0 (0.00)	1 (0.56)
RETIFANLIMAB	0 (0.00)	1 (0.56)
Anti-angiogenic	33 (31.13)	75 (42.13)
LENVATINIB	19 (17.92)	64 (35.96)
BEVACIZUMAB	12 (11.32)	9 (5.06)
CEDIRANIB	2 (1.89)	2 (1.12)
BEVACIZUMAB AWWB	2 (1.89)	0 (0.00)
BEVACIZUMAB BVZR	0 (0.00)	1 (0.56)
Chemotherapy	33 (31.13)	35 (19.66)
DOXORUBICIN	10 (9.43)	8 (4.49)
CARBOPLATIN	7 (6.60)	12 (6.74)
PACLITAXEL	5 (4.72)	14 (7.87)
LIPOSOMAL DOXORUBICIN	9 (8.49)	5 (2.81)
PEGYLATED LIPOSOMAL DOXORUBICIN HYDROCHLORIDE	6 (5.66)	3 (1.69)
CISPLATIN	2 (1.89)	3 (1.69)
LIPOSOMAL DOXORUBICIN HYDROCHLORIDE	3 (2.83)	1 (0.56)
TOPOTECAN	3 (2.83)	0 (0.00)
GEMCITABINE	2 (1.89)	1 (0.56)
PEGYLATED LIPOSOMAL DOXORUBICIN	0 (0.00)	2 (1.12)
DOCETAXEL	0 (0.00)	1 (0.56)
OTHER THERAPEUTIC PRODUCTS	0 (0.00)	1 (0.56)
Hormonal agents	12 (11.32)	16 (8.99)
LETROZOLE	7 (6.60)	9 (5.06)
MEGESTROL	4 (3.77)	4 (2.25)
TAMOXIFEN	3 (2.83)	5 (2.81)
ANASTROZOLE	1 (0.94)	2 (1.12)
Other Investigational or Approved Agents	10 (9.43)	21 (11.80)
EVEROLIMUS	3 (2.83)	7 (3.93)
OLAPARIB	1 (0.94)	5 (2.81)
TRASTUZUMAB	3 (2.83)	1 (0.56)
CAPIVASERTIB	0 (0.00)	3 (1.69)
ONAPRISTONE	1 (0.94)	1 (0.56)
ETIGILIMAB	0 (0.00)	2 (1.12)
VIBOSTOLIMAB	0 (0.00)	2 (1.12)
ABEMACICLIB	1 (0.94)	0 (0.00)
AFATINIB	1 (0.94)	0 (0.00)
TRASTUZUMAB DERUXTECAN NXKI	1 (0.94)	0 (0.00)
MARGETUXIMAB	0 (0.00)	1 (0.56)
METHOTREXATE	0 (0.00)	1 (0.56)
REBASTINIB	0 (0.00)	1 (0.56)
TEBOTELIMAB	0 (0.00)	1 (0.56)
PROCEDURES, OTHER NON-THERAPEUTIC PRODUCTS OR AGENTS	0 (0.00)	3 (1.69)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Category[b] **Sub-category**[c]	**Paclitaxel + Carboplatin + Pembrolizumab (N^d=106)**	**Paclitaxel + Carboplatin + Placebo (N^d=178)**
DENOSUMAB	0 (0.00)	2 (1.12)
ALL OTHER NON-THERAPEUTIC PRODUCTS	0 (0.00)	1 (0.56)
RADIOTHERAPY	11 (10.38)	18 (10.11)
RADIOTHERAPY	11 (10.38)	18 (10.11)

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: A specific medication class appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding. A participant with multiple first subsequent systemic therapies within a medication class is counted a single time for that medication class

c: Every participant is counted a single time for each applicable systemic therapy

d: Number of participants: intention-to-treat population who progressed based on investigator assessment per RECIST 1.1

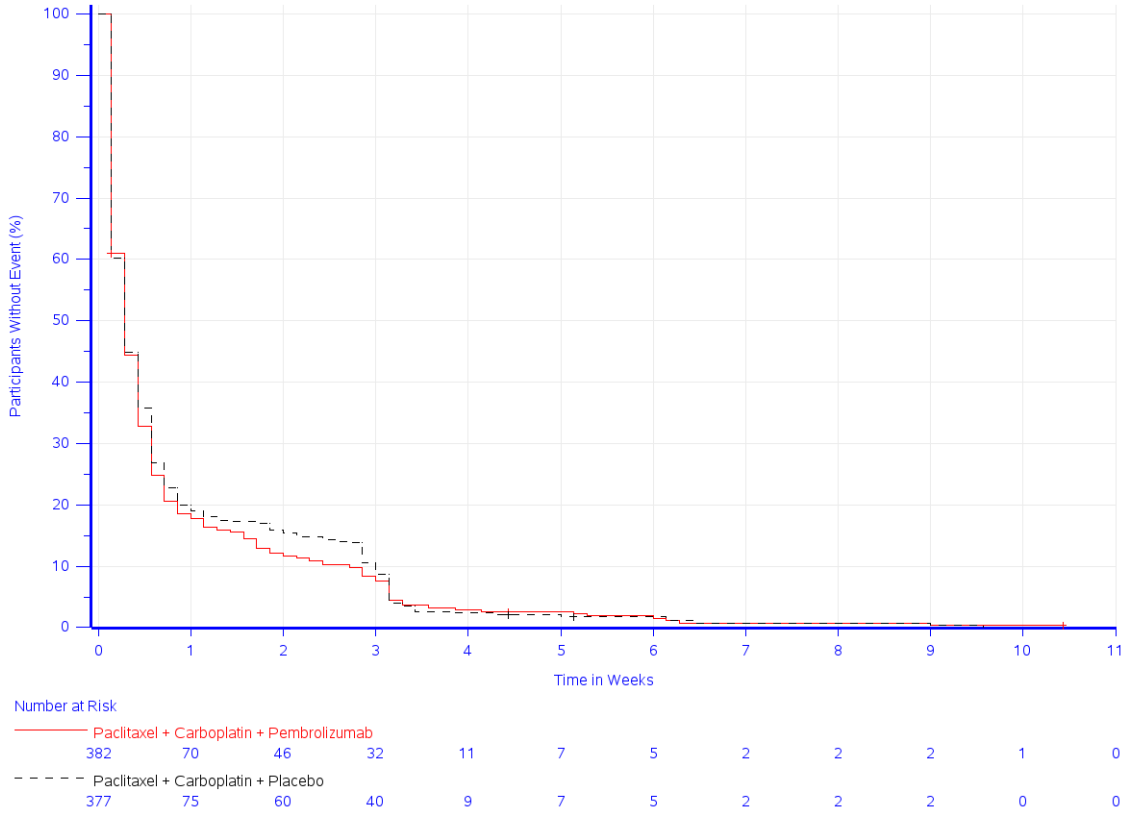
dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair; RECIST: Response Evaluation Criteria In Solid Tumors

Table 4.1-12
Time to Event Analysis for Adverse Event Related Endpoints
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Adverse Events	382	376 (98.4)	0.3 [-; -]	377	375 (99.5)	0.3 [-; -]	1.03 [0.90; 1.19]	0.654
Serious Adverse Events	382	132 (34.6)	80.9 [60.6; -]	377	73 (19.4)	Not reached [-; -]	1.84 [1.38; 2.45]	< 0.001
Severe Adverse Events (CTCAE-Grade 3-5)	382	225 (58.9)	17.9 [13.1; 20.7]	377	174 (46.2)	24.1 [17.9; -]	1.32 [1.08; 1.61]	0.006
Treatment Discontinuations Due to Adverse Events/Side Effects/Complications	382	53 (13.9)	Not reached [-; -]	377	23 (6.1)	Not reached [-; -]	1.81 [1.10; 2.96]	0.018

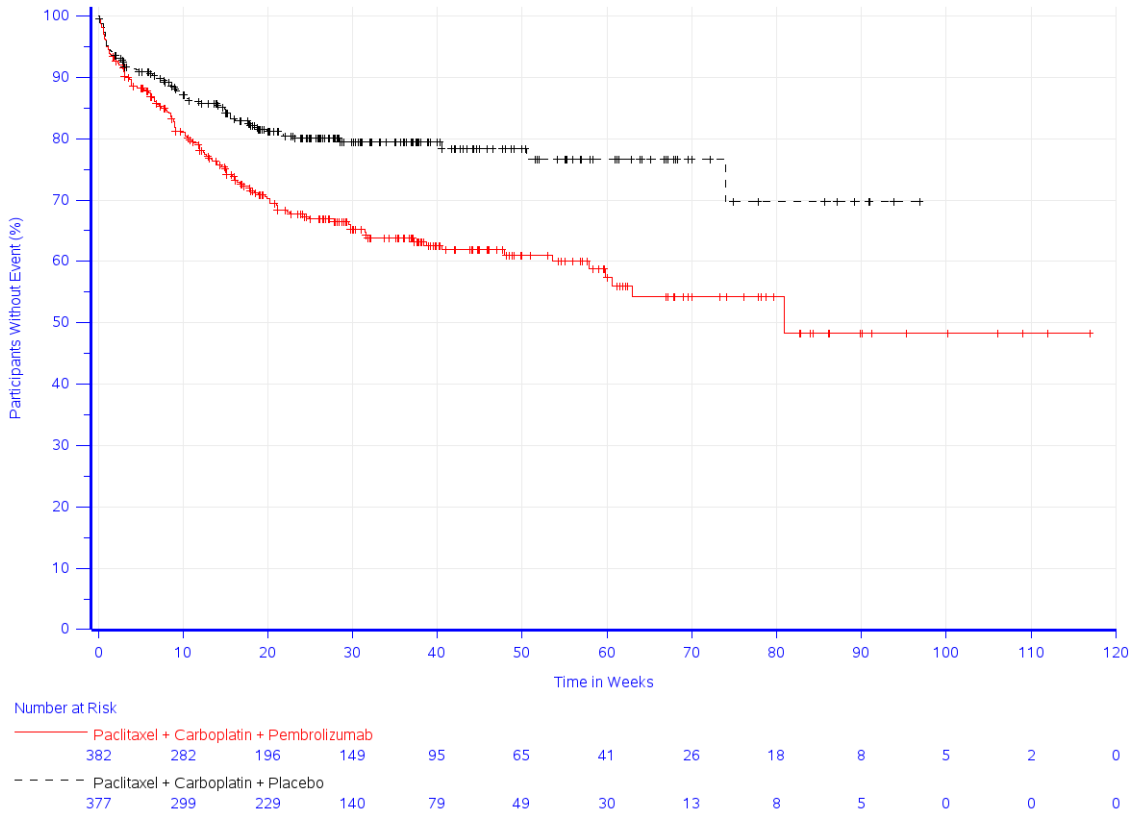
a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.1-7
Time to Adverse Event - Kaplan-Meier Curve
in All-comers Participants
(All-Participants-as-Treated Population)



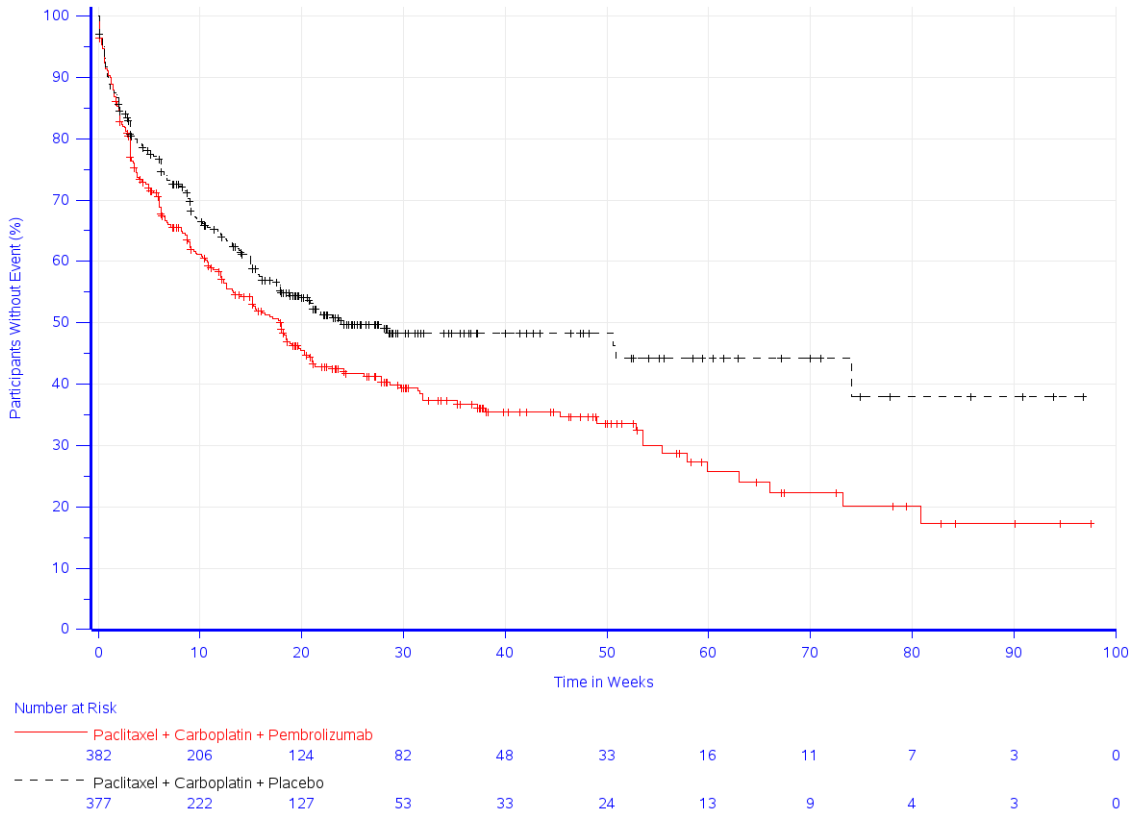
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event

Figure 4.1-8
Time to Serious Adverse Event - Kaplan-Meier Curve
in All-comers Participants
(All-Participants-as-Treated Population)



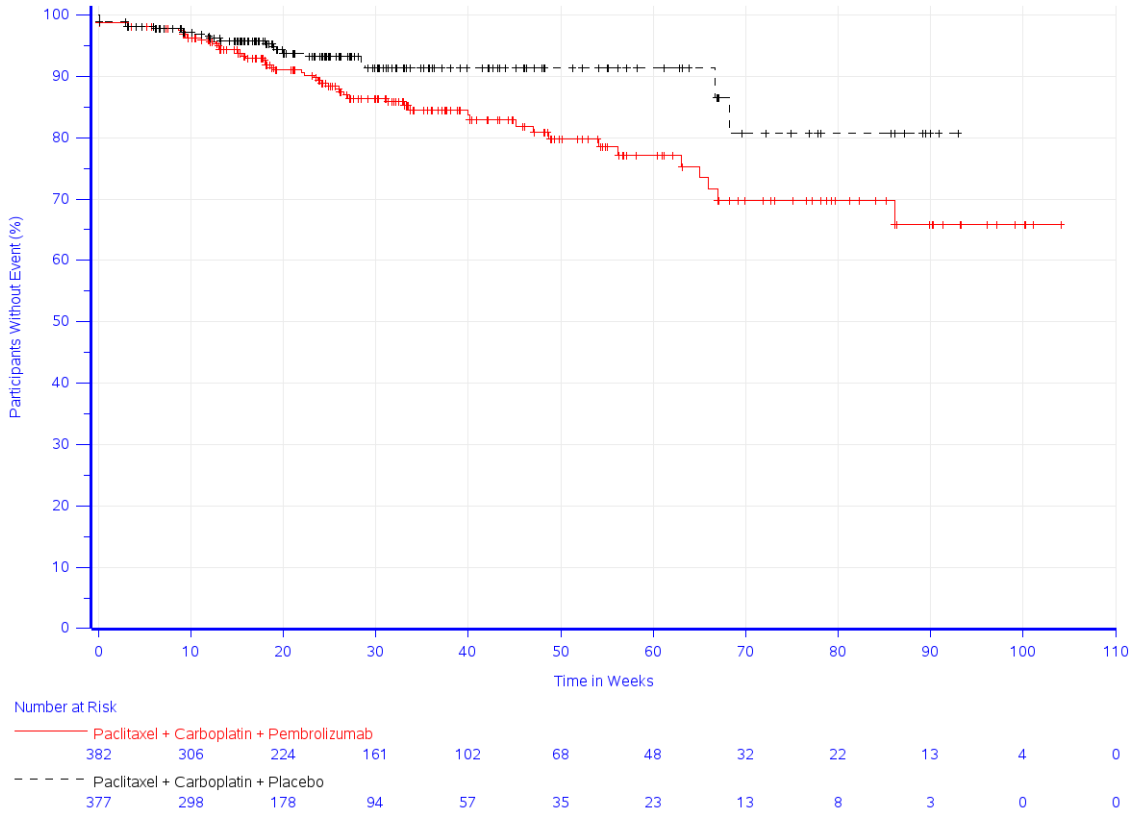
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Serious Adverse Event

Figure 4.1-9
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5)

Figure 4.1-10
Time to Treatment Discontinuation Due to Adverse Events/Side Effects/Complications - Kaplan-Meier Curve
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Time to Treatment Discontinuation Due to Adverse Events/Side Effects/Complications

Table 4.2-13
Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Blood and lymphatic system disorders	232 (60.7)	12.0 [9.3; 14.7]	218 (57.8)	12.0 [9.1; 15.0]	1.07 [0.89; 1.29]	0.471	0.785
Anaemia	212 (55.5)	14.7 [11.9; 17.1]	205 (54.4)	14.9 [11.9; 17.7]	1.04 [0.86; 1.26]	0.677	n.s.
Febrile neutropenia	13 (3.4)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.60 [0.93; 7.29]	0.069	n.s.
Neutropenia	22 (5.8)	Not reached [-; -]	22 (5.8)	Not reached [-; -]	0.99 [0.55; 1.79]	0.977	n.s.
Thrombocytopenia	15 (3.9)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	1.11 [0.53; 2.34]	0.782	n.s.
Cardiac disorders	50 (13.1)	Not reached [-; -]	28 (7.4)	Not reached [-; -]	1.72 [1.08; 2.74]	0.021	0.142
Palpitations	10 (2.6)	Not reached [-; -]	2 (0.5)	Not reached [-; -]	4.79 [1.05; 21.89]	0.043	n.s.
Sinus tachycardia	11 (2.9)	Not reached [-; -]	9 (2.4)	Not reached [-; -]	1.12 [0.46; 2.72]	0.798	n.s.
Tachycardia	13 (3.4)	Not reached [-; -]	6 (1.6)	Not reached [-; -]	2.10 [0.80; 5.53]	0.133	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Ear and labyrinth disorders	22 (5.8)	Not reached [-; -]	21 (5.6)	Not reached [-; -]	0.95 [0.52; 1.72]	0.855	0.900
Tinnitus	13 (3.4)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.56 [0.65; 3.78]	0.320	n.s.
Endocrine disorders	64 (16.8)	Not reached [-; -]	25 (6.6)	Not reached [-; -]	2.50 [1.57; 3.97]	< 0.001	0.002
Hyperthyroidism	25 (6.5)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	2.38 [1.14; 4.97]	0.021	0.048
Hypothyroidism	47 (12.3)	Not reached [-; -]	14 (3.7)	Not reached [-; -]	3.25 [1.79; 5.91]	< 0.001	< 0.001
Eye disorders	64 (16.8)	Not reached [-; -]	45 (11.9)	Not reached [-; -]	1.34 [0.91; 1.96]	0.137	0.330
Dry eye	16 (4.2)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	2.12 [0.87; 5.17]	0.097	n.s.
Vision blurred	38 (9.9)	Not reached [-; -]	24 (6.4)	Not reached [-; -]	1.52 [0.91; 2.54]	0.106	n.s.
Gastrointestinal disorders	330 (86.4)	1.7 [0.9; 2.9]	309 (82.0)	2.0 [1.0; 3.0]	1.09 [0.93; 1.27]	0.295	0.590

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Abdominal distension	15 (3.9)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	0.74 [0.37; 1.48]	0.398	n.s.
Abdominal pain	58 (15.2)	Not reached [-; -]	52 (13.8)	Not reached [-; -]	1.04 [0.72; 1.52]	0.826	n.s.
Abdominal pain upper	13 (3.4)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.38 [0.85; 6.70]	0.101	n.s.
Constipation	175 (45.8)	44.1 [15.0; -]	154 (40.8)	Not reached [36.1; -]	1.11 [0.89; 1.38]	0.346	n.s.
Diarrhoea	148 (38.7)	63.0 [38.9; -]	129 (34.2)	Not reached [-; -]	1.10 [0.86; 1.39]	0.452	n.s.
Dry mouth	24 (6.3)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	3.16 [1.36; 7.34]	0.008	n.s.
Dyspepsia	24 (6.3)	Not reached [-; -]	15 (4.0)	Not reached [-; -]	1.53 [0.80; 2.92]	0.198	n.s.
Gastrooesophageal reflux disease	14 (3.7)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	1.08 [0.50; 2.34]	0.849	n.s.
Nausea	183 (47.9)	28.0 [14.3; -]	165 (43.8)	56.0 [24.0; -]	1.10 [0.89; 1.36]	0.357	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Stomatitis	34 (8.9)	Not reached [-; -]	19 (5.0)	Not reached [-; -]	1.71 [0.98; 3.01]	0.061	n.s.
Vomiting	76 (19.9)	Not reached [-; -]	48 (12.7)	Not reached [-; -]	1.58 [1.10; 2.26]	0.014	n.s.
General disorders and administration site conditions	301 (78.8)	3.9 [3.3; 5.7]	265 (70.3)	6.1 [3.3; 8.1]	1.22 [1.04; 1.44]	0.016	0.142
Asthenia	16 (4.2)	Not reached [-; -]	16 (4.2)	Not reached [-; -]	0.96 [0.48; 1.91]	0.901	n.s.
Chills	20 (5.2)	Not reached [-; -]	6 (1.6)	Not reached [-; -]	3.16 [1.27; 7.89]	0.013	n.s.
Fatigue	257 (67.3)	6.7 [5.9; 9.3]	226 (59.9)	9.1 [6.1; 12.1]	1.14 [0.95; 1.36]	0.150	n.s.
Mucosal inflammation	11 (2.9)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	1.43 [0.55; 3.71]	0.461	n.s.
Oedema peripheral	46 (12.0)	Not reached [-; -]	38 (10.1)	Not reached [-; -]	1.15 [0.74; 1.76]	0.537	n.s.
Pain	23 (6.0)	Not reached [-; -]	21 (5.6)	Not reached [-; -]	1.04 [0.58; 1.89]	0.890	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Pyrexia	30 (7.9)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	2.79 [1.36; 5.71]	0.005	n.s.
Immune system disorders	19 (5.0)	Not reached [-; -]	20 (5.3)	Not reached [85.4; -]	0.92 [0.49; 1.73]	0.794	0.882
Hypersensitivity	6 (1.6)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	0.59 [0.22; 1.63]	0.311	n.s.
Infections and infestations	154 (40.3)	47.7 [32.0; 59.9]	119 (31.6)	63.7 [38.4; -]	1.23 [0.97; 1.56]	0.092	0.262
COVID-19	30 (7.9)	Not reached [-; -]	26 (6.9)	Not reached [-; -]	0.88 [0.52; 1.50]	0.651	n.s.
Folliculitis	10 (2.6)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.24 [0.49; 3.14]	0.653	n.s.
Sinusitis	12 (3.1)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.06 [0.72; 5.89]	0.176	n.s.
Upper respiratory tract infection	10 (2.6)	Not reached [-; -]	9 (2.4)	Not reached [-; -]	0.91 [0.37; 2.26]	0.842	n.s.
Urinary tract infection	53 (13.9)	Not reached [-; -]	41 (10.9)	Not reached [78.1; -]	1.22 [0.81; 1.84]	0.335	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Injury, poisoning and procedural complications	111 (29.1)	Not reached [-; -]	81 (21.5)	Not reached [-; -]	1.33 [1.00; 1.77]	0.051	0.204
Contusion	13 (3.4)	Not reached [-; -]	11 (2.9)	Not reached [-; -]	1.11 [0.49; 2.47]	0.806	n.s.
Fall	35 (9.2)	Not reached [-; -]	24 (6.4)	Not reached [-; -]	1.35 [0.80; 2.28]	0.255	n.s.
Infusion related reaction	54 (14.1)	Not reached [-; -]	51 (13.5)	Not reached [-; -]	1.03 [0.70; 1.51]	0.869	n.s.
Investigations	264 (69.1)	8.7 [6.1; 9.1]	250 (66.3)	8.9 [6.1; 11.7]	1.03 [0.87; 1.23]	0.731	0.860
Alanine aminotransferase increased	58 (15.2)	Not reached [92.0; -]	39 (10.3)	Not reached [79.0; -]	1.38 [0.92; 2.08]	0.120	n.s.
Aspartate aminotransferase increased	49 (12.8)	Not reached [-; -]	26 (6.9)	Not reached [-; -]	1.79 [1.11; 2.88]	0.017	n.s.
Blood alkaline phosphatase increased	49 (12.8)	Not reached [92.0; -]	46 (12.2)	Not reached [89.3; -]	0.99 [0.66; 1.48]	0.942	n.s.
Blood bilirubin increased	12 (3.1)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	1.50 [0.59; 3.83]	0.395	n.s.

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Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Blood creatinine increased	68 (17.8)	Not reached [-; -]	30 (8.0)	Not reached [-; -]	2.12 [1.38; 3.27]	< 0.001	n.s.
Blood glucose increased	10 (2.6)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	0.80 [0.35; 1.86]	0.608	n.s.
Blood magnesium decreased	12 (3.1)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	0.94 [0.42; 2.09]	0.873	n.s.
Blood thyroid stimulating hormone increased	21 (5.5)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	1.60 [0.78; 3.25]	0.196	n.s.
Haemoglobin decreased	13 (3.4)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	1.30 [0.57; 2.97]	0.530	n.s.
Lymphocyte count decreased	80 (20.9)	Not reached [-; -]	71 (18.8)	Not reached [-; -]	1.10 [0.80; 1.51]	0.577	n.s.
Neutrophil count decreased	99 (25.9)	Not reached [-; -]	100 (26.5)	Not reached [-; -]	0.96 [0.72; 1.26]	0.755	n.s.
Platelet count decreased	113 (29.6)	Not reached [-; -]	89 (23.6)	Not reached [-; -]	1.27 [0.96; 1.68]	0.092	n.s.
Weight decreased	36 (9.4)	Not reached [-; -]	31 (8.2)	Not reached [-; -]	1.07 [0.66; 1.74]	0.778	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Weight increased	15 (3.9)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	1.25 [0.56; 2.79]	0.590	n.s.
White blood cell count decreased	119 (31.2)	Not reached [-; -]	126 (33.4)	Not reached [-; -]	0.88 [0.69; 1.14]	0.336	n.s.
Metabolism and nutrition disorders	234 (61.3)	10.0 [7.1; 14.0]	223 (59.2)	11.7 [8.4; 14.9]	1.03 [0.86; 1.24]	0.718	0.860
Decreased appetite	82 (21.5)	Not reached [-; -]	81 (21.5)	Not reached [-; -]	0.97 [0.71; 1.32]	0.846	n.s.
Dehydration	19 (5.0)	Not reached [-; -]	22 (5.8)	Not reached [-; -]	0.81 [0.44; 1.50]	0.505	n.s.
Hypercalcaemia	16 (4.2)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	1.15 [0.55; 2.40]	0.706	n.s.
Hyperglycaemia	82 (21.5)	Not reached [-; -]	67 (17.8)	Not reached [-; -]	1.18 [0.85; 1.63]	0.321	n.s.
Hyperkalaemia	12 (3.1)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	0.60 [0.29; 1.25]	0.172	n.s.
Hypoalbuminaemia	46 (12.0)	Not reached [-; -]	33 (8.8)	Not reached [-; -]	1.33 [0.85; 2.09]	0.208	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Hypocalcaemia	27 (7.1)	Not reached [-; -]	28 (7.4)	Not reached [-; -]	0.91 [0.54; 1.55]	0.742	n.s.
Hypoglycaemia	5 (1.3)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	0.36 [0.13; 1.02]	0.055	n.s.
Hypokalaemia	49 (12.8)	Not reached [-; -]	69 (18.3)	Not reached [-; -]	0.66 [0.45; 0.95]	0.024	n.s.
Hypomagnesaemia	71 (18.6)	Not reached [-; -]	60 (15.9)	Not reached [-; -]	1.12 [0.79; 1.58]	0.518	n.s.
Hyponatraemia	52 (13.6)	Not reached [-; -]	33 (8.8)	Not reached [-; -]	1.48 [0.95; 2.29]	0.080	n.s.
Musculoskeletal and connective tissue disorders	256 (67.0)	3.9 [3.1; 8.1]	243 (64.5)	5.1 [3.1; 7.7]	1.05 [0.88; 1.25]	0.618	0.857
Arthralgia	114 (29.8)	Not reached [81.0; -]	133 (35.3)	Not reached [-; -]	0.76 [0.59; 0.98]	0.035	n.s.
Back pain	41 (10.7)	Not reached [-; -]	44 (11.7)	Not reached [-; -]	0.82 [0.54; 1.26]	0.377	n.s.
Bone pain	35 (9.2)	Not reached [-; -]	35 (9.3)	Not reached [-; -]	0.98 [0.61; 1.56]	0.922	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Muscle spasms	26 (6.8)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	1.32 [0.72; 2.42]	0.364	n.s.
Muscular weakness	38 (9.9)	Not reached [-; -]	23 (6.1)	Not reached [86.1; -]	1.62 [0.96; 2.71]	0.070	n.s.
Myalgia	74 (19.4)	Not reached [-; -]	64 (17.0)	Not reached [-; -]	1.14 [0.82; 1.60]	0.432	n.s.
Pain in extremity	58 (15.2)	Not reached [-; -]	44 (11.7)	Not reached [-; -]	1.28 [0.87; 1.90]	0.213	n.s.
Nervous system disorders	323 (84.6)	3.3 [3.1; 4.1]	309 (82.0)	4.1 [3.4; 6.0]	1.08 [0.92; 1.26]	0.339	0.617
Dizziness	63 (16.5)	Not reached [93.3; -]	57 (15.1)	Not reached [-; -]	1.03 [0.72; 1.47]	0.886	n.s.
Dysgeusia	36 (9.4)	Not reached [-; -]	42 (11.1)	Not reached [-; -]	0.84 [0.54; 1.31]	0.442	n.s.
Headache	66 (17.3)	Not reached [87.6; -]	48 (12.7)	Not reached [-; -]	1.28 [0.88; 1.86]	0.196	n.s.
Hypoaesthesia	11 (2.9)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	0.81 [0.36; 1.81]	0.608	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Neuropathy peripheral	122 (31.9)	Not reached [-; -]	108 (28.6)	Not reached [-; -]	1.14 [0.88; 1.48]	0.318	n.s.
Paraesthesia	39 (10.2)	Not reached [-; -]	37 (9.8)	Not reached [-; -]	1.03 [0.66; 1.61]	0.902	n.s.
Peripheral motor neuropathy	13 (3.4)	Not reached [-; -]	6 (1.6)	Not reached [-; -]	2.11 [0.80; 5.55]	0.131	n.s.
Peripheral sensory neuropathy	138 (36.1)	Not reached [-; -]	145 (38.5)	Not reached [-; -]	0.92 [0.73; 1.16]	0.479	n.s.
Restless legs syndrome	11 (2.9)	Not reached [-; -]	9 (2.4)	Not reached [-; -]	1.22 [0.50; 2.94]	0.661	n.s.
Syncope	13 (3.4)	Not reached [-; -]	14 (3.7)	Not reached [-; -]	0.88 [0.41; 1.87]	0.737	n.s.
Taste disorder	14 (3.7)	Not reached [-; -]	9 (2.4)	Not reached [-; -]	1.49 [0.64; 3.44]	0.354	n.s.
Tremor	11 (2.9)	Not reached [-; -]	4 (1.1)	Not reached [-; -]	2.63 [0.84; 8.27]	0.098	n.s.
Psychiatric disorders	91 (23.8)	Not reached [-; -]	80 (21.2)	Not reached [-; -]	1.07 [0.79; 1.45]	0.642	0.857

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
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(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Anxiety	40 (10.5)	Not reached [-; -]	31 (8.2)	Not reached [-; -]	1.20 [0.75; 1.92]	0.441	n.s.
Depression	10 (2.6)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	0.90 [0.38; 2.18]	0.824	n.s.
Insomnia	47 (12.3)	Not reached [-; -]	39 (10.3)	Not reached [-; -]	1.12 [0.73; 1.72]	0.600	n.s.
Renal and urinary disorders	91 (23.8)	Not reached [-; -]	67 (17.8)	Not reached [-; -]	1.34 [0.97; 1.83]	0.072	0.239
Dysuria	21 (5.5)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	1.09 [0.58; 2.06]	0.779	n.s.
Haematuria	12 (3.1)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	1.10 [0.47; 2.55]	0.825	n.s.
Micturition urgency	14 (3.7)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.57 [0.66; 3.77]	0.311	n.s.
Pollakiuria	22 (5.8)	Not reached [-; -]	11 (2.9)	Not reached [-; -]	1.89 [0.91; 3.90]	0.086	n.s.
Urinary incontinence	21 (5.5)	Not reached [-; -]	15 (4.0)	Not reached [-; -]	1.28 [0.66; 2.48]	0.471	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
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(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Reproductive system and breast disorders	54 (14.1)	Not reached [-; -]	51 (13.5)	Not reached [-; -]	0.98 [0.67; 1.44]	0.914	0.914
Pelvic pain	7 (1.8)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	0.48 [0.19; 1.20]	0.117	n.s.
Vaginal discharge	9 (2.4)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	0.85 [0.34; 2.10]	0.725	n.s.
Vaginal haemorrhage	21 (5.5)	Not reached [-; -]	21 (5.6)	Not reached [-; -]	0.88 [0.48; 1.61]	0.676	n.s.
Respiratory, thoracic and mediastinal disorders	165 (43.2)	37.9 [20.0; -]	144 (38.2)	53.9 [33.6; -]	1.18 [0.94; 1.48]	0.148	0.330
Cough	56 (14.7)	Not reached [-; -]	50 (13.3)	Not reached [-; -]	1.02 [0.70; 1.50]	0.915	n.s.
Dyspnoea	87 (22.8)	Not reached [95.0; -]	65 (17.2)	Not reached [-; -]	1.34 [0.97; 1.85]	0.075	n.s.
Epistaxis	11 (2.9)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.30 [0.52; 3.24]	0.572	n.s.
Nasal congestion	14 (3.7)	Not reached [-; -]	11 (2.9)	Not reached [-; -]	1.06 [0.47; 2.35]	0.892	n.s.

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
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(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Oropharyngeal pain	14 (3.7)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	0.94 [0.44; 2.01]	0.871	n.s.
Pulmonary embolism	12 (3.1)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	0.88 [0.40; 1.94]	0.758	n.s.
Rhinitis allergic	12 (3.1)	Not reached [-; -]	6 (1.6)	Not reached [-; -]	1.88 [0.71; 5.03]	0.206	n.s.
Rhinorrhoea	8 (2.1)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	0.60 [0.25; 1.48]	0.271	n.s.
Skin and subcutaneous tissue disorders	280 (73.3)	3.1 [3.0; 3.4]	251 (66.6)	3.1 [3.1; 4.3]	1.20 [1.01; 1.42]	0.039	0.193
Alopecia	207 (54.2)	6.1 [4.0; 10.3]	213 (56.5)	5.9 [3.1; 11.9]	0.95 [0.78; 1.15]	0.577	0.577
Dry skin	25 (6.5)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	1.32 [0.72; 2.43]	0.368	0.429
Pruritus	62 (16.2)	Not reached [-; -]	42 (11.1)	Not reached [-; -]	1.41 [0.95; 2.09]	0.084	0.117
Rash	56 (14.7)	Not reached [-; -]	36 (9.5)	Not reached [-; -]	1.49 [0.98; 2.27]	0.063	0.111

Time to Event Analysis for Adverse Events by System Organ Class and Preferred Term
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(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Rash maculo-papular	50 (13.1)	Not reached [-; -]	19 (5.0)	Not reached [-; -]	2.60 [1.53; 4.42]	< 0.001	0.001
Vascular disorders	119 (31.2)	Not reached [-; -]	109 (28.9)	Not reached [-; -]	1.07 [0.83; 1.39]	0.606	0.857
Embolism	13 (3.4)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	1.65 [0.65; 4.14]	0.290	n.s.
Flushing	19 (5.0)	Not reached [-; -]	11 (2.9)	Not reached [-; -]	1.71 [0.81; 3.59]	0.158	n.s.
Hot flush	21 (5.5)	Not reached [-; -]	17 (4.5)	Not reached [-; -]	1.20 [0.63; 2.27]	0.580	n.s.
Hypertension	53 (13.9)	Not reached [-; -]	59 (15.6)	Not reached [-; -]	0.86 [0.59; 1.24]	0.409	n.s.
Hypotension	9 (2.4)	Not reached [-; -]	16 (4.2)	Not reached [-; -]	0.54 [0.24; 1.21]	0.135	n.s.

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

c: A system organ class or 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 treatment groups

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

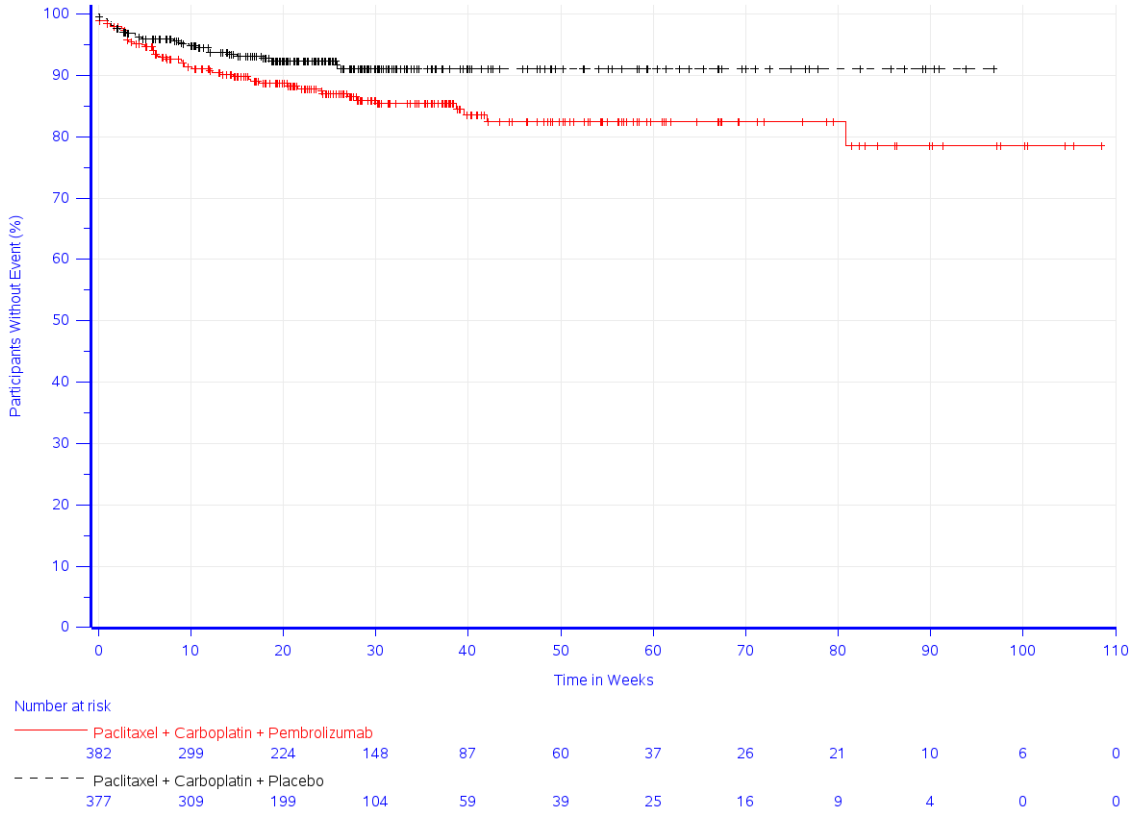
e: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

f: Two-sided p-value using Wald test

g: Adjusted p-values for treatment comparisons of adverse events at the SOC level were computed using the FDR procedure, and they were computed using the double FDR procedure for comparisons of adverse events at the PT level. Not significant (i.e., 'n.s.') is reported for PTs in a SOC when the SOC did not meet the threshold p-value criteria in the first step of the double FDR procedure. Adjusted p-values should be used for evaluating the results in order to reduce the number of false discoveries (i.e., statistical findings) when numerous statistical tests are performed

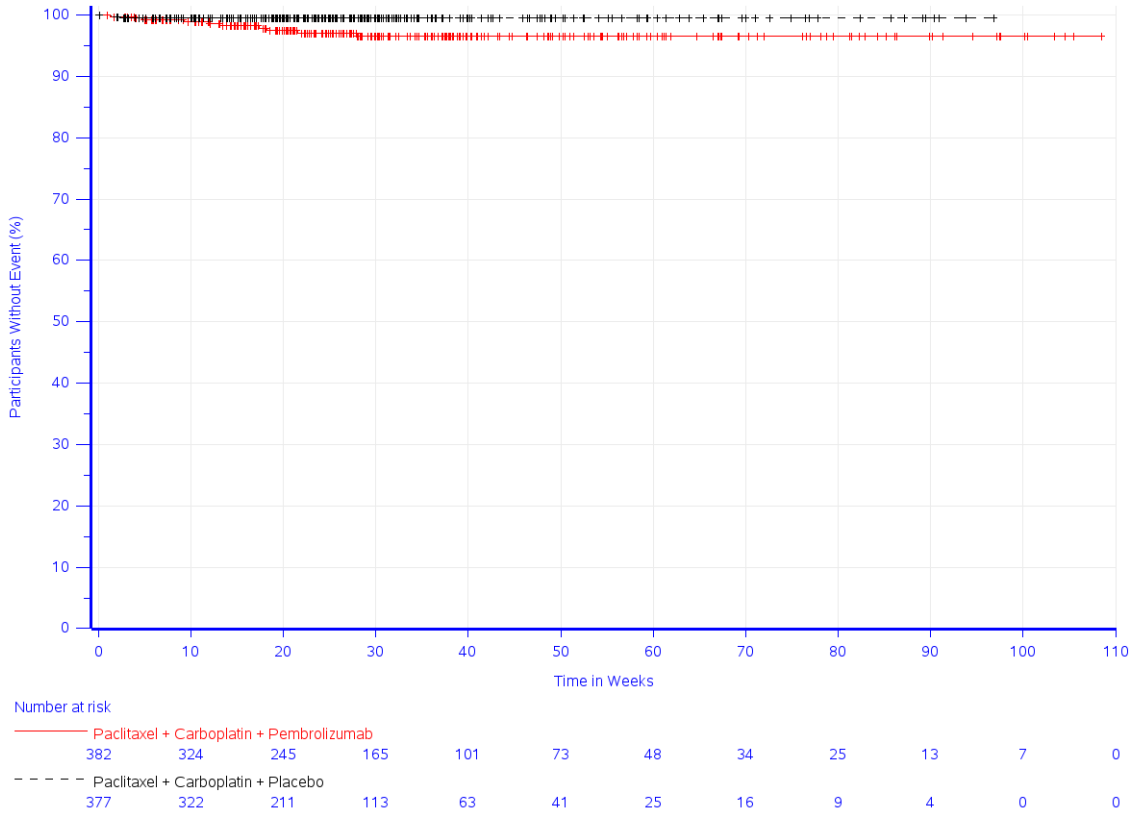
CI: Confidence Interval; COVID-19: Coronavirus Disease 2019; dMMR: Deficient Mismatch Repair; FDR: False Discovery Rate; n.s.: Non-Significant (adjusted p-value ≥ 0.05); pMMR: Proficient Mismatch Repair; PT: Preferred Term; SOC: System Organ Class

Figure 4.2-11
Time to Adverse Event - Kaplan-Meier Curve
for System Organ Class: Cardiac disorders
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



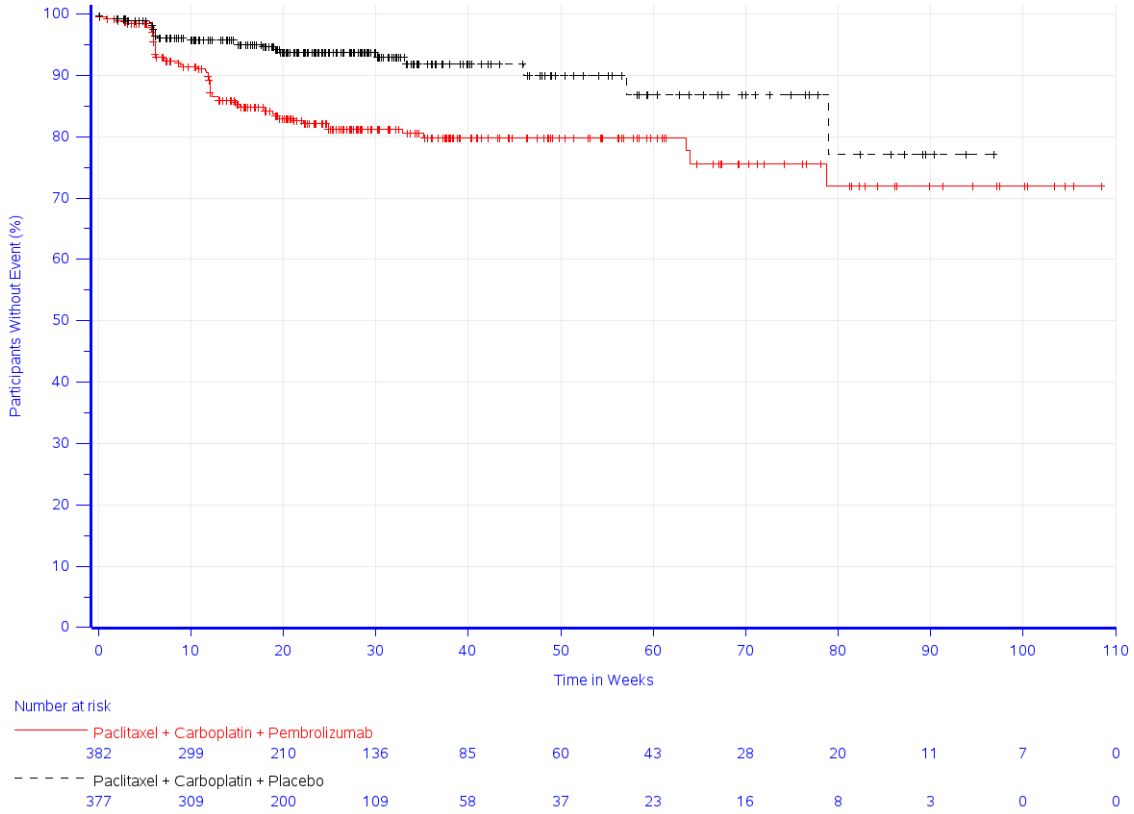
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - System Organ Class: Cardiac disorders

Figure 4.2-12
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Palpitations
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



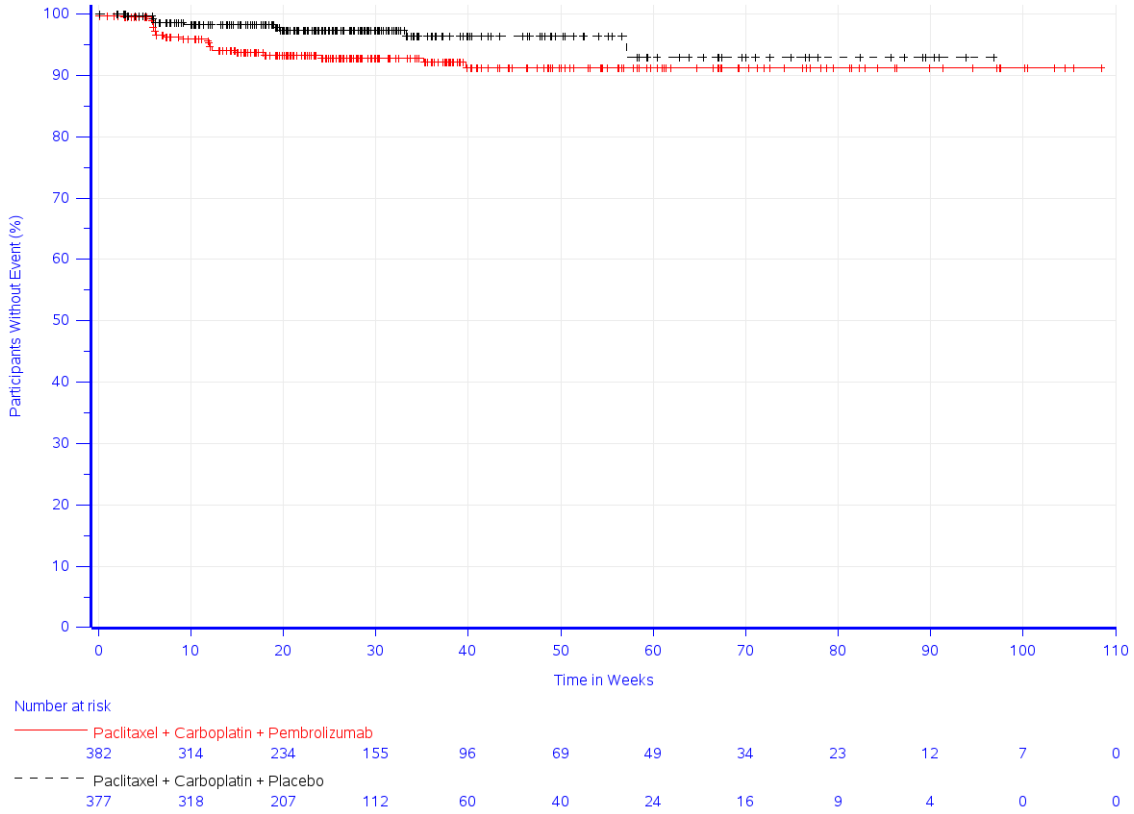
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Palpitations

Figure 4.2-13
Time to Adverse Event - Kaplan-Meier Curve
for System Organ Class: Endocrine disorders
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



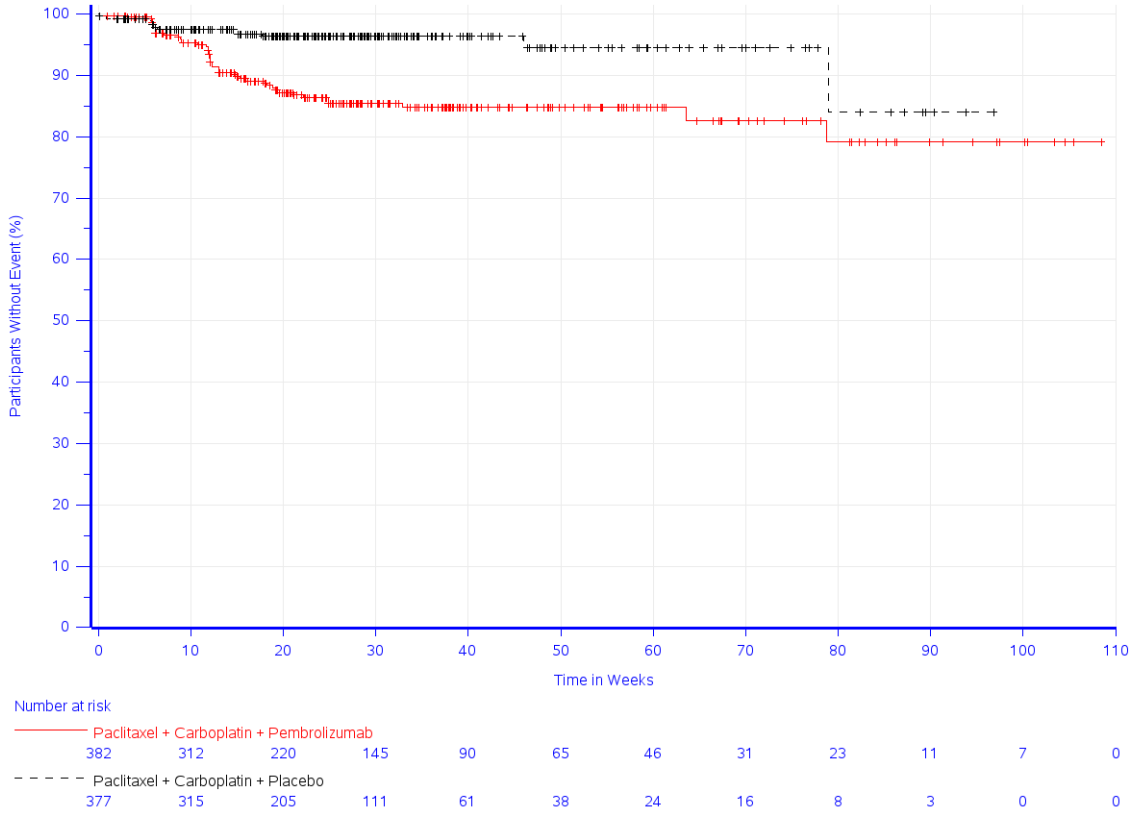
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - System Organ Class: Endocrine disorders

Figure 4.2-14
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Hyperthyroidism
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



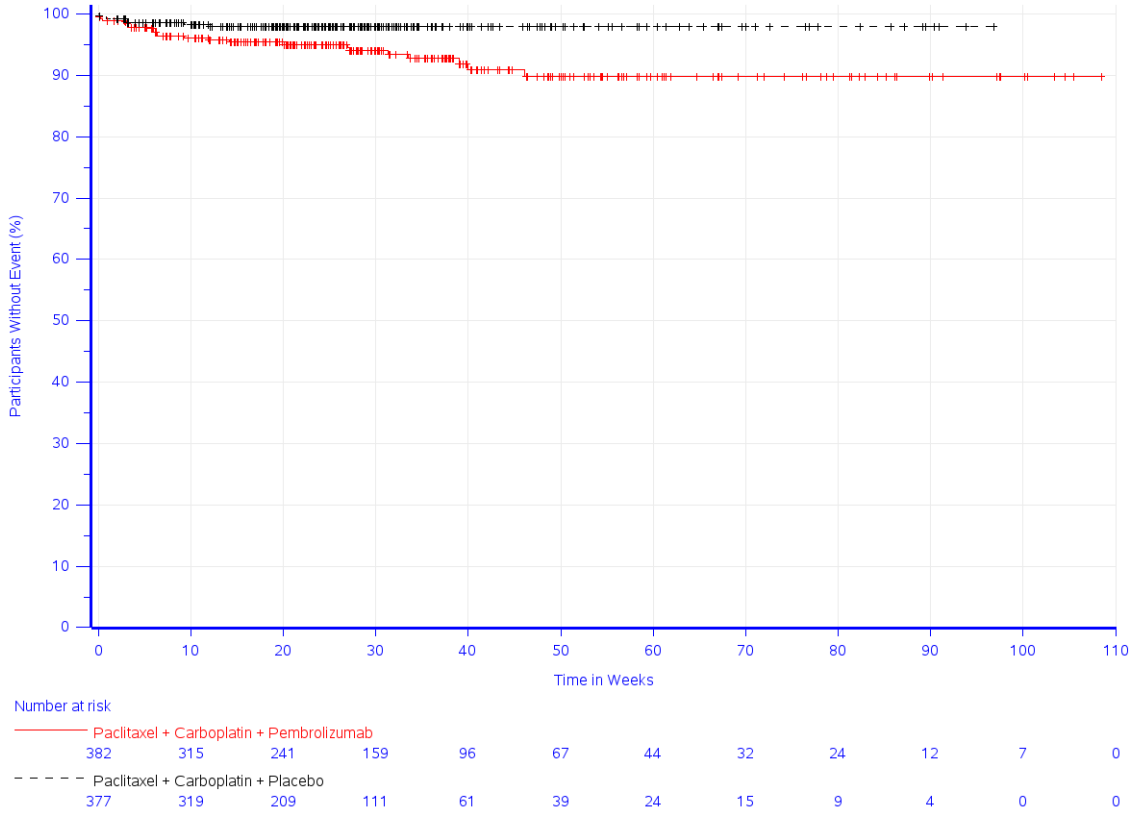
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hyperthyroidism

Figure 4.2-15
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Hypothyroidism
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



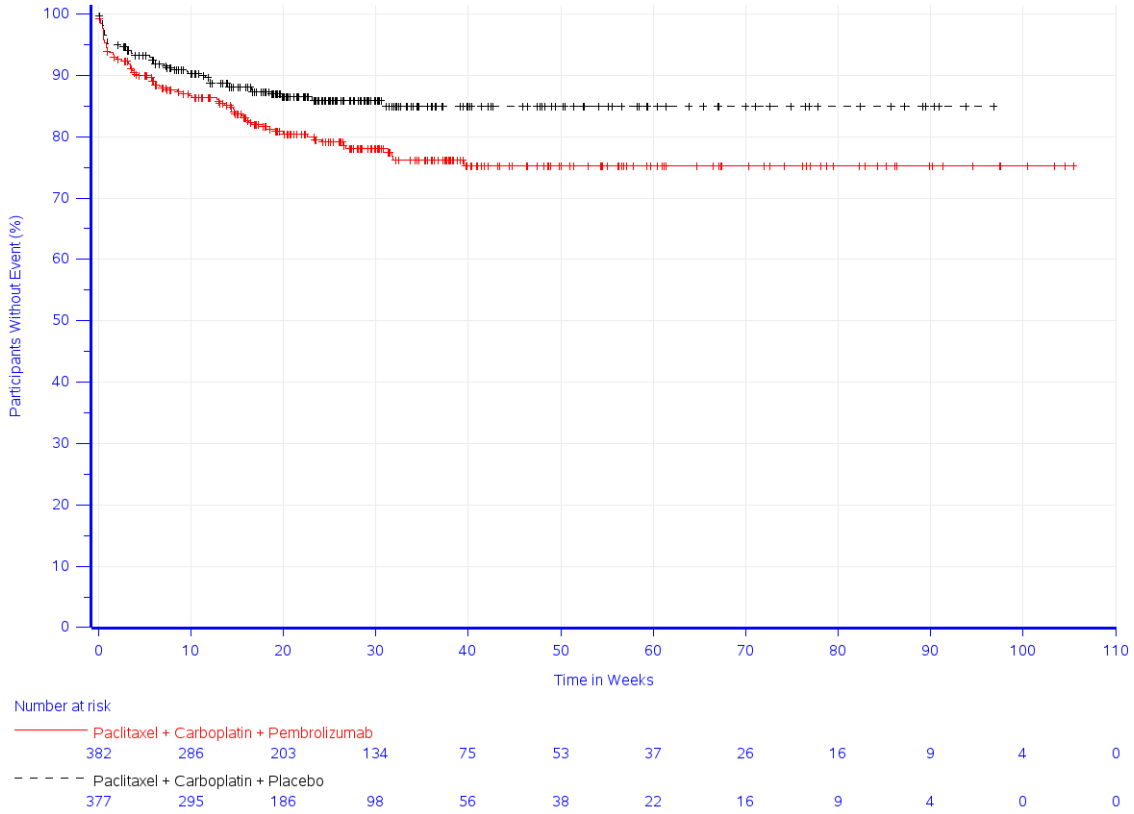
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hypothyroidism

Figure 4.2-16
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Dry mouth
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



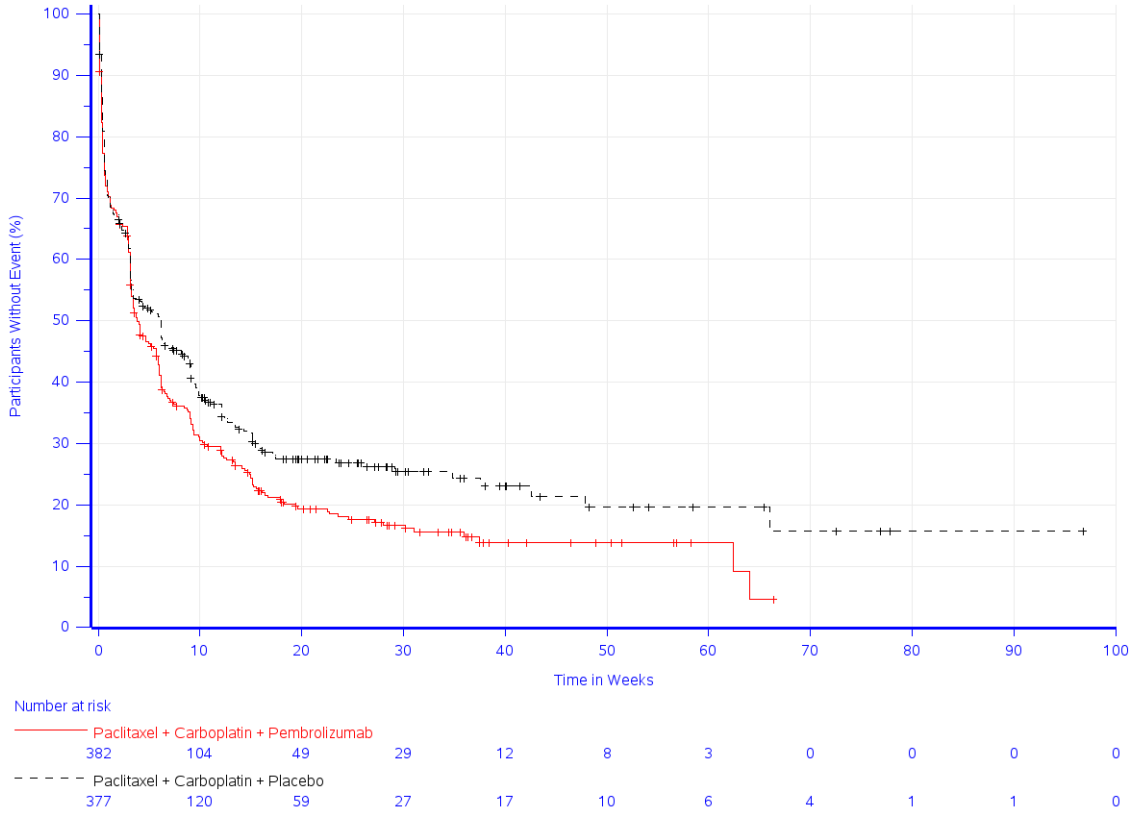
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Dry mouth

Figure 4.2-17
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Vomiting
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



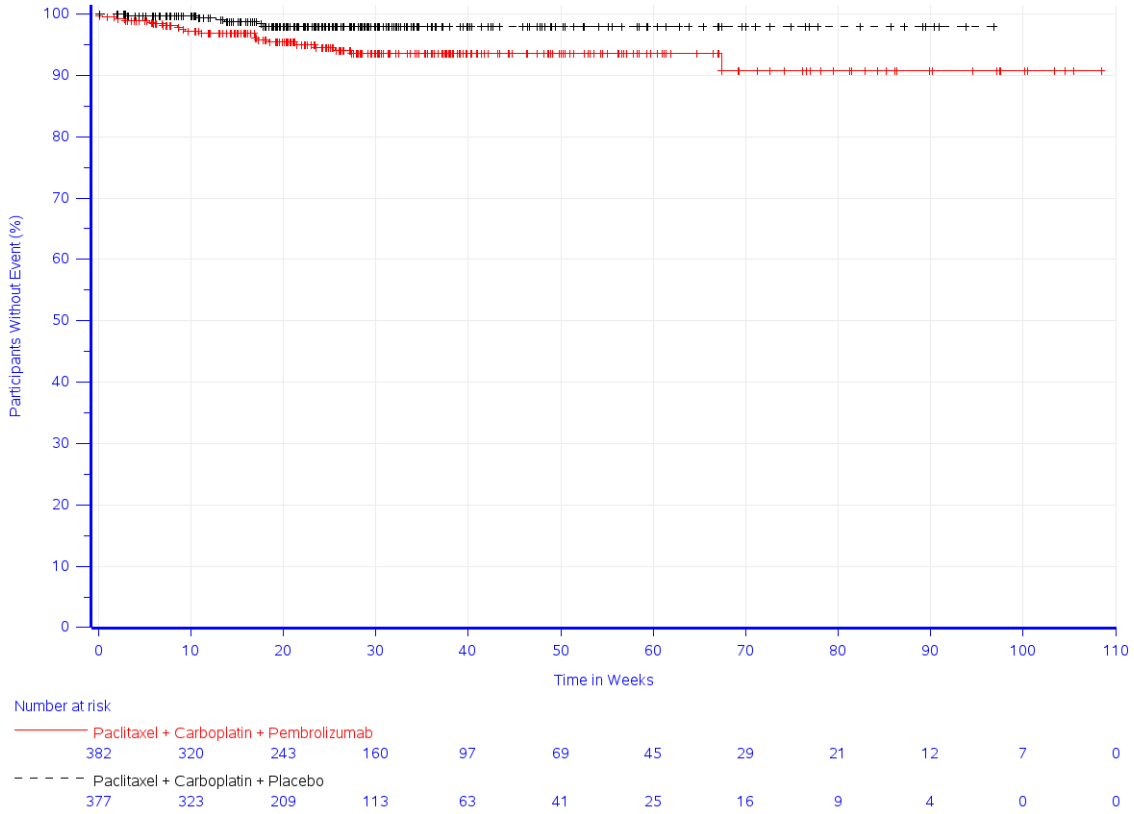
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Vomiting

Figure 4.2-18
Time to Adverse Event - Kaplan-Meier Curve
for System Organ Class: General disorders and administration site conditions
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



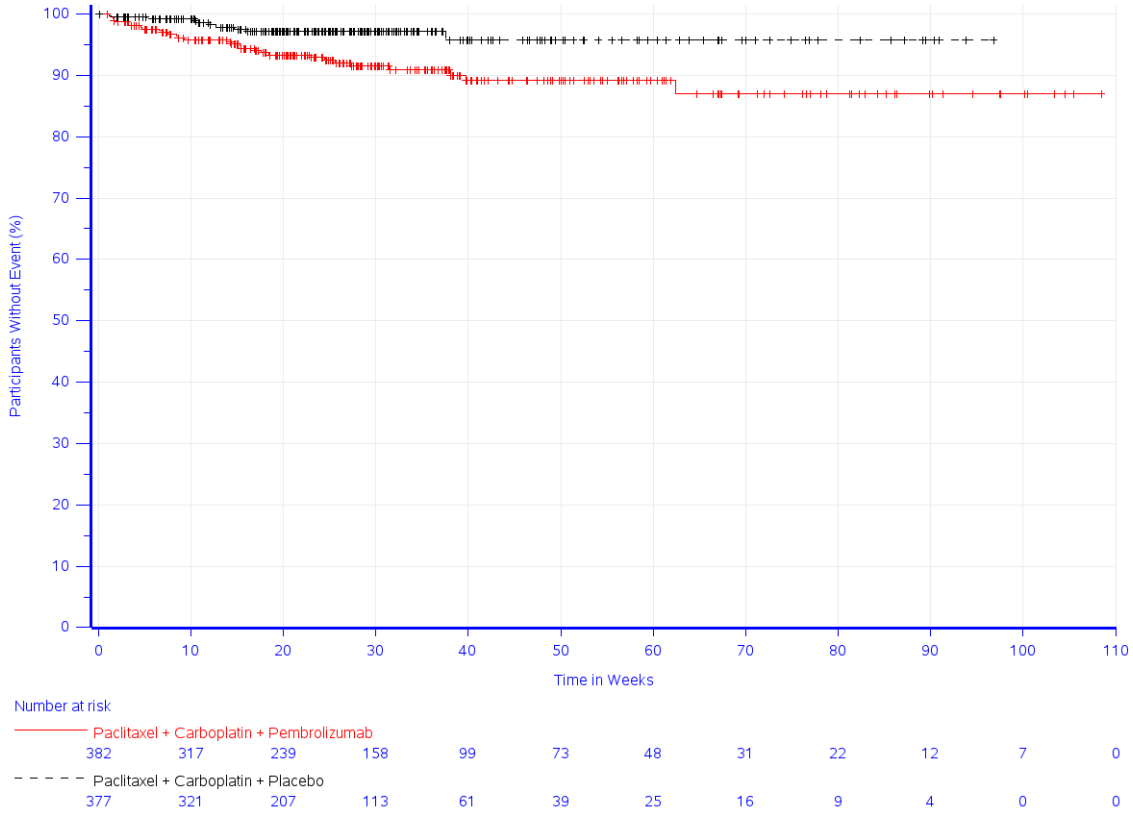
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - System Organ Class: General disorders and administration site conditions

Figure 4.2-19
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Chills
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



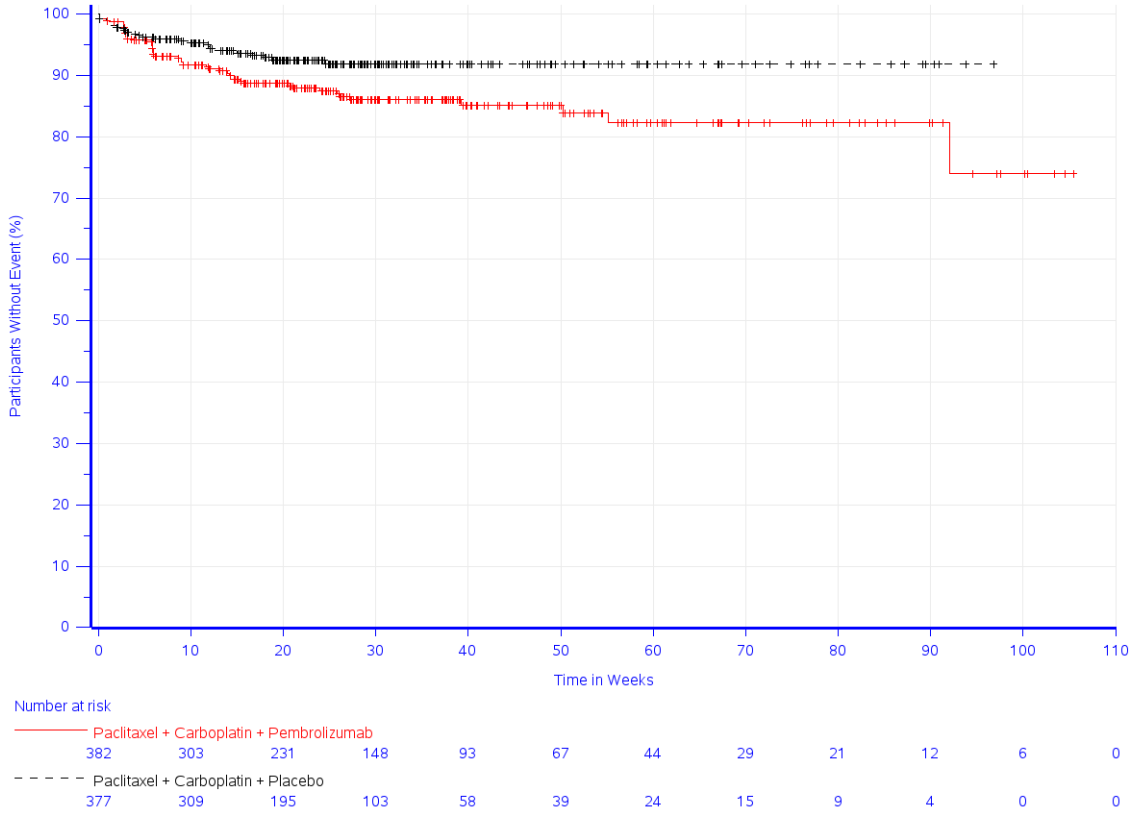
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Chills

Figure 4.2-20
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Pyrexia
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



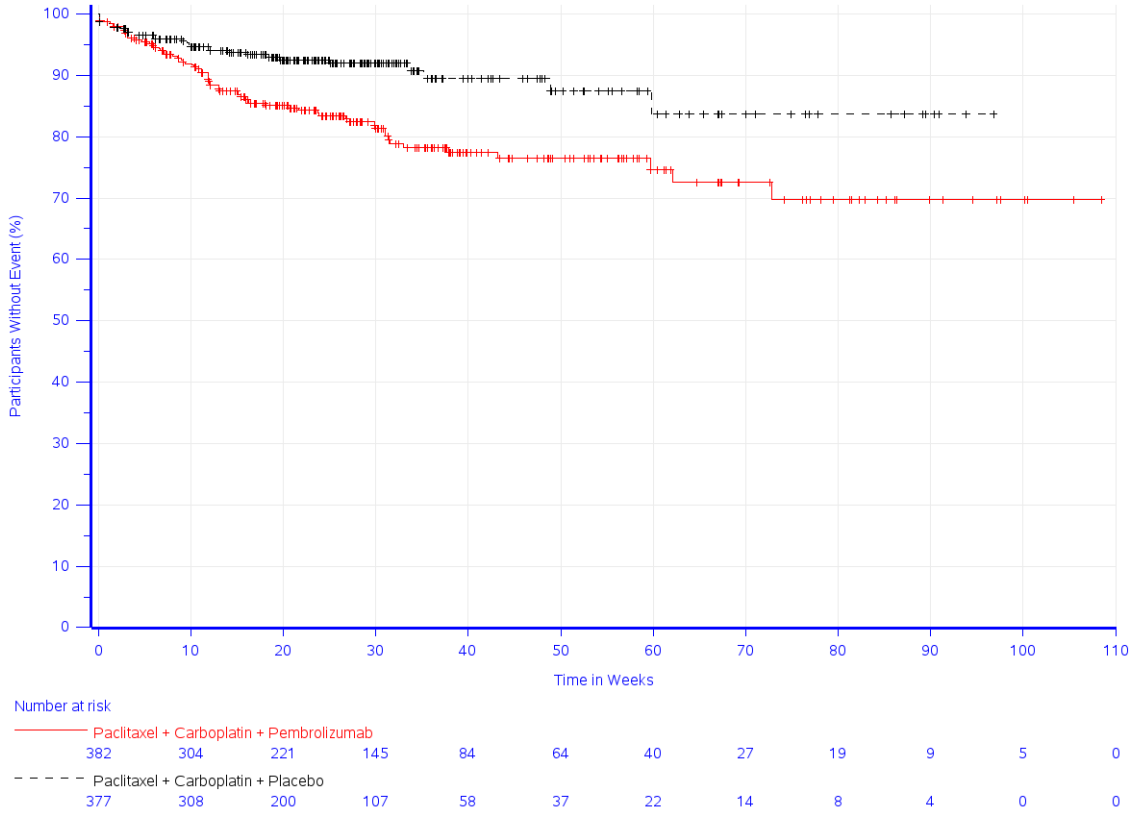
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Pyrexia

Figure 4.2-21
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Aspartate aminotransferase increased
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



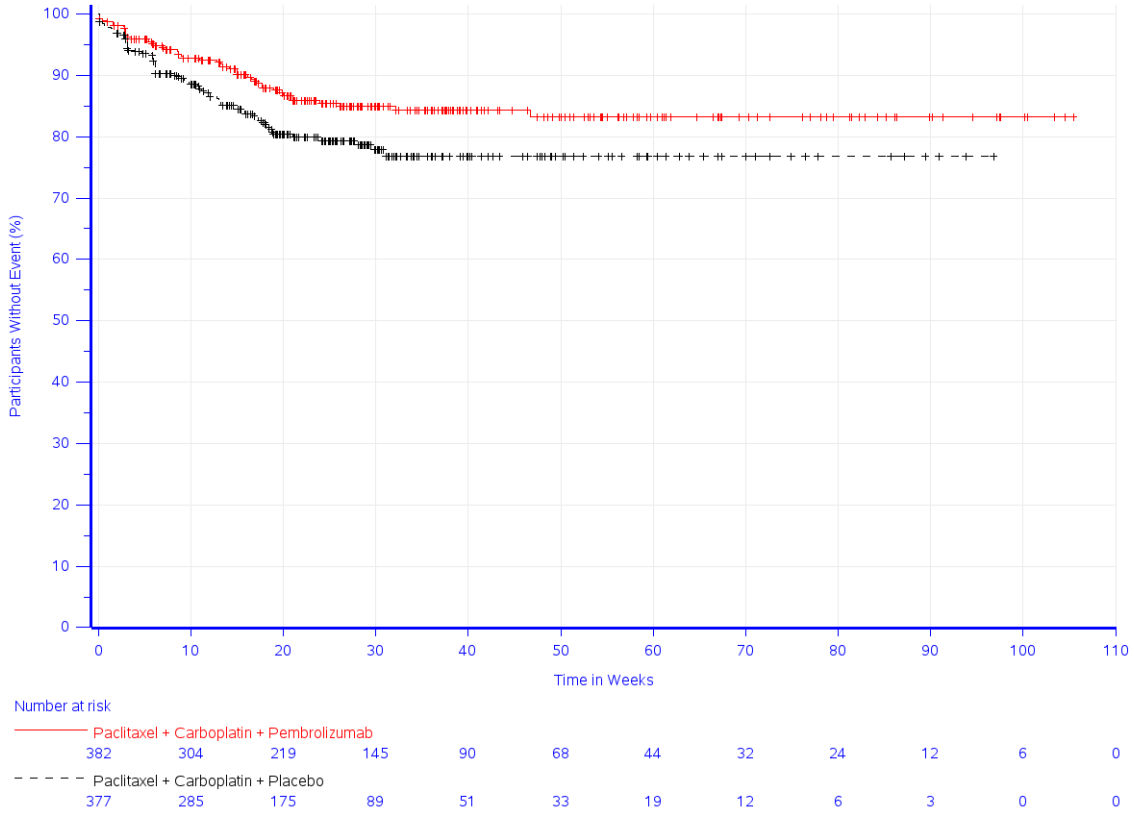
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Aspartate aminotransferase increased

Figure 4.2-22
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Blood creatinine increased
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



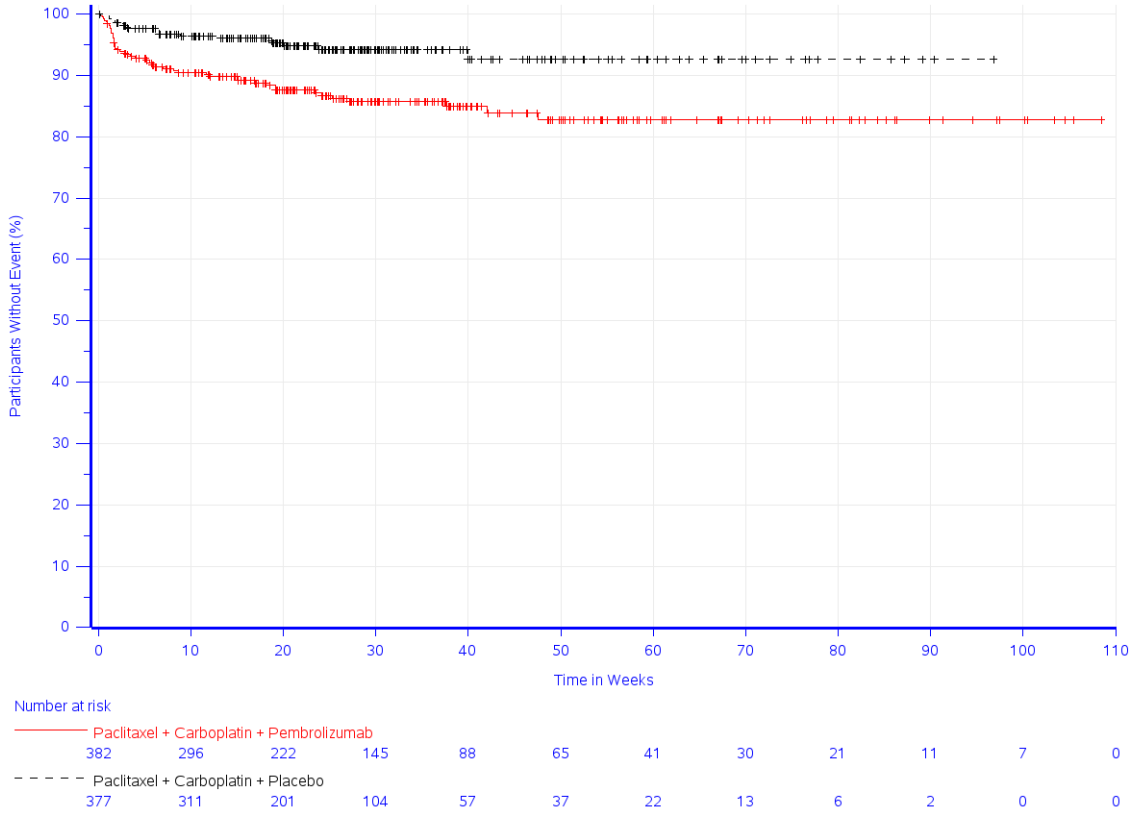
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Blood creatinine increased

Figure 4.2-23
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Hypokalaemia
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hypokalaemia

Figure 4.2-24
Time to Adverse Event - Kaplan-Meier Curve
for Preferred Term: Rash maculo-papular
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Rash maculo-papular

Table 4.2-14
Time to Event Analysis for Serious Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Serious Adverse Events by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
Blood and lymphatic system disorders	27 (7.1)	Not reached [-; -]	20 (5.3)	Not reached [-; -]	1.34 [0.75; 2.38]	0.326	0.407
Anaemia	16 (4.2)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	1.20 [0.58; 2.49]	0.631	n.s.
Febrile neutropenia	11 (2.9)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.20 [0.77; 6.34]	0.143	n.s.
Cardiac disorders	13 (3.4)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.38 [0.84; 6.70]	0.101	0.148
Gastrointestinal disorders	25 (6.5)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	1.32 [0.72; 2.42]	0.372	0.414
Infections and infestations	32 (8.4)	Not reached [-; -]	18 (4.8)	Not reached [-; -]	1.67 [0.93; 2.98]	0.083	0.148
Investigations	26 (6.8)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	2.53 [1.22; 5.25]	0.013	0.073
Metabolism and nutrition disorders	22 (5.8)	Not reached [-; -]	11 (2.9)	Not reached [-; -]	1.86 [0.90; 3.85]	0.093	0.148
Nervous system disorders	22 (5.8)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	2.74 [1.22; 6.16]	0.015	0.073

Time to Event Analysis for Serious Adverse Events by System Organ Class and Preferred Term
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Serious Adverse Events by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Renal and urinary disorders	11 (2.9)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	1.46 [0.56; 3.77]	0.438	0.438
Respiratory, thoracic and mediastinal disorders	22 (5.8)	Not reached [-; -]	9 (2.4)	Not reached [-; -]	2.32 [1.07; 5.05]	0.033	0.111
Vascular disorders	15 (3.9)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	2.11 [0.86; 5.17]	0.104	0.148

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

c: A system organ class or specific adverse event appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups

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

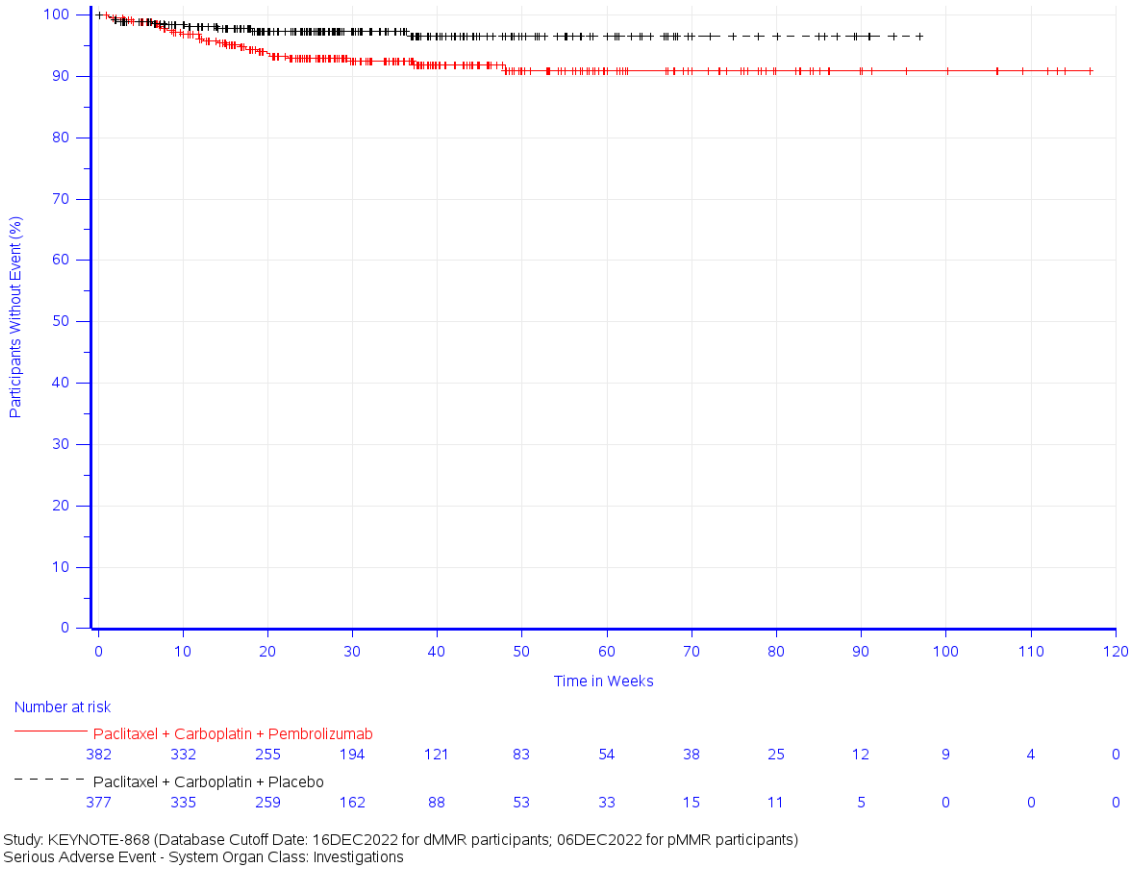
e: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

f: Two-sided p-value using Wald test

g: Adjusted p-values for treatment comparisons of adverse events at the SOC level were computed using the FDR procedure, and they were computed using the double FDR procedure for comparisons of adverse events at the PT level. Not significant (i.e., 'n.s.') is reported for PTs in a SOC when the SOC did not meet the threshold p-value criteria in the first step of the double FDR procedure. Adjusted p-values should be used for evaluating the results in order to reduce the number of false discoveries (i.e., statistical findings) when numerous statistical tests are performed

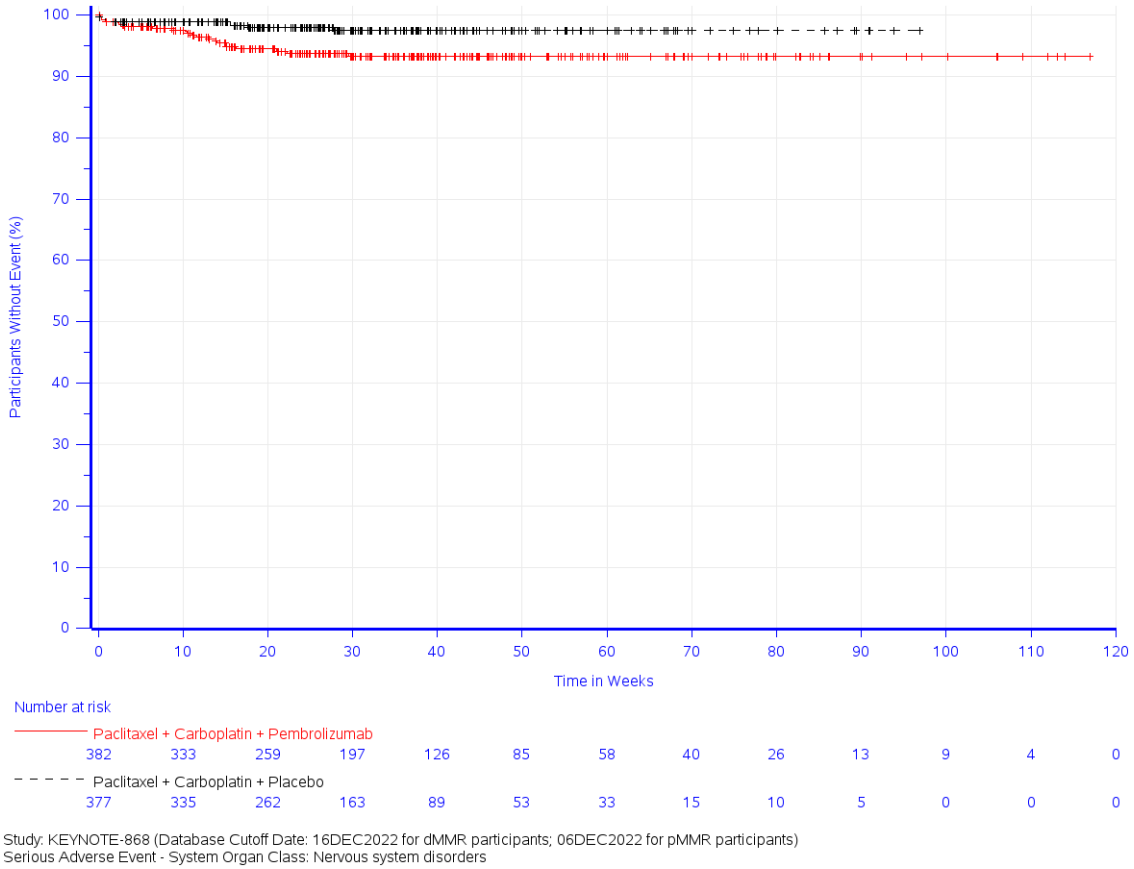
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; FDR: False Discovery Rate; n.s.: Non-Significant (adjusted p-value ≥ 0.05); pMMR: Proficient Mismatch Repair; PT: Preferred Term; SOC: System Organ Class

Figure 4.2-25
Time to Serious Adverse Event - Kaplan-Meier Curve
for System Organ Class: Investigations
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



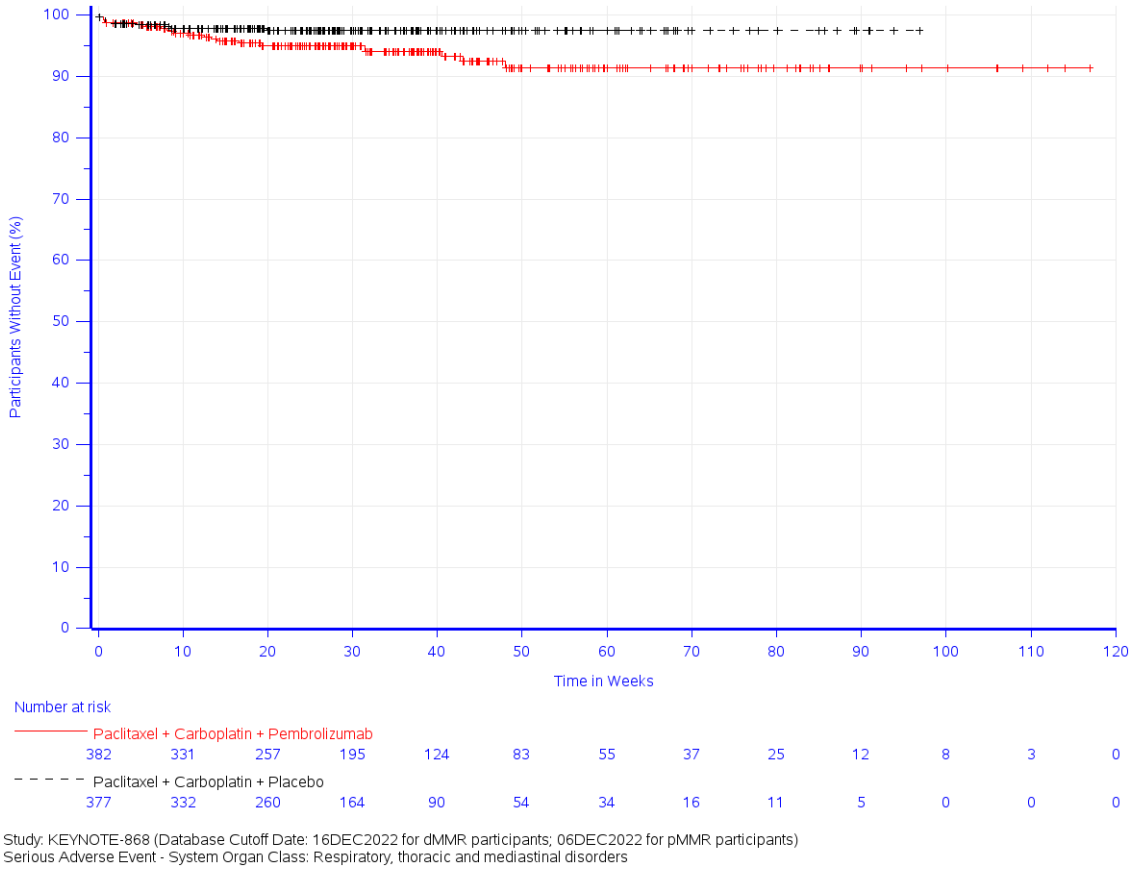
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Serious Adverse Event - System Organ Class: Investigations

Figure 4.2-26
Time to Serious Adverse Event - Kaplan-Meier Curve
for System Organ Class: Nervous system disorders
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Serious Adverse Event - System Organ Class: Nervous system disorders

Figure 4.2-27
Time to Serious Adverse Event - Kaplan-Meier Curve
for System Organ Class: Respiratory, thoracic and mediastinal disorders
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Serious Adverse Event - System Organ Class: Respiratory, thoracic and mediastinal disorders

Table 4.2-15
Time to Event Analysis for Severe Adverse Events (CTCAE-Grade 3-5) by System Organ Class and Preferred Term (Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups) in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Blood and lymphatic system disorders	77 (20.2)	Not reached [-; -]	47 (12.5)	Not reached [-; -]	1.66 [1.15; 2.38]	0.006	0.084
Anaemia	59 (15.4)	Not reached [-; -]	38 (10.1)	Not reached [-; -]	1.54 [1.03; 2.32]	0.037	n.s.
Febrile neutropenia	13 (3.4)	Not reached [-; -]	4 (1.1)	Not reached [-; -]	3.26 [1.06; 9.98]	0.039	n.s.
Neutropenia	15 (3.9)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	1.47 [0.66; 3.28]	0.342	n.s.
Cardiac disorders	11 (2.9)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.22 [0.49; 3.05]	0.675	0.700
Gastrointestinal disorders	30 (7.9)	Not reached [-; -]	23 (6.1)	Not reached [-; -]	1.18 [0.68; 2.03]	0.559	0.700
General disorders and administration site conditions	15 (3.9)	Not reached [-; -]	12 (3.2)	Not reached [-; -]	1.16 [0.54; 2.49]	0.700	0.700
Fatigue	5 (1.3)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	0.48 [0.16; 1.39]	0.176	n.s.
Infections and infestations	45 (11.8)	Not reached [-; -]	22 (5.8)	Not reached [-; -]	1.84 [1.10; 3.06]	0.020	0.131

Time to Event Analysis for Severe Adverse Events (CTCAE-Grade 3-5) by System Organ Class and Preferred Term
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Urinary tract infection	14 (3.7)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.64 [0.69; 3.92]	0.266	n.s.
Investigations	92 (24.1)	Not reached [-; -]	72 (19.1)	Not reached [-; -]	1.24 [0.91; 1.69]	0.172	0.373
Lymphocyte count decreased	23 (6.0)	Not reached [-; -]	17 (4.5)	Not reached [-; -]	1.33 [0.71; 2.50]	0.368	n.s.
Neutrophil count decreased	51 (13.4)	Not reached [-; -]	49 (13.0)	Not reached [-; -]	1.01 [0.69; 1.50]	0.942	n.s.
Platelet count decreased	16 (4.2)	Not reached [-; -]	7 (1.9)	Not reached [-; -]	2.13 [0.88; 5.18]	0.096	n.s.
White blood cell count decreased	33 (8.6)	Not reached [-; -]	29 (7.7)	Not reached [-; -]	1.12 [0.68; 1.85]	0.652	n.s.
Metabolism and nutrition disorders	35 (9.2)	Not reached [-; -]	27 (7.2)	Not reached [-; -]	1.16 [0.70; 1.91]	0.575	0.700
Hyperglycaemia	10 (2.6)	Not reached [-; -]	2 (0.5)	Not reached [-; -]	4.15 [0.90; 19.08]	0.068	n.s.
Hypokalaemia	10 (2.6)	Not reached [-; -]	14 (3.7)	Not reached [-; -]	0.67 [0.30; 1.50]	0.330	n.s.

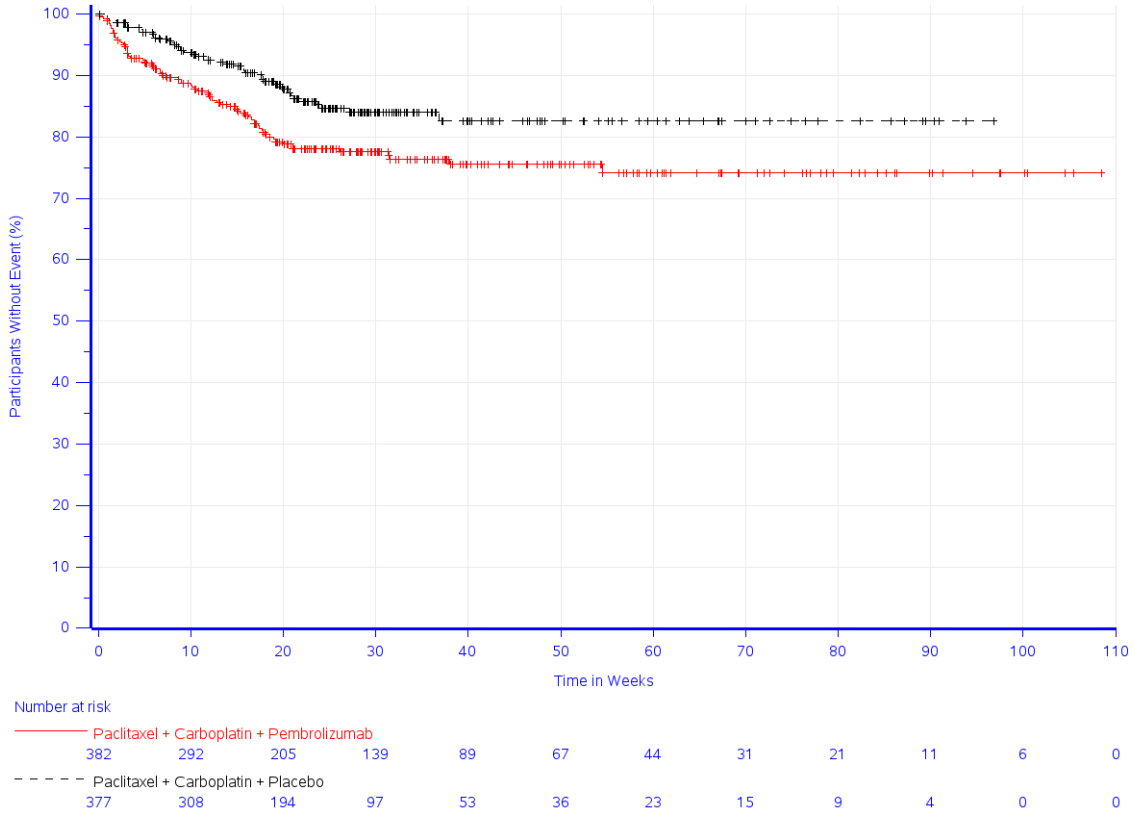
Time to Event Analysis for Severe Adverse Events (CTCAE-Grade 3-5) by System Organ Class and Preferred Term
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)**		**Paclitaxel + Carboplatin + Placebo (N[b]=377)**		**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT[c]	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio[e] [95 %-CI]**	**p-Value[e,f]**	**Adjusted p-Value[g]**
Musculoskeletal and connective tissue disorders	14 (3.7)	Not reached [-; -]	15 (4.0)	Not reached [-; -]	0.86 [0.42; 1.79]	0.697	0.700
Nervous system disorders	34 (8.9)	Not reached [-; -]	21 (5.6)	Not reached [-; -]	1.51 [0.88; 2.61]	0.137	0.357
Syncope	13 (3.4)	Not reached [-; -]	14 (3.7)	Not reached [-; -]	0.88 [0.41; 1.87]	0.737	n.s.
Renal and urinary disorders	14 (3.7)	Not reached [-; -]	8 (2.1)	Not reached [-; -]	1.54 [0.64; 3.68]	0.335	0.623
Respiratory, thoracic and mediastinal disorders	27 (7.1)	Not reached [-; -]	13 (3.4)	Not reached [-; -]	1.96 [1.01; 3.81]	0.047	0.157
Pulmonary embolism	10 (2.6)	Not reached [-; -]	10 (2.7)	Not reached [-; -]	0.96 [0.40; 2.31]	0.928	n.s.
Skin and subcutaneous tissue disorders	15 (3.9)	Not reached [-; -]	5 (1.3)	Not reached [-; -]	2.78 [1.01; 7.67]	0.048	0.157
Vascular disorders	31 (8.1)	Not reached [-; -]	26 (6.9)	Not reached [-; -]	1.16 [0.69; 1.96]	0.575	0.700
Hypertension	18 (4.7)	Not reached [-; -]	20 (5.3)	Not reached [-; -]	0.88 [0.47; 1.67]	0.697	n.s.

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: all-participants-as-treated population
c: A system organ class or specific adverse event appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
f: Two-sided p-value using Wald test

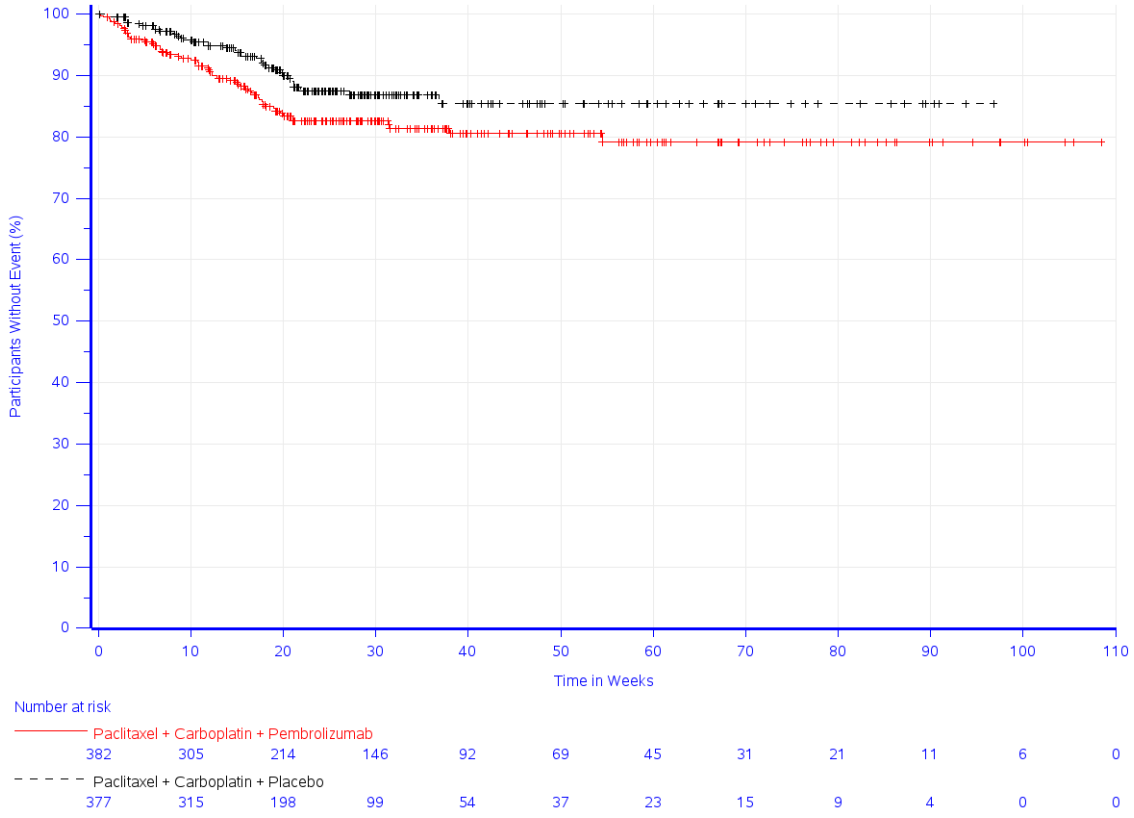
Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab (N[b]=382)		Paclitaxel + Carboplatin + Placebo (N[b]=377)		Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio[e] [95 %-CI]	p-Value[e,f]	Adjusted p-Value[g]
g: Adjusted p-values for treatment comparisons of adverse events at the SOC level were computed using the FDR procedure, and they were computed using the double FDR procedure for comparisons of adverse events at the PT level. Not significant (i.e., 'n.s.') is reported for PTs in a SOC when the SOC did not meet the threshold p-value criteria in the first step of the double FDR procedure. Adjusted p-values should be used for evaluating the results in order to reduce the number of false discoveries (i.e., statistical findings) when numerous statistical tests are performed							
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; FDR: False Discovery Rate; n.s.: Non-Significant (adjusted p-value ≥ 0.05); pMMR: Proficient Mismatch Repair; PT : Preferred Term; SOC: System Organ Class							

Figure 4.2-28
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for System Organ Class: Blood and lymphatic system disorders
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



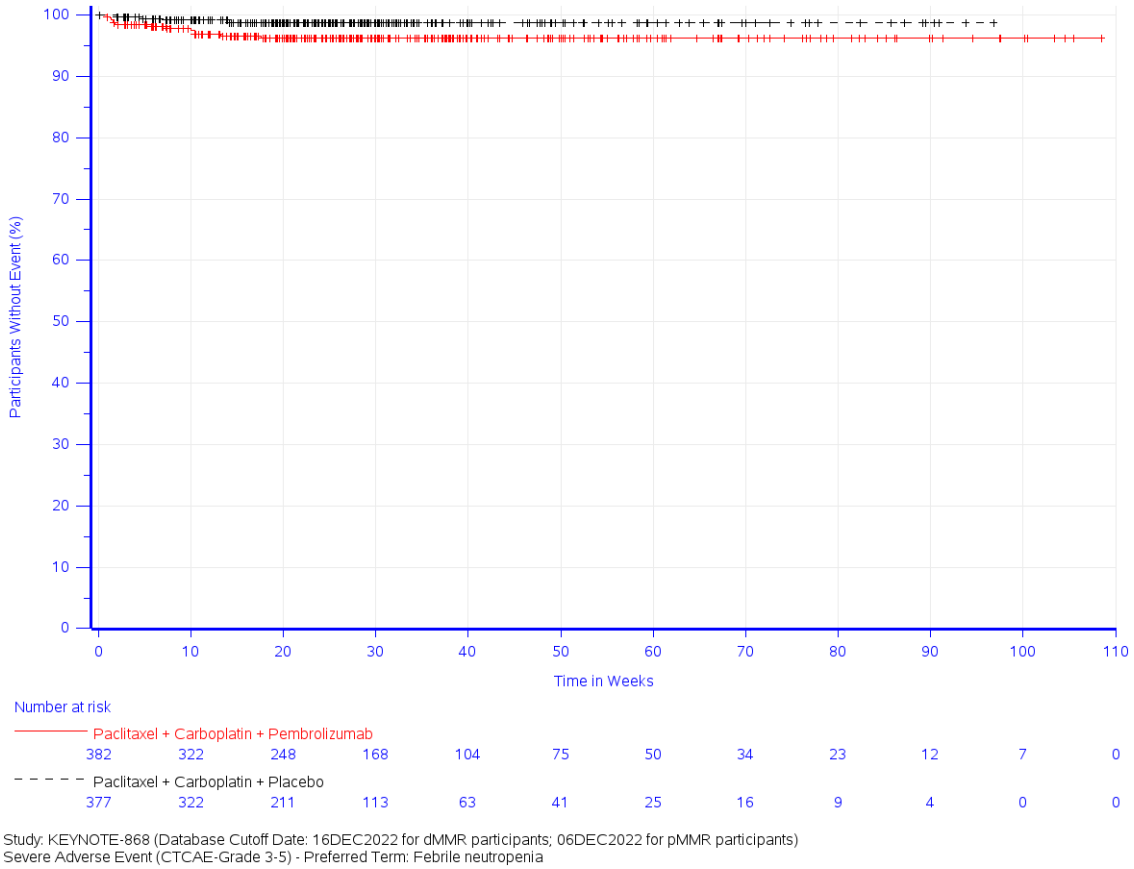
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - System Organ Class: Blood and lymphatic system disorders

Figure 4.2-29
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for Preferred Term: Anaemia
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



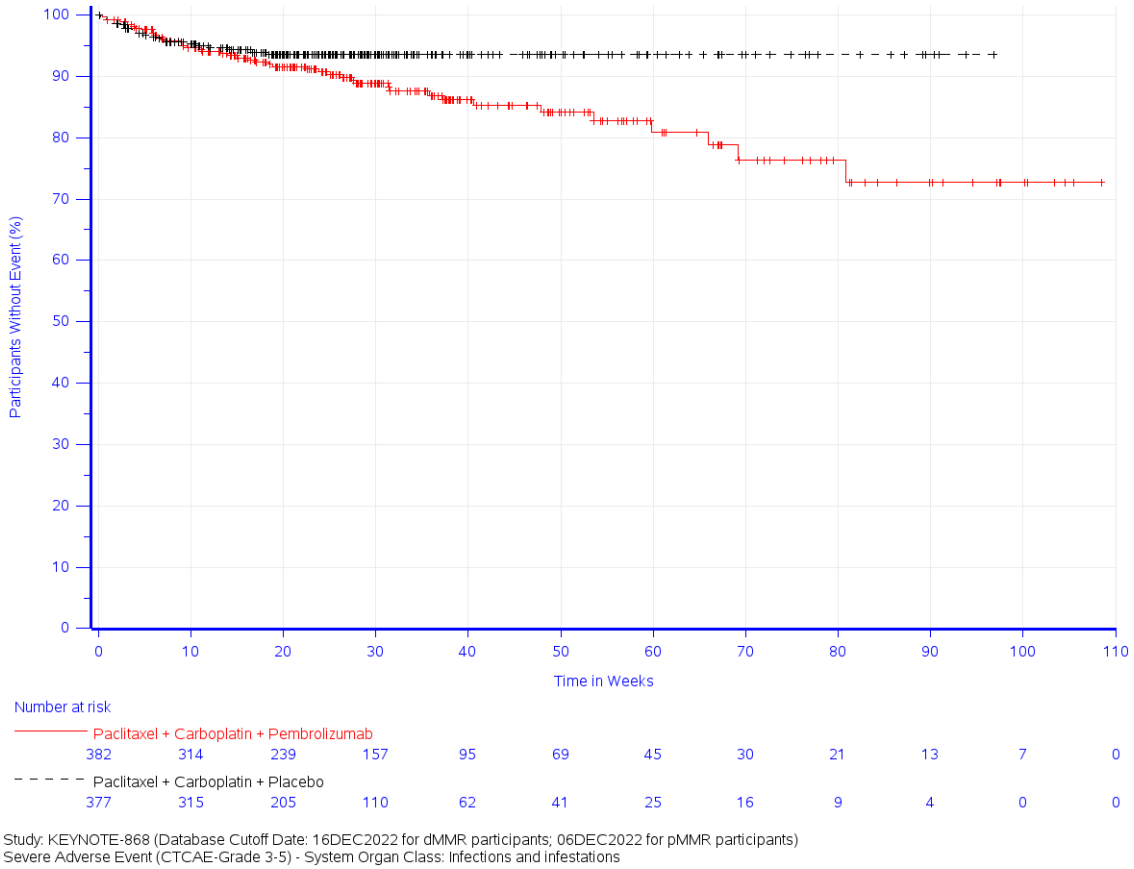
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - Preferred Term: Anaemia

Figure 4.2-30
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for Preferred Term: Febrile neutropenia
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



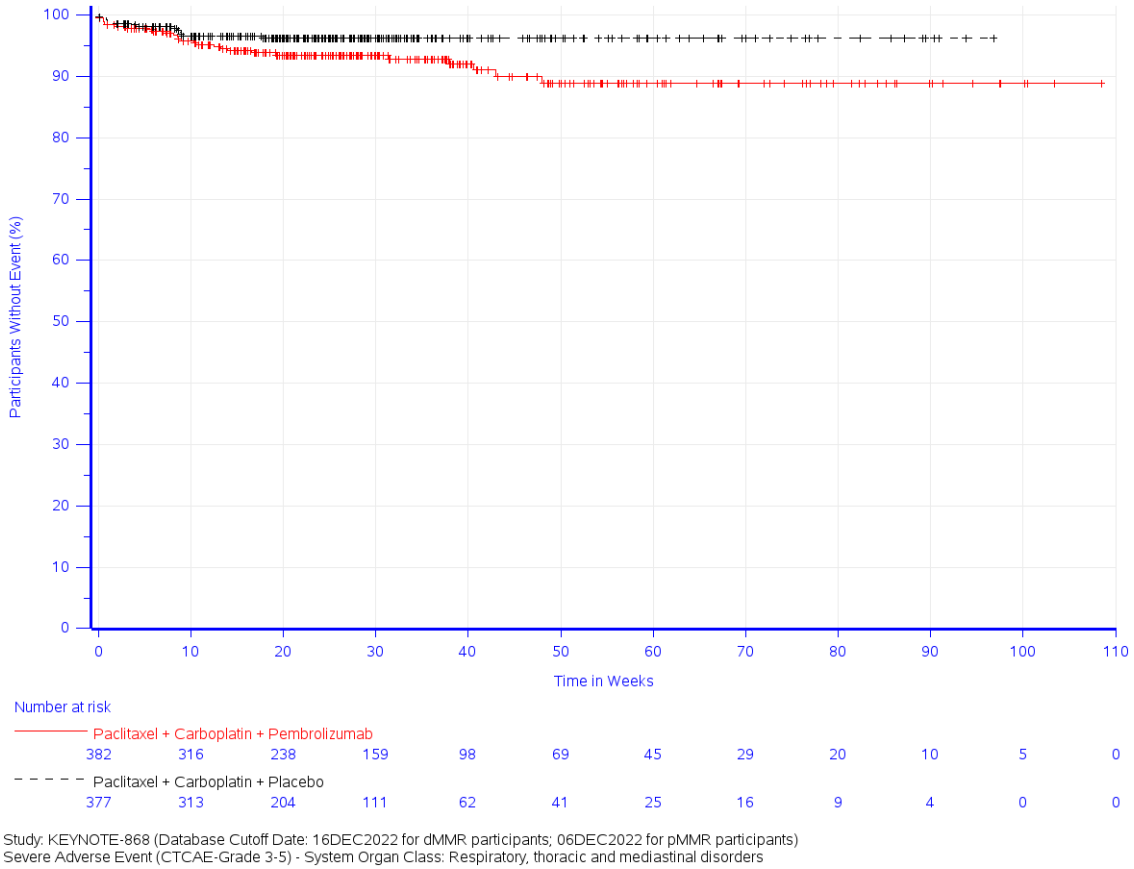
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - Preferred Term: Febrile neutropenia

Figure 4.2-31
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for System Organ Class: Infections and infestations
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



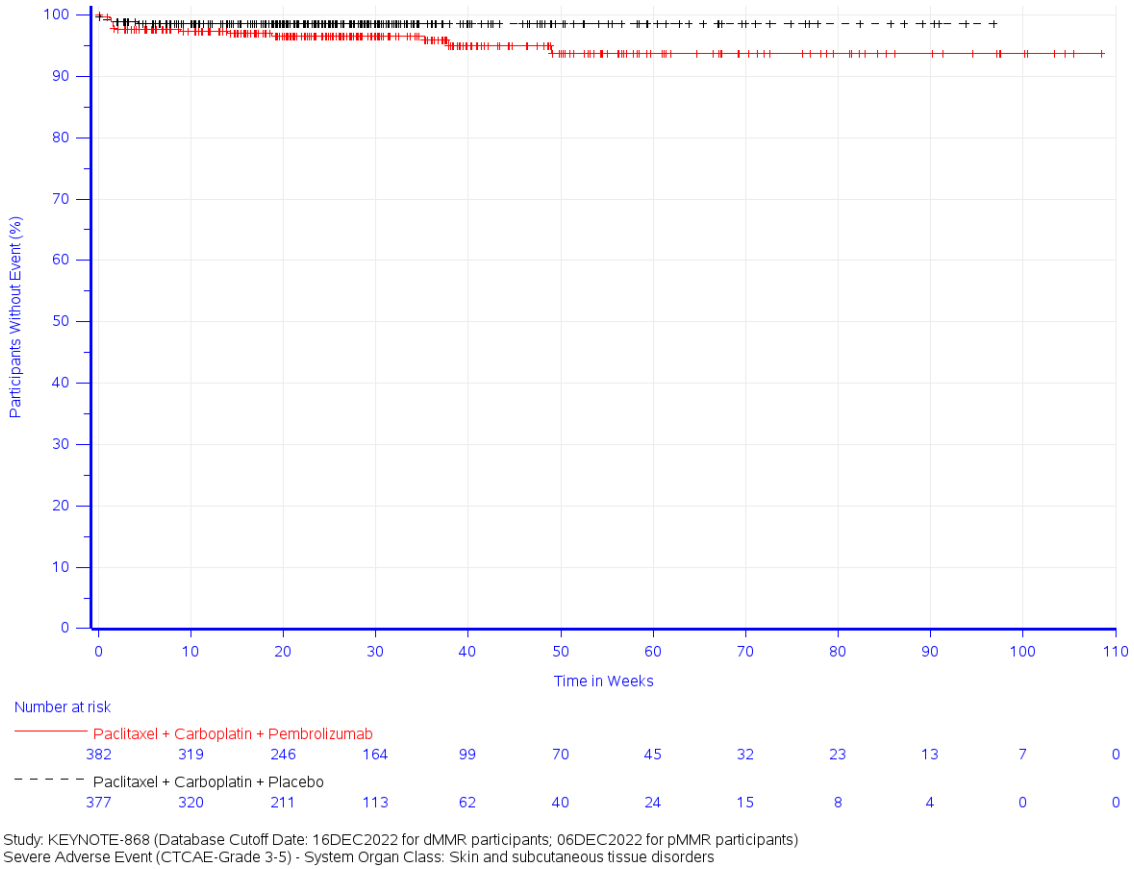
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - System Organ Class: Infections and infestations

Figure 4.2-32
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for System Organ Class: Respiratory, thoracic and mediastinal disorders
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - System Organ Class: Respiratory, thoracic and mediastinal disorders

Figure 4.2-33
Time to Severe Adverse Event (CTCAE-Grade 3-5) - Kaplan-Meier Curve
for System Organ Class: Skin and subcutaneous tissue disorders
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event (CTCAE-Grade 3-5) - System Organ Class: Skin and subcutaneous tissue disorders

Table 4.3-16
Summary of Adverse Events Noted Around Treatment Discontinuation Date
by System Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Participants with one or more adverse events	48 (12.6)	23 (6.1)
Blood and lymphatic system disorders	22 (5.8)	8 (2.1)
Anaemia	17 (4.5)	8 (2.1)
Neutropenia	4 (1.0)	0 (0.0)
Thrombocytopenia	2 (0.5)	1 (0.3)
Febrile neutropenia	2 (0.5)	0 (0.0)
Haemolysis	1 (0.3)	0 (0.0)
Cardiac disorders	6 (1.6)	3 (0.8)
Bradycardia	1 (0.3)	2 (0.5)
Atrial fibrillation	1 (0.3)	1 (0.3)
Sinus tachycardia	2 (0.5)	0 (0.0)
Myocardial infarction	1 (0.3)	0 (0.0)
Palpitations	1 (0.3)	0 (0.0)
Ear and labyrinth disorders	0 (0.0)	1 (0.3)
Vertigo	0 (0.0)	1 (0.3)
Endocrine disorders	2 (0.5)	0 (0.0)
Adrenal insufficiency	1 (0.3)	0 (0.0)
Hypophysitis	1 (0.3)	0 (0.0)
Hypothyroidism	1 (0.3)	0 (0.0)
Eye disorders	2 (0.5)	1 (0.3)
Eye disorder	0 (0.0)	1 (0.3)
Lacrimation increased	1 (0.3)	0 (0.0)
Vitreous floaters	1 (0.3)	0 (0.0)
Gastrointestinal disorders	25 (6.5)	9 (2.4)
Diarrhoea	11 (2.9)	6 (1.6)
Constipation	6 (1.6)	2 (0.5)
Nausea	6 (1.6)	2 (0.5)
Abdominal pain	4 (1.0)	2 (0.5)
Vomiting	4 (1.0)	2 (0.5)
Stomatitis	4 (1.0)	0 (0.0)
Anal incontinence	1 (0.3)	2 (0.5)
Oral pain	2 (0.5)	1 (0.3)
Colitis	2 (0.5)	0 (0.0)
Dyspepsia	2 (0.5)	0 (0.0)
Abdominal discomfort	0 (0.0)	1 (0.3)
Abdominal distension	1 (0.3)	0 (0.0)
Anal inflammation	1 (0.3)	0 (0.0)

Summary of Adverse Events Noted Around Treatment Discontinuation Date by System Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Ascites	1 (0.3)	0 (0.0)
Dry mouth	1 (0.3)	0 (0.0)
Duodenal perforation	1 (0.3)	0 (0.0)
Duodenal ulcer	1 (0.3)	0 (0.0)
Dysphagia	1 (0.3)	0 (0.0)
Gingival bleeding	0 (0.0)	1 (0.3)
Haematochezia	1 (0.3)	0 (0.0)
Hiatus hernia	1 (0.3)	0 (0.0)
Ileus	1 (0.3)	0 (0.0)
Pancreatitis	1 (0.3)	0 (0.0)
Rectal haemorrhage	1 (0.3)	0 (0.0)
General disorders and administration site conditions	18 (4.7)	7 (1.9)
Fatigue	11 (2.9)	5 (1.3)
Oedema peripheral	3 (0.8)	1 (0.3)
Pyrexia	3 (0.8)	0 (0.0)
Asthenia	2 (0.5)	0 (0.0)
Chills	2 (0.5)	0 (0.0)
Localised oedema	1 (0.3)	0 (0.0)
Pain	1 (0.3)	0 (0.0)
Physical deconditioning	0 (0.0)	1 (0.3)
Ulcer	1 (0.3)	0 (0.0)
Immune system disorders	0 (0.0)	1 (0.3)
Hypersensitivity	0 (0.0)	1 (0.3)
Infections and infestations	17 (4.5)	6 (1.6)
Urinary tract infection	6 (1.6)	1 (0.3)
COVID-19	2 (0.5)	1 (0.3)
Pneumonia	3 (0.8)	0 (0.0)
Candida infection	1 (0.3)	1 (0.3)
Nasopharyngitis	1 (0.3)	1 (0.3)
Abdominal infection	0 (0.0)	1 (0.3)
Abscess oral	0 (0.0)	1 (0.3)
Bacteraemia	1 (0.3)	0 (0.0)
Cellulitis	0 (0.0)	1 (0.3)
Clostridium difficile infection	1 (0.3)	0 (0.0)
Encephalitis	1 (0.3)	0 (0.0)
Eye infection	1 (0.3)	0 (0.0)
Meningitis	1 (0.3)	0 (0.0)

Summary of Adverse Events Noted Around Treatment Discontinuation Date
by System Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Sepsis	1 (0.3)	0 (0.0)
Urosepsis	1 (0.3)	0 (0.0)
Vestibular neuronitis	1 (0.3)	0 (0.0)
Injury, poisoning and procedural complications	6 (1.6)	1 (0.3)
Infusion related reaction	4 (1.0)	0 (0.0)
Fall	1 (0.3)	1 (0.3)
Radiation proctitis	1 (0.3)	0 (0.0)
Skin abrasion	1 (0.3)	0 (0.0)
Investigations	28 (7.3)	8 (2.1)
White blood cell count decreased	9 (2.4)	4 (1.1)
Platelet count decreased	6 (1.6)	5 (1.3)
Lymphocyte count decreased	8 (2.1)	2 (0.5)
Neutrophil count decreased	8 (2.1)	2 (0.5)
Blood creatinine increased	7 (1.8)	1 (0.3)
Aspartate aminotransferase increased	6 (1.6)	1 (0.3)
Alanine aminotransferase increased	5 (1.3)	1 (0.3)
Blood alkaline phosphatase increased	4 (1.0)	1 (0.3)
Blood bilirubin increased	3 (0.8)	1 (0.3)
Weight decreased	3 (0.8)	1 (0.3)
Blood bicarbonate decreased	3 (0.8)	0 (0.0)
Blood magnesium decreased	1 (0.3)	1 (0.3)
Blood phosphorus decreased	1 (0.3)	1 (0.3)
Blood potassium decreased	2 (0.5)	0 (0.0)
Troponin T increased	2 (0.5)	0 (0.0)
Activated partial thromboplastin time prolonged	1 (0.3)	0 (0.0)
Amylase increased	1 (0.3)	0 (0.0)
Aspartate aminotransferase	1 (0.3)	0 (0.0)
Blood chloride decreased	1 (0.3)	0 (0.0)
Blood lactic acid increased	1 (0.3)	0 (0.0)
Blood sodium decreased	1 (0.3)	0 (0.0)
Blood urea increased	1 (0.3)	0 (0.0)
Brain natriuretic peptide increased	1 (0.3)	0 (0.0)
Haemoglobin decreased	1 (0.3)	0 (0.0)
Heart rate irregular	1 (0.3)	0 (0.0)
International normalised ratio increased	1 (0.3)	0 (0.0)
Oxygen saturation decreased	1 (0.3)	0 (0.0)
Troponin I increased	1 (0.3)	0 (0.0)

Summary of Adverse Events Noted Around Treatment Discontinuation Date
by System Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Troponin increased	1 (0.3)	0 (0.0)
Weight increased	1 (0.3)	0 (0.0)
Metabolism and nutrition disorders	19 (5.0)	6 (1.6)
Hypokalaemia	7 (1.8)	1 (0.3)
Hyponatraemia	6 (1.6)	2 (0.5)
Decreased appetite	5 (1.3)	2 (0.5)
Hypomagnesaemia	7 (1.8)	0 (0.0)
Hypoalbuminaemia	5 (1.3)	1 (0.3)
Hyperglycaemia	3 (0.8)	1 (0.3)
Dehydration	2 (0.5)	2 (0.5)
Hypocalcaemia	2 (0.5)	1 (0.3)
Hyperkalaemia	1 (0.3)	1 (0.3)
Hypophosphataemia	1 (0.3)	1 (0.3)
Hyperphosphataemia	2 (0.5)	0 (0.0)
Acidosis	1 (0.3)	0 (0.0)
Diabetic ketoacidosis	1 (0.3)	0 (0.0)
Failure to thrive	0 (0.0)	1 (0.3)
Hypercalcaemia	1 (0.3)	0 (0.0)
Hypoglycaemia	1 (0.3)	0 (0.0)
Hypophagia	0 (0.0)	1 (0.3)
Metabolic acidosis	1 (0.3)	0 (0.0)
Musculoskeletal and connective tissue disorders	11 (2.9)	7 (1.9)
Arthralgia	4 (1.0)	2 (0.5)
Back pain	2 (0.5)	3 (0.8)
Muscular weakness	3 (0.8)	2 (0.5)
Myalgia	1 (0.3)	2 (0.5)
Pain in extremity	2 (0.5)	1 (0.3)
Arthritis	0 (0.0)	1 (0.3)
Nervous system disorders	21 (5.5)	10 (2.7)
Neuropathy peripheral	4 (1.0)	5 (1.3)
Peripheral sensory neuropathy	5 (1.3)	1 (0.3)
Dizziness	3 (0.8)	2 (0.5)
Headache	4 (1.0)	0 (0.0)
Balance disorder	3 (0.8)	0 (0.0)
Paraesthesia	1 (0.3)	1 (0.3)
Peripheral motor neuropathy	2 (0.5)	0 (0.0)
Seizure	2 (0.5)	0 (0.0)

Summary of Adverse Events Noted Around Treatment Discontinuation Date
by System Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Syncope	2 (0.5)	0 (0.0)
Taste disorder	2 (0.5)	0 (0.0)
Brachial plexopathy	1 (0.3)	0 (0.0)
Burning sensation	0 (0.0)	1 (0.3)
Cognitive disorder	1 (0.3)	0 (0.0)
Dyskinesia	1 (0.3)	0 (0.0)
Encephalopathy	1 (0.3)	0 (0.0)
Guillain-Barre syndrome	1 (0.3)	0 (0.0)
Hemiparesis	1 (0.3)	0 (0.0)
Hypoaesthesia	1 (0.3)	0 (0.0)
Memory impairment	1 (0.3)	0 (0.0)
Peripheral sensorimotor neuropathy	1 (0.3)	0 (0.0)
Polyneuropathy	1 (0.3)	0 (0.0)
Psychiatric disorders	5 (1.3)	3 (0.8)
Insomnia	3 (0.8)	1 (0.3)
Confusional state	1 (0.3)	1 (0.3)
Agitation	1 (0.3)	0 (0.0)
Anxiety	0 (0.0)	1 (0.3)
Depression	1 (0.3)	0 (0.0)
Hallucination	0 (0.0)	1 (0.3)
Mental status changes	1 (0.3)	0 (0.0)
Renal and urinary disorders	9 (2.4)	3 (0.8)
Acute kidney injury	3 (0.8)	0 (0.0)
Dysuria	2 (0.5)	1 (0.3)
Urinary incontinence	1 (0.3)	1 (0.3)
Urinary retention	1 (0.3)	1 (0.3)
Haematuria	1 (0.3)	0 (0.0)
Hydronephrosis	1 (0.3)	0 (0.0)
Proteinuria	1 (0.3)	0 (0.0)
Reproductive system and breast disorders	1 (0.3)	1 (0.3)
Vaginal haemorrhage	0 (0.0)	1 (0.3)
Vulvovaginal inflammation	1 (0.3)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	12 (3.1)	2 (0.5)
Dyspnoea	5 (1.3)	0 (0.0)
Cough	3 (0.8)	0 (0.0)
Pneumonitis	2 (0.5)	1 (0.3)
Pulmonary embolism	1 (0.3)	1 (0.3)

Summary of Adverse Events Noted Around Treatment Discontinuation Date by System Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Participants with Event n (%)**	
Adverse Events Noted Around Treatment Discontinuation Date by SOC and PT[b,c]	**Paclitaxel + Carboplatin + Pembrolizumab (N[d]=382)**	**Paclitaxel + Carboplatin + Placebo (N[d]=377)**
Dyspnoea exertional	2 (0.5)	0 (0.0)
Hypoxia	1 (0.3)	0 (0.0)
Pleural effusion	1 (0.3)	0 (0.0)
Upper-airway cough syndrome	1 (0.3)	0 (0.0)
Skin and subcutaneous tissue disorders	16 (4.2)	5 (1.3)
Alopecia	5 (1.3)	1 (0.3)
Rash	4 (1.0)	2 (0.5)
Pruritus	3 (0.8)	1 (0.3)
Rash maculo-papular	3 (0.8)	0 (0.0)
Decubitus ulcer	1 (0.3)	1 (0.3)
Dry skin	1 (0.3)	0 (0.0)
Palmar-plantar erythrodysaesthesia syndrome	1 (0.3)	0 (0.0)
Rash pruritic	0 (0.0)	1 (0.3)
Skin disorder	1 (0.3)	0 (0.0)
Skin irritation	0 (0.0)	1 (0.3)
Skin ulcer	1 (0.3)	0 (0.0)
Stasis dermatitis	1 (0.3)	0 (0.0)
Vascular disorders	8 (2.1)	2 (0.5)
Hypertension	4 (1.0)	1 (0.3)
Hypotension	1 (0.3)	1 (0.3)
Deep vein thrombosis	1 (0.3)	0 (0.0)
Embolism	1 (0.3)	0 (0.0)
Hypovolaemic shock	1 (0.3)	0 (0.0)
Vasculitis	1 (0.3)	0 (0.0)

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: A SOC or specific adverse event appears on this report only if its incidence is > 0% in one or more treatment groups

c: Adverse events noted around treatment discontinuation date include adverse events started within +/- 30 days from the treatment discontinuation date, for those participants who discontinued treatment due to 'Adverse Event/Side Effects/Complications' (captured in the participant disposition case report form)

d: Number of participants: all-participants-as-treated population

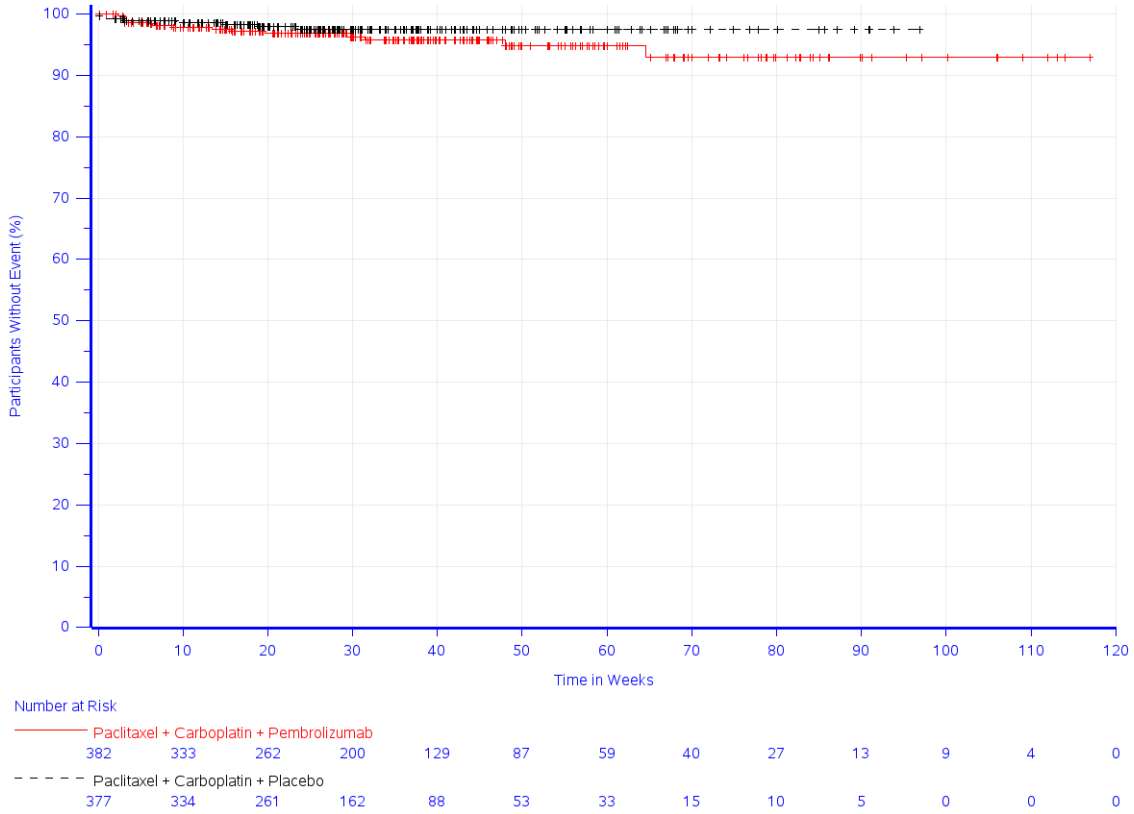
COVID-19: Coronavirus Disease 2019; dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair; PT: Preferred Term; SOC: System Organ Class

Table 4.4-17
Time to Event Analysis for Adverse Event of Special Interest Related Endpoints in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo	
	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]
Serious AEOSI	382	15 (3.9)	Not reached [-; -]	377	8 (2.1)	Not reached [-; -]	1.74 [0.74; 4.12]	0.206
Severe AEOSI (CTCAE-Grade 3-5)	382	33 (8.6)	Not reached [-; -]	377	16 (4.2)	Not reached [-; -]	1.90 [1.04; 3.46]	0.036

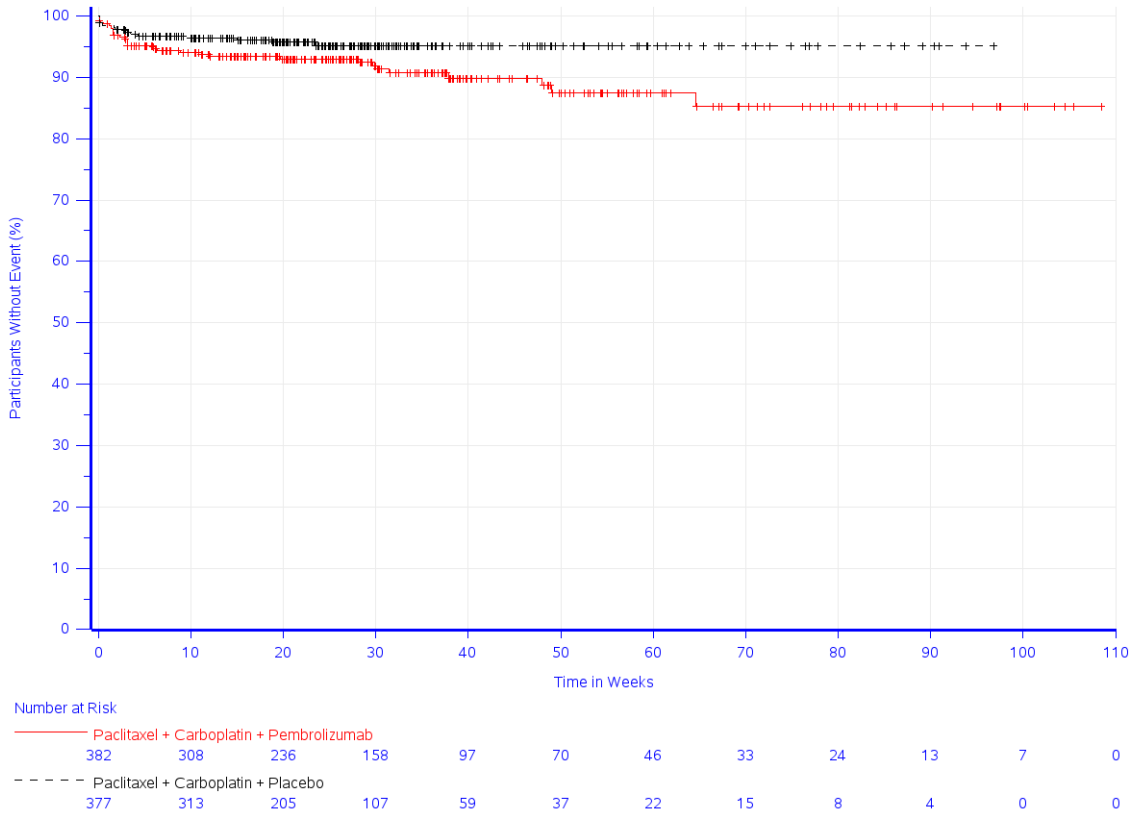
a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
AEOSI: Adverse Events Of Special Interest; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.4-34
Time to Serious Adverse Event of Special Interest - Kaplan-Meier Curve
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Serious Adverse Event of Special Interest

Figure 4.4-35
Time to Severe Adverse Event of Special Interest (CTCAE-Grade 3-5) - Kaplan-Meier Curve in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Severe Adverse Event of Special Interest (CTCAE-Grade 3-5)

Table 4.1-18
Overview of Subgroup Analyses for Overall Survival
Treatment by Subgroup Interaction
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Mortality					
Overall Survival	0.697	0.698	n.c.	0.296	**0.025[c]**

Overview of Subgroup Analyses for Overall Survival
Treatment by Subgroup Interaction
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**					
	Age group (< 65 vs. ≥ 65 to <75 vs. ≥ 75)	**Race (White vs. All Others)**	**Histology (Endometrioid vs. Other)**	**Prior Radiation Therapy (Yes vs. No)**	**Measurable Disease at Baseline (Yes vs. No)**	**Status of Disease (Primary vs. Recurrent/Persistent)**
Mortality						
Overall Survival	0.829	0.384	0.141	**0.021[c]**	0.051	0.206

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

c: p-value for interaction test smaller than 0.05

dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.2-19
Overview of Subgroup Analyses for Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule)
Treatment by Subgroup Interaction
in All-comers Participants
(Intention-to- Treat Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Morbidity					
Progression-Free Survival (INV Primary Censoring Rule)	0.488	0.643	n.c.	**0.026[c]**	**0.025[c]**

Overview of Subgroup Analyses for Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule)
Treatment by Subgroup Interaction
in All-comers Participants
(Intention-to- Treat Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**					
	Age group (< 65 vs. ≥ 65 to <75 vs. ≥ 75)	**Race (White vs. All Others)**	**Histology (Endometrioid vs. Other)**	**Prior Radiation Therapy (Yes vs. No)**	**Measurable Disease at Baseline (Yes vs. No)**	**Status of Disease (Primary vs. Recurrent/Persistent)**
Morbidity						
Progression-Free Survival (INV Primary Censoring Rule)	0.626	0.264	0.298	**0.014[c]**	0.063	0.098

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

c: p-value for interaction test smaller than 0.05
dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; INV: Investigator; 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); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.2-20
Overview of Subgroup Analyses for Time to Subsequent Therapy or Death
Treatment by Subgroup Interaction
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Time to Subsequent Therapy or Death					
Time to Subsequent Oncologic Therapy or Death	0.721	0.953	n.c.	**0.021[c]**	0.051

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
c: p-value for interaction test smaller than 0.05
dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.6-21
Overview of Subgroup Analyses for Time to Adverse Event Related Endpoints
Treatment by Subgroup Interaction
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Adverse Events - Time to Event					
Adverse Events	0.346	0.581	n.c.	0.352	0.054
Serious Adverse Events	0.571	0.746	n.c.	0.770	0.794
Severe Adverse Events (CTCAE-Grade 3-5)	0.291	0.241	n.c.	0.607	0.113
Treatment Discontinuations Due to Adverse Events/Side Effects/Complications	**0.032[c]**	0.283	n.c.	0.992	0.259

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

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

c: p-value for interaction test smaller than 0.05

CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; WHO: World Health Organization

Table 4.7-22
Overview of Subgroup Analyses for Time to Adverse Event Related Endpoints
Treatment by Subgroup Interaction
by System Organ Class and Preferred Term
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Adverse Events by SOC and PT[c] - Time to Event					
Cardiac disorders	0.139	0.357	n.c.	0.089	0.093
Palpitations	n.c.	0.997	n.c.	n.c.	**0.039[d]**
Endocrine disorders	0.279	0.519	n.c.	0.069	0.213
Hyperthyroidism	0.120	0.539	n.c.	0.363	0.704
Hypothyroidism	0.899	**0.038[d]**	n.c.	**0.007[d]**	**0.024[d]**
Gastrointestinal disorders	n.p.	n.p.	n.p.	n.p.	n.p.

Overview of Subgroup Analyses for Time to Adverse Event Related Endpoints
Treatment by Subgroup Interaction
by System Organ Class and Preferred Term
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Dry mouth	0.064	0.672	n.c.	**0.006[d]**	0.149
Vomiting	0.791	0.642	n.c.	0.166	**0.007[d]**
General disorders and administration site conditions	0.477	0.797	n.c.	0.193	0.578
Chills	0.112	0.991	n.c.	0.803	0.508
Pyrexia	0.402	0.369	n.c.	0.628	0.741
Investigations	n.p.	n.p.	n.p.	n.p.	n.p.
Aspartate aminotransferase increased	0.260	0.433	n.c.	0.574	0.108

Overview of Subgroup Analyses for Time to Adverse Event Related Endpoints
Treatment by Subgroup Interaction
by System Organ Class and Preferred Term
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Blood creatinine increased	0.700	0.582	n.c.	0.991	0.431
Metabolism and nutrition disorders	n.p.	n.p.	n.p.	n.p.	n.p.
Hypokalaemia	0.402	0.183	n.c.	0.755	0.767
Musculoskeletal and connective tissue disorders	n.p.	n.p.	n.p.	n.p.	n.p.
Arthralgia	0.193	0.493	n.c.	0.888	0.258
Skin and subcutaneous tissue disorders	**0.042[d]**	0.575	n.c.	0.443	0.480
Rash maculo-papular	**0.006[d]**	0.898	n.c.	0.302	0.290

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

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

c: A system organ class or 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 treatment groups and p-value of main treatment effect smaller than 0.05

d: p-value for interaction test smaller than 0.05

dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); n.p.: not performed (subgroup analysis not performed as nominal p-value of main treatment effect greater or equal than 0.05); pMMR: Proficient Mismatch Repair; PT:Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-23
Overview of Subgroup Analyses for Time to Serious Adverse Event Related Endpoints
Treatment by Subgroup Interaction
by System Organ Class and Preferred Term
(Incidence ≥ 5 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Serious Adverse Events by SOC and PT[c] - Time to Event					
Investigations	0.903	0.594	n.c.	0.317	0.164
Nervous system disorders	0.500	0.585	n.c.	0.502	0.972
Respiratory, thoracic and mediastinal disorders	0.876	0.809	n.c.	0.653	0.891

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

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

c: A system organ class or specific adverse event appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect smaller than 0.05

dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; PT:Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-24
Overview of Subgroup Analyses for Time to Severe Adverse Event (CTCAE-Grade 3-5) Related Endpoints
Treatment by Subgroup Interaction
by System Organ Class and Preferred Term
(Incidence ≥ 5 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**P-Values of Treatment by Subgroup Interaction Test[b]**				
	Age group (< 65 vs. ≥ 65)	**ECOG (0 vs. 1 or 2)**	**Region (WHO Stratum A vs. Rest of World)**	**Mismatch repair deficient (dMMR) (Yes vs. No)**	**Prior Chemotherapy (Yes vs. No)**
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT[c] - Time to Event					
Blood and lymphatic system disorders	0.907	0.586	n.c.	0.892	0.508
Anaemia	0.473	0.529	n.c.	0.704	0.952
Febrile neutropenia	0.720	0.425	n.c.	0.112	0.469
Infections and infestations	0.251	0.781	n.c.	0.964	0.305
Respiratory, thoracic and mediastinal disorders	0.817	0.855	n.c.	0.300	0.860
Skin and subcutaneous tissue disorders	0.967	0.396	n.c.	0.827	0.685

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

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

c: A system organ class or specific adverse event appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect smaller than 0.05

CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; PT:Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Table 4.1-25
Analyses of Overall Survival
for Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**	**p-Value for Interaction Test[f]**
Prior Chemotherapy									
Yes	80	17 (21.3)	20.9 [16.8; -]	81	10 (12.3)	29.3 [18.5; -]	1.54 [0.71; 3.37]	0.278	0.025
No	324	38 (11.7)	Not reached [-; -]	325	61 (18.8)	32.2 [21.3; -]	0.57 [0.38; 0.86]	0.007	
Prior radiation therapy									
Yes	160	30 (18.8)	Not reached [24.8; -]	178	28 (15.7)	Not reached [19.1; -]	1.12 [0.67; 1.88]	0.657	0.021
No	244	25 (10.2)	Not reached [28.0; -]	228	43 (18.9)	29.3 [21.3; -]	0.48 [0.29; 0.79]	0.004	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: intention-to-treat population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CI: confidence interval; dMMR: deficient mismatch repair; pMMR: proficient mismatch repair

Table 4.2-26
Analysis of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule) for Subgroups With P-Value for Interaction test < 0.05 in All-comers Participants (Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Progression-Free Survival (INV Primary Censoring Rule)	**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]**
Mismatch repair deficient (dMMR)									
Yes	110	29 (26.4)	Not reached [30.7; -]	112	60 (53.6)	8.3 [6.5; 12.3]	0.34 [0.22; 0.53]	< 0.001	0.026
No	294	95 (32.3)	13.1 [10.6; 19.5]	294	138 (46.9)	8.7 [8.4; 11.0]	0.57 [0.44; 0.74]	< 0.001	
Prior Chemotherapy									
Yes	80	37 (46.3)	9.1 [8.3; 11.5]	81	39 (48.1)	8.3 [6.5; 8.8]	0.74 [0.47; 1.17]	0.195	0.025
No	324	87 (26.9)	30.7 [17.1; -]	325	159 (48.9)	8.7 [8.3; 11.3]	0.42 [0.32; 0.55]	< 0.001	
Prior radiation therapy									
Yes	160	63 (39.4)	12.0 [9.3; 15.1]	178	89 (50.0)	8.7 [8.3; 11.2]	0.66 [0.47; 0.91]	0.011	0.014
No	244	61 (25.0)	Not reached [18.8; -]	228	109 (47.8)	8.5 [6.9; 10.9]	0.38 [0.28; 0.53]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

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

d: Based on unstratified Cox regression model with treatment as a covariate for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model with treatment as a covariate stratified by prior chemotherapy. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

f: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CI: Confidence Interval; dMMR: deficient mismatch repair; INV: Investigator; pMMR: proficient mismatch repair

Table 4.2-27
Analysis of Time to Subsequent Therapy or Death
for Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Time to Subsequent Therapy or Death	N[b]	Participants with Event n (%)	Median Time[c] in Months [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Months [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
Mismatch repair deficient (dMMR)									
Yes	110	27 (24.5)	Not reached [-; -]	112	63 (56.3)	8.7 [7.3; 11.4]	0.30 [0.19; 0.48]	< 0.001	0.021
No	294	94 (32.0)	13.6 [11.9; 20.7]	294	137 (46.6)	9.5 [8.2; 10.6]	0.54 [0.42; 0.71]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

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

d: Based on unstratified Cox regression model with treatment as a covariate for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model with treatment as a covariate stratified by prior chemotherapy. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

f: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CI: confidence interval; dMMR: deficient mismatch repair; pMMR: proficient mismatch repair

Table 4.6-28
Analyses of Time to Treatment Discontinuation Due to Adverse Events/Side Effects/Complications for Subgroups with p-Value for Interaction Test < 0.05 in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Treatment Discontinuation Due to Adverse Events/Side Effects/Complications	**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]**
Age group									
< 65	172	19 (11.0)	Not reached [-; -]	174	3 (1.7)	Not reached [66.7; -]	4.68 [1.38; 15.93]	0.013	0.032
≥65	210	34 (16.2)	Not reached [86.1; -]	203	20 (9.9)	Not reached [-; -]	1.35 [0.78; 2.36]	0.286	

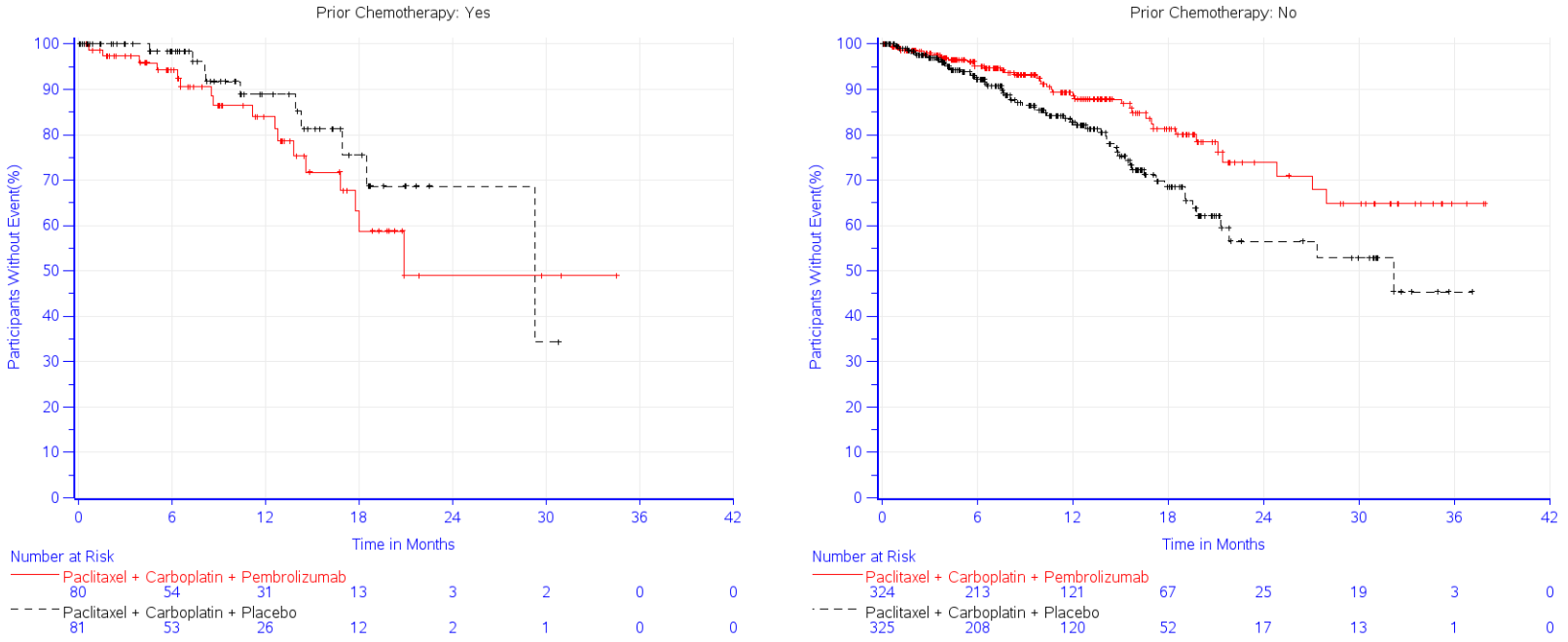
a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Table 4.5-29
Summary of Best Overall Response Based on Investigator Assessment per RECIST 1.1
in All-comers Participants
(ITT Population with Measurable Disease at Baseline)

Response Evaluation	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo		
	n	%	95% CI[a]	n	%	95% CI[a]
Participants in population	315			330		
Complete Response (CR)	51	16.2	(12.3, 20.7)	27	8.2	(5.5, 11.7)
Partial Response (PR)	158	50.2	(44.5, 55.8)	160	48.5	(43.0, 54.0)
Overall Response (CR+PR)	**209**	**66.3**	**(60.8, 71.6)**	**187**	**56.7**	**(51.1, 62.1)**
Stable Disease (SD)	39	12.4	(9.0, 16.5)	69	20.9	(16.6, 25.7)
Disease Control (CR+PR+SD≥8Weeks)	**235**	**74.6**	**(69.4, 79.3)**	**238**	**72.1**	**(66.9, 76.9)**
Clinical Benefit (CR+PR+ SD≥23Weeks)	**217**	**68.9**	**(63.5, 74.0)**	**199**	**60.3**	**(54.8, 65.6)**
Progressive Disease (PD)	17	5.4	(3.2, 8.5)	22	6.7	(4.2, 9.9)
NE	2	0.6	(0.1, 2.3)	3	0.9	(0.2, 2.6)
No Assessment	48	15.2	(11.5, 19.7)	49	14.8	(11.2, 19.2)

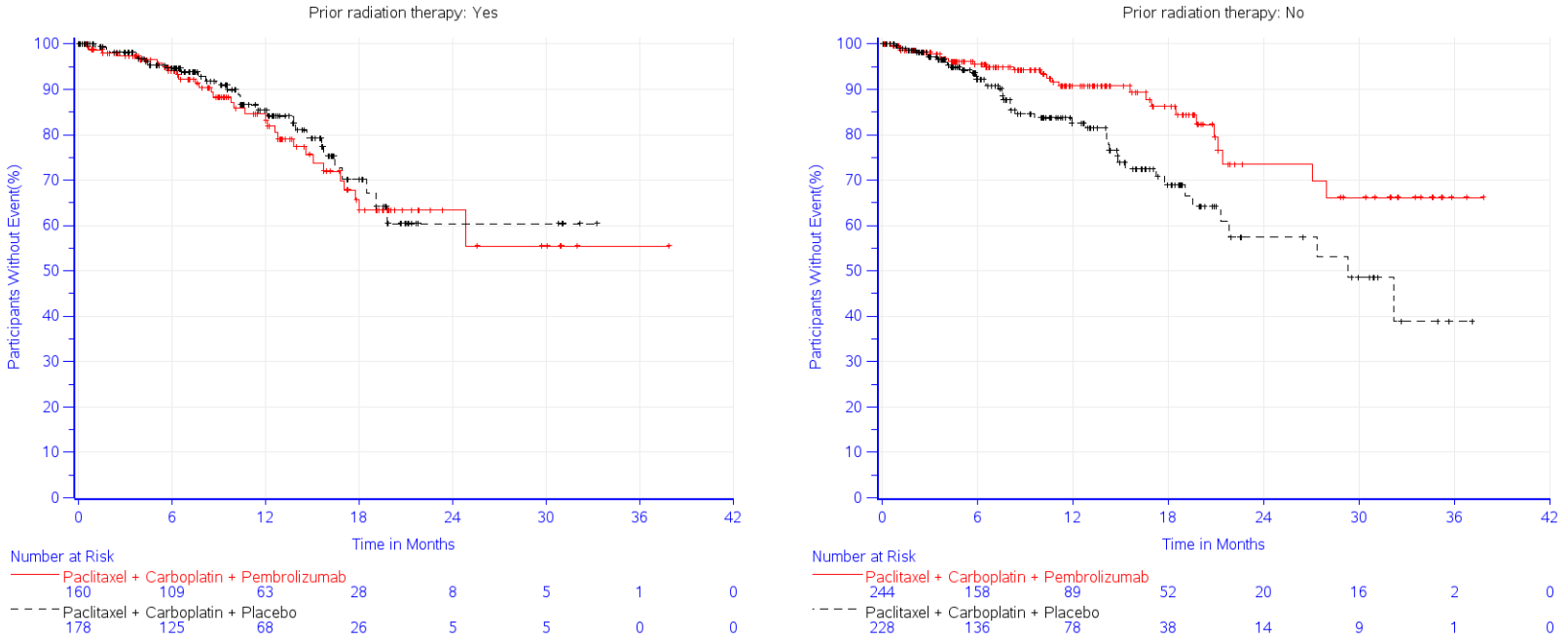
[a] Based on binomial exact confidence interval method.
Non-evaluable: Post-baseline assessment(s) available, but not evaluable.
No Assessment: No post-baseline assessment available for response evaluation.
Patients who enter the study with no measurable disease are excluded from the calculation.
Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
dMMR: Deficient Mismatch Repair; pMMR: Proficient Mismatch Repair

Figure 4.1-36
Kaplan-Meier Curves of Overall Survival
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Prior Chemotherapy
(Intention-to-Treat Population)



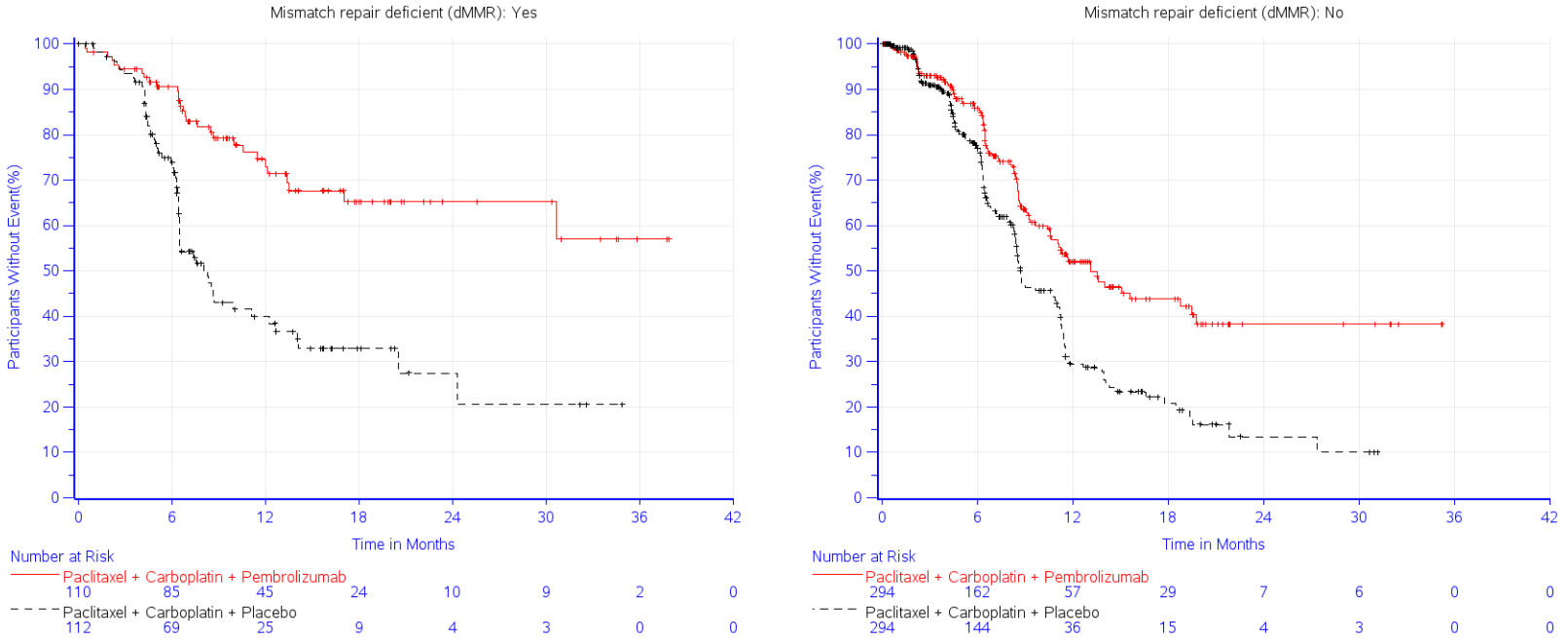
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Overall Survival

Figure 4.1-37
Kaplan-Meier Curves of Overall Survival
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Prior radiation therapy
(Intention-to-Treat Population)



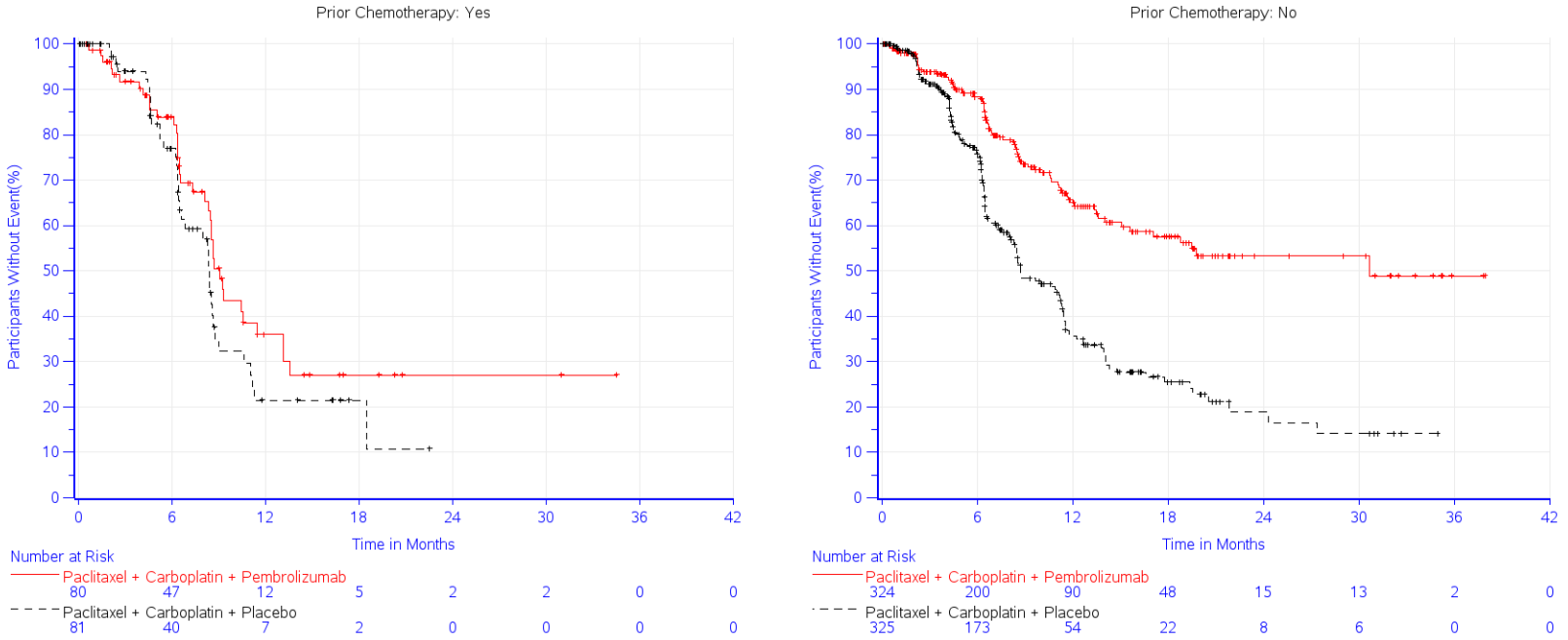
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Overall Survival

Figure 4.2-38
Kaplan-Meier Curves of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Mismatch repair deficient (dMMR)
(Intention-to-Treat Population)



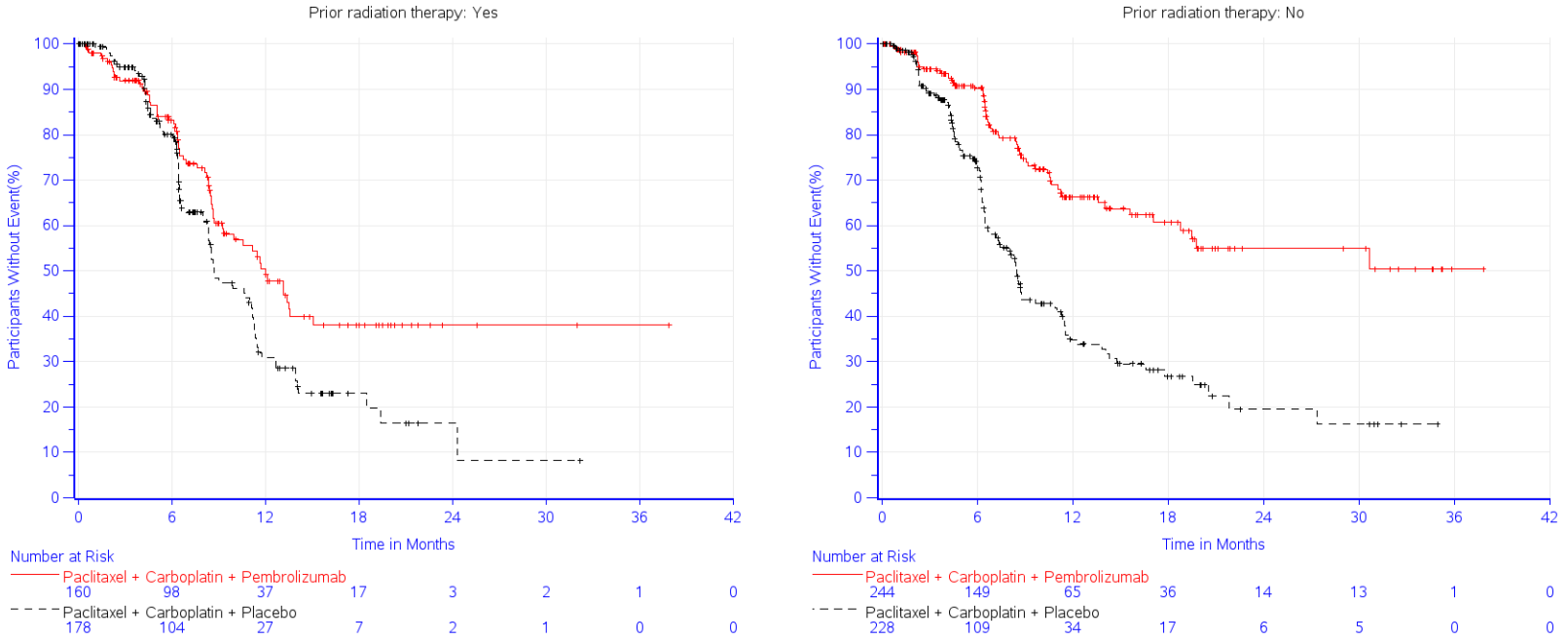
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival (INV Primary Censoring Rule)

Figure 4.2-39
Kaplan-Meier Curves of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Prior Chemotherapy
(Intention-to-Treat Population)



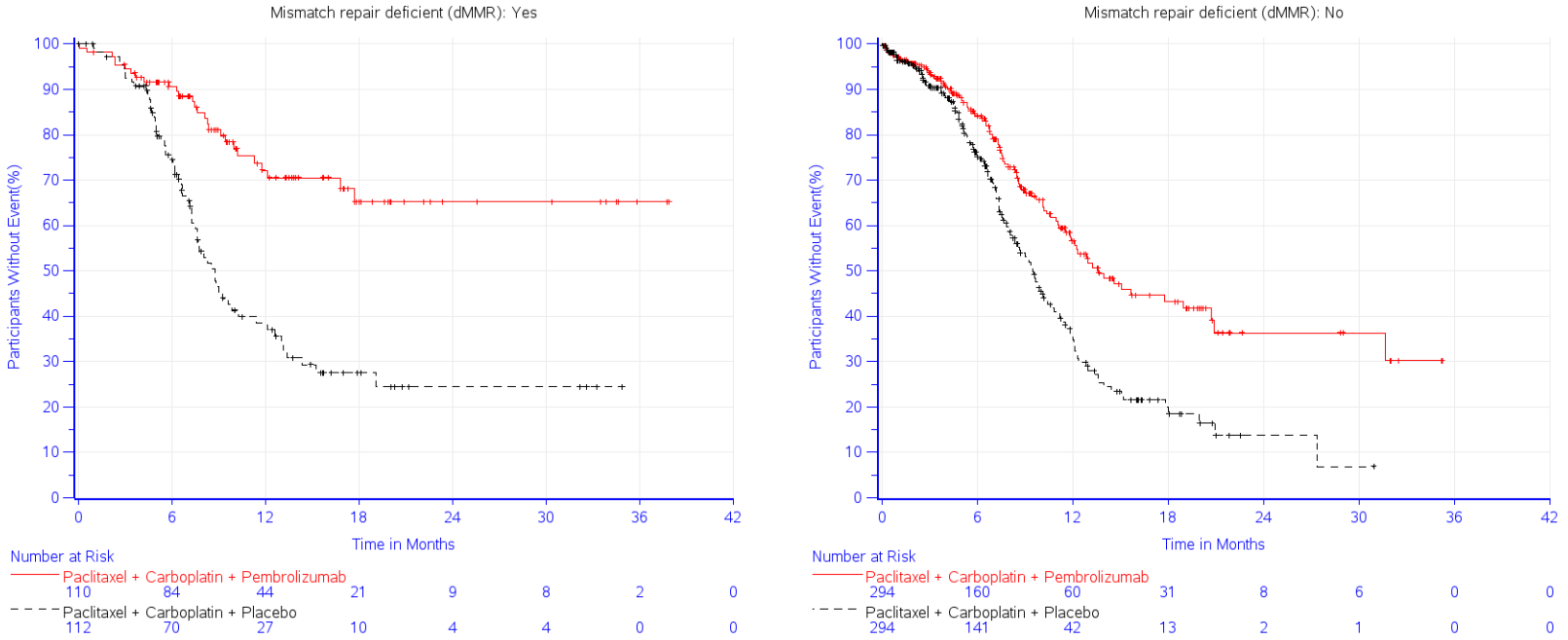
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival (INV Primary Censoring Rule)

Figure 4.2-40
Kaplan-Meier Curves of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Prior radiation therapy
(Intention-to-Treat Population)



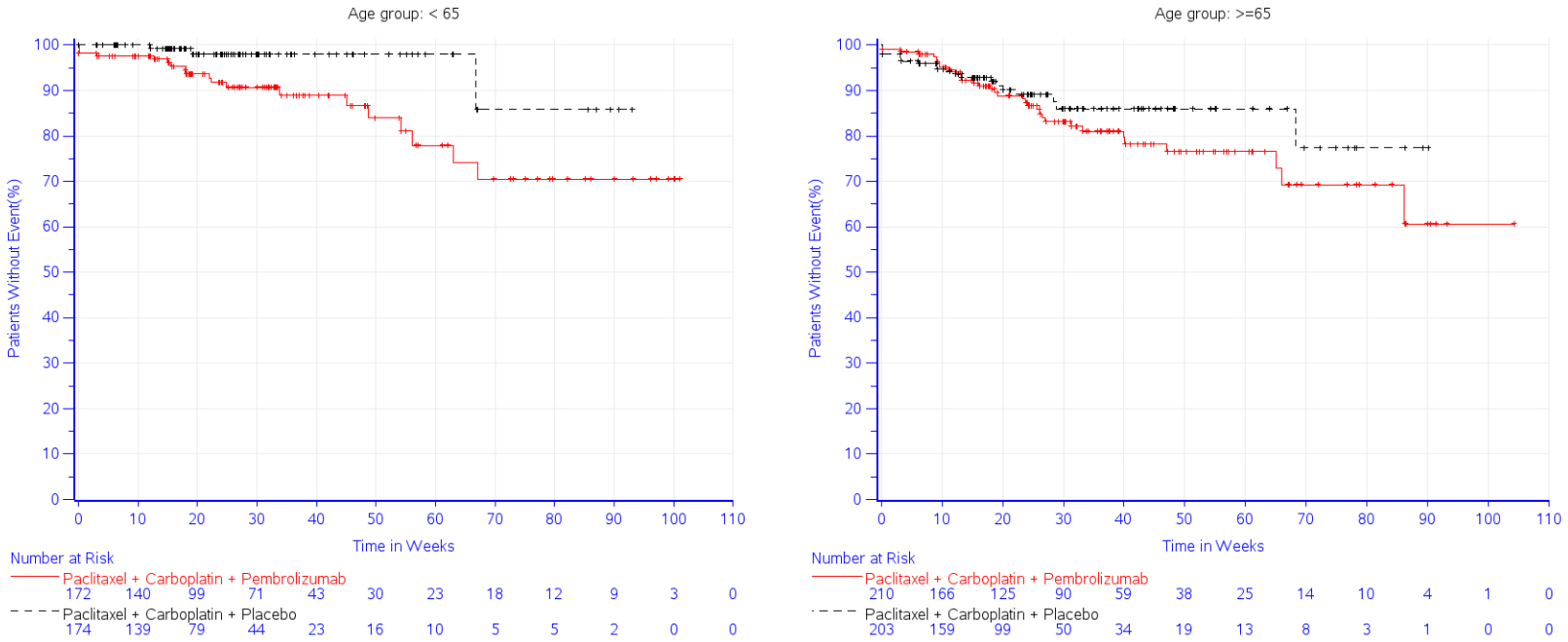
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Progression-Free Survival (INV Primary Censoring Rule)

Figure 4.2-41
Kaplan-Meier Curves of Time to Subsequent Therapy or Death
by Subgroups With P-Value for Interaction test < 0.05
in All-comers Participants
Mismatch repair deficient (dMMR)
(Intention-to-Treat Population)



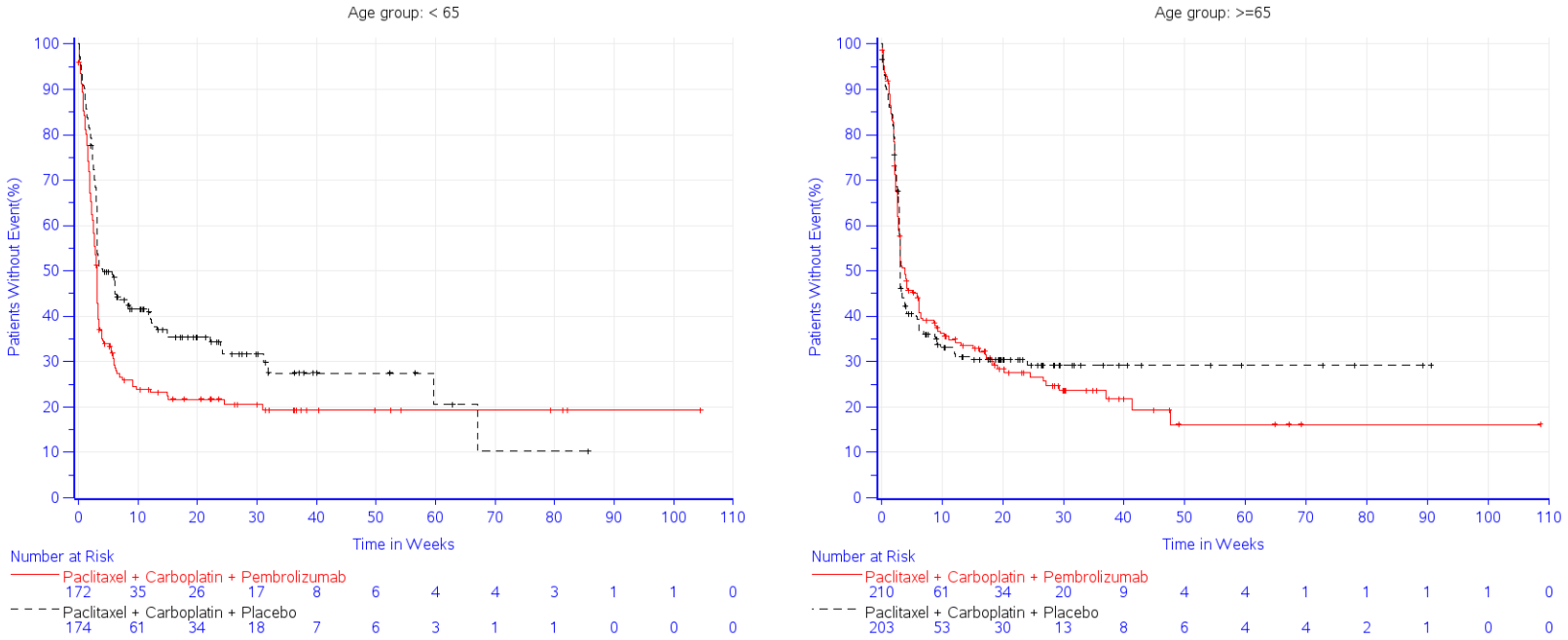
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Time to Subsequent Therapy or Death

Figure 4.6-42
Analysis of Time to Treatment Discontinuation Due to Adverse Events/Side Effects/Complications by Subgroup with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
Age group
in All-comers Participants
(All-Participants-as-Treated Population)



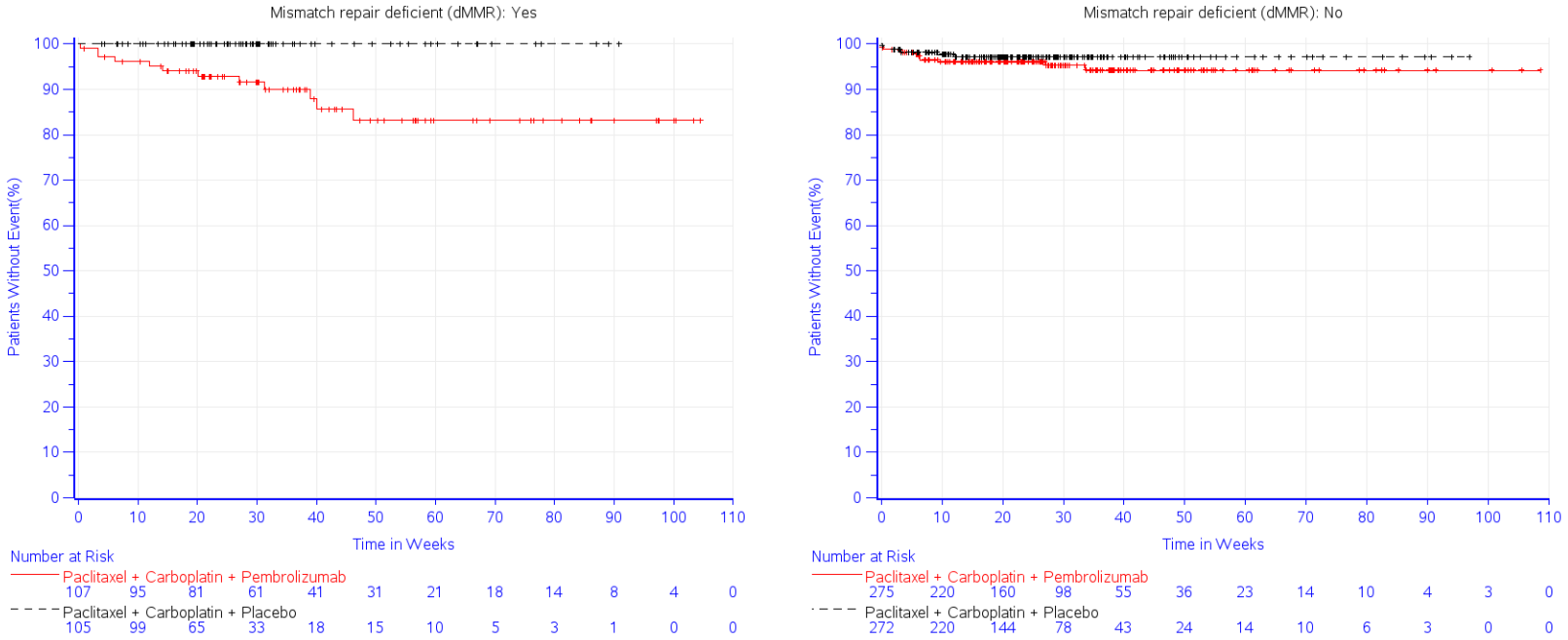
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Treatment Discontinuation Due to Adverse Events/Side Effects/Complications

Figure 4.7-43
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Skin and subcutaneous tissue disorders
Age group
in All-comers Participants
(All-Participants-as-Treated Population)



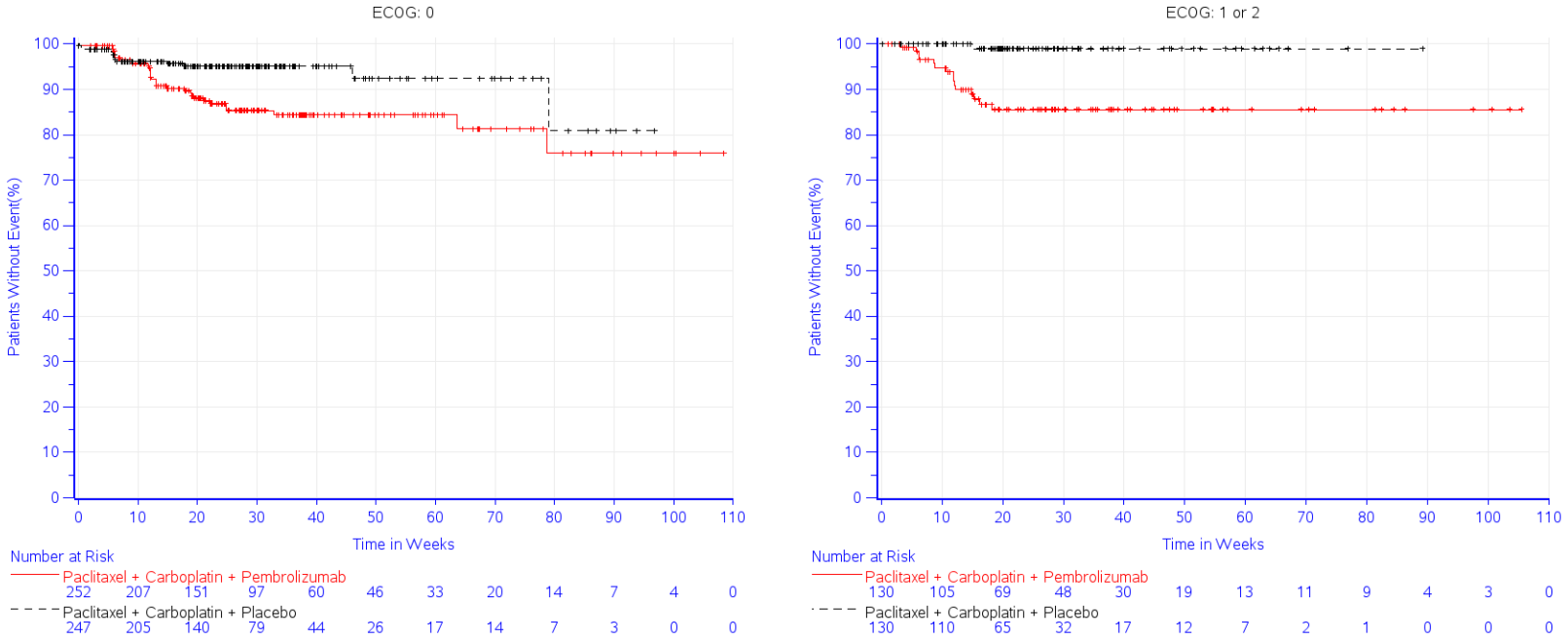
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - System Organ Class: Skin and subcutaneous tissue disorders

Figure 4.7-44
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Dry mouth
Mismatch repair deficient (dMMR)
in All-comers Participants
(All-Participants-as-Treated Population)



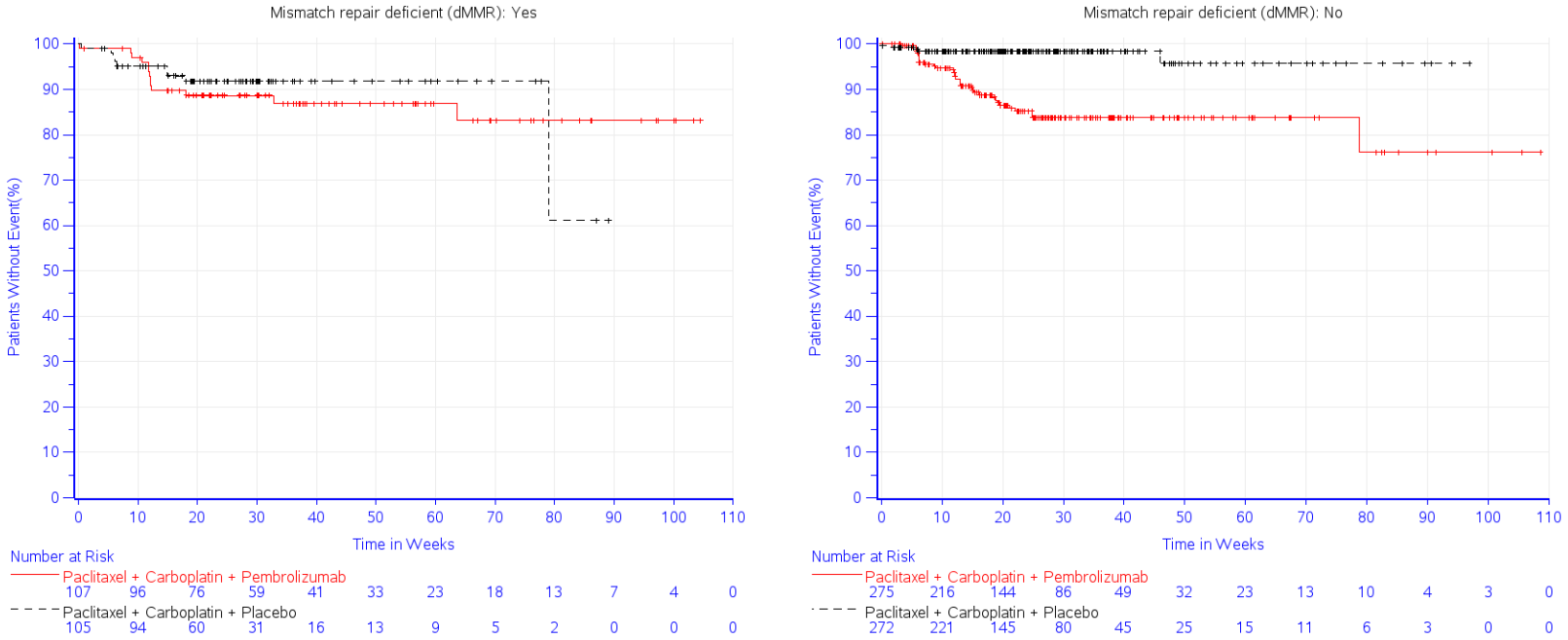
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Dry mouth

Figure 4.7-45
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Hypothyroidism
ECOG
in All-comers Participants
(All-Participants-as-Treated Population)



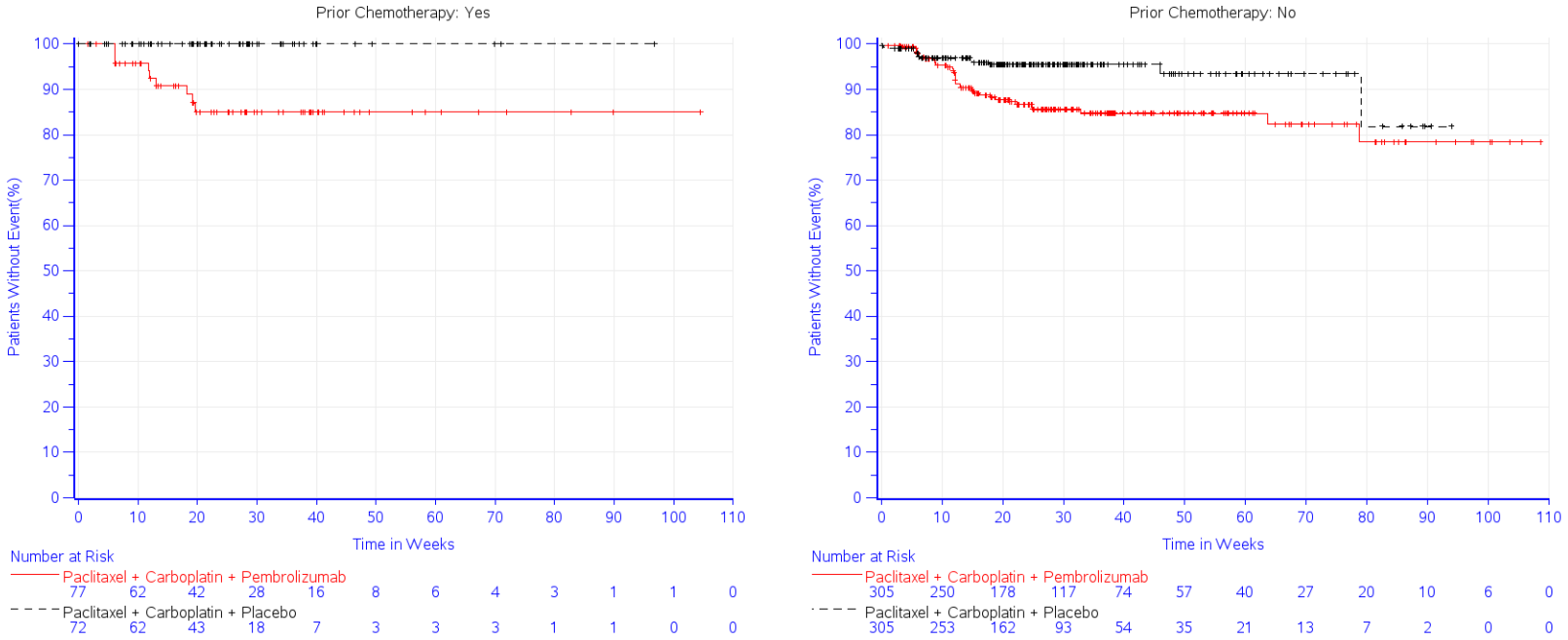
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hypothyroidism

Figure 4.7-46
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Hypothyroidism
Mismatch repair deficient (dMMR)
in All-comers Participants
(All-Participants-as-Treated Population)



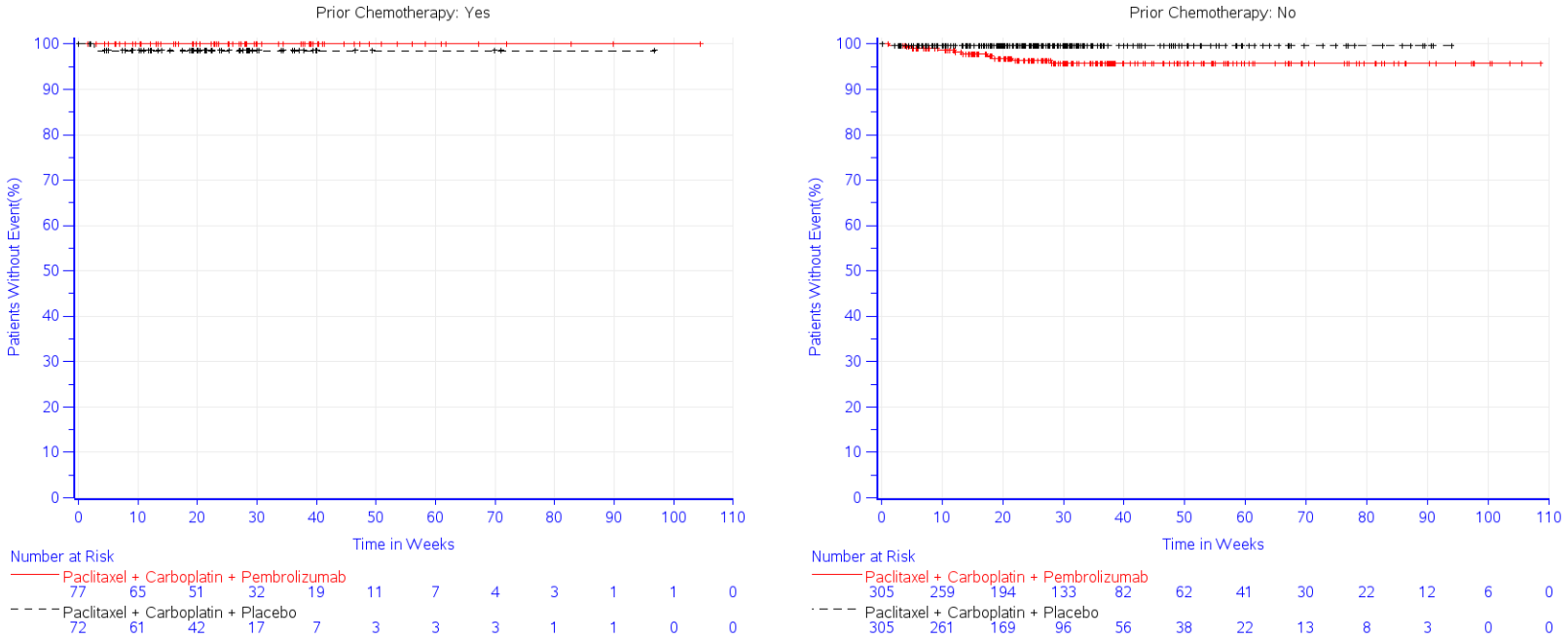
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hypothyroidism

Figure 4.7-47
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Hypothyroidism
Prior Chemotherapy
in All-comers Participants
(All-Participants-as-Treated Population)



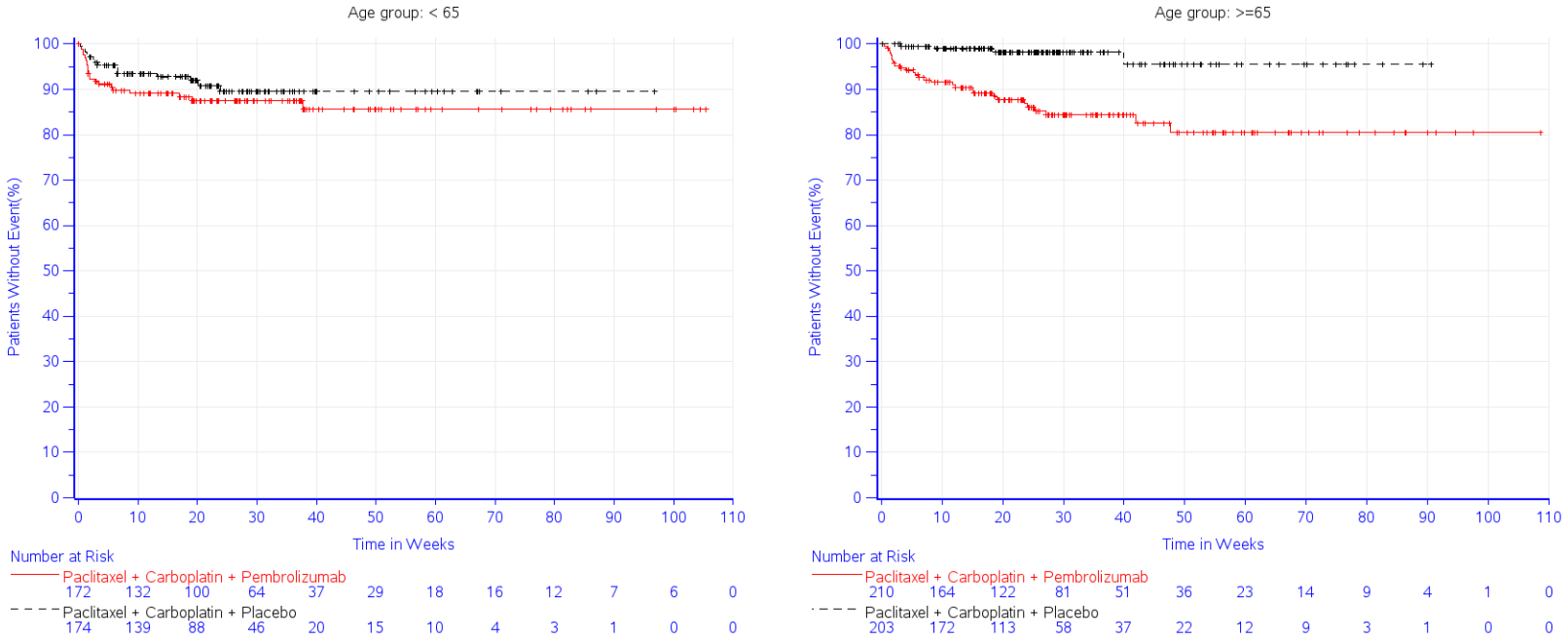
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Hypothyroidism

Figure 4.7-48
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Palpitations
Prior Chemotherapy
in All-comers Participants
(All-Participants-as-Treated Population)



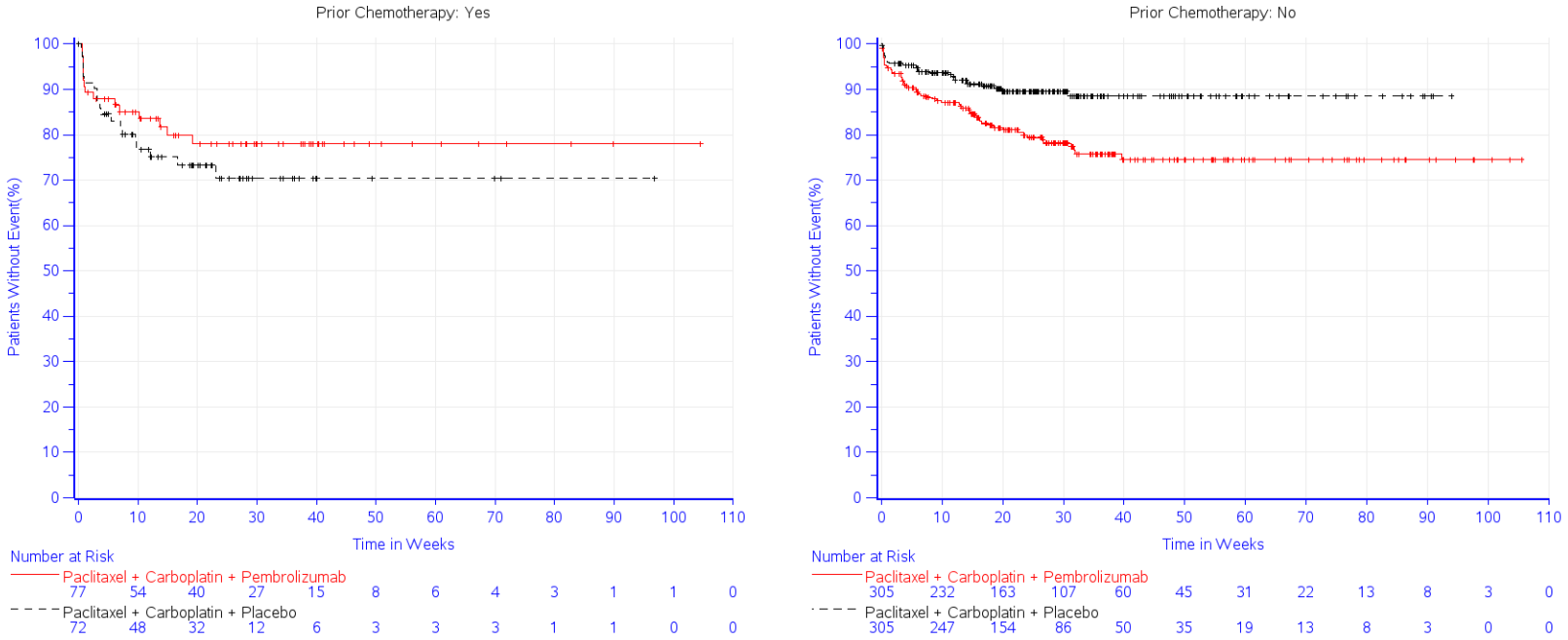
Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Palpitations

Figure 4.7-49
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Rash maculo-papular
Age group
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Rash maculo-papular

Figure 4.7-50
Analysis of Time to Adverse Event by Subgroup
with p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for System Organ Class/Preferred Term: Vomiting
Prior Chemotherapy
in All-comers Participants
(All-Participants-as-Treated Population)



Study: KEYNOTE-868 (Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants)
Adverse Event - Preferred Term: Vomiting

Table 4.1-30
Analyses of Overall Survival
for Subgroups With P-Value for Interaction test ≥ 0.05 or not Calculated
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**	**p-Value for Interaction Test[f]**
Age group									
< 65	182	19 (10.4)	Not reached [-; -]	187	26 (13.9)	Not reached [27.4; -]	0.68 [0.38; 1.23]	0.202	0.697
≥65	222	36 (16.2)	27.0 [20.9; -]	219	45 (20.5)	21.8 [19.5; -]	0.74 [0.48; 1.15]	0.180	
ECOG									
0	262	27 (10.3)	Not reached [-; -]	264	32 (12.1)	Not reached [27.4; -]	0.76 [0.46; 1.27]	0.301	0.698
1 or 2	142	28 (19.7)	27.0 [21.1; -]	142	39 (27.5)	19.1 [15.3; 29.3]	0.67 [0.41; 1.09]	0.103	
Region									
WHO Stratum A	400	55 (13.8)	n.c.	402	71 (17.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	4	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	110	10 (9.1)	Not reached [-; -]	112	17 (15.2)	Not reached [-; -]	0.55 [0.25; 1.19]	0.129	0.296
No	294	45 (15.3)	28.0 [21.4; -]	294	54 (18.4)	27.4 [19.5; -]	0.79 [0.53; 1.17]	0.233	
Age group									
< 65	182	19 (10.4)	Not reached [-; -]	187	26 (13.9)	Not reached [27.4; -]	0.68 [0.38; 1.23]	0.202	0.829
≥65 to <75	162	25 (15.4)	28.0 [20.9; -]	164	31 (18.9)	29.3 [17.8; -]	0.71 [0.42; 1.20]	0.198	
≥75	60	11 (18.3)	21.1 [16.8; -]	55	14 (25.5)	21.8 [19.5; -]	0.91 [0.41; 2.04]	0.815	
Race									
White	303	42 (13.9)	Not reached [-; -]	297	47 (15.8)	Not reached [21.8; -]	0.83 [0.55; 1.26]	0.392	0.384
All Others	80	12 (15.0)	27.0 [21.4; -]	85	17 (20.0)	19.1 [17.2; -]	0.55 [0.26; 1.16]	0.115	

Analyses of Overall Survival for Subgroups With P-Value for Interaction test ≥ 0.05 or not Calculated in All-comers Participants (Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**	**p-Value for Interaction Test[f]**
Histology									
Endometrioid	246	26 (10.6)	Not reached [-; -]	239	40 (16.7)	Not reached [21.3; -]	0.58 [0.35; 0.95]	0.030	0.141
Other	158	29 (18.4)	21.4 [19.8; -]	166	30 (18.1)	29.3 [19.5; -]	0.94 [0.56; 1.57]	0.808	
Measurable disease at baseline									
Yes	315	44 (14.0)	Not reached [28.0; -]	330	66 (20.0)	27.4 [19.8; -]	0.63 [0.43; 0.92]	0.018	0.051
No	89	11 (12.4)	Not reached [19.8; -]	76	5 (6.6)	Not reached [-; -]	1.88 [0.65; 5.40]	0.244	
Status of Disease									
Primary	164	21 (12.8)	Not reached [27.0; -]	173	35 (20.2)	32.2 [19.1; -]	0.54 [0.31; 0.93]	0.025	0.206
Recurrent/Persistent	240	34 (14.2)	Not reached [24.8; -]	233	36 (15.5)	Not reached [27.4; -]	0.87 [0.55; 1.40]	0.575	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

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

d: Based on unstratified Cox regression model with treatment as a covariate for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model with treatment as a covariate stratified by prior chemotherapy. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

f: Based on unstratified Cox regression model with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) for all subgroups with the exception of mismatch repair deficient (dMMR) which utilized the Cox regression model stratified by prior chemotherapy with treatment, subgroup as covariates and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CI: confidence interval; dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.2-31
Analysis of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule)
for Subgroups With P-Value for Interaction test ≥ 0.05 or not Calculated
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Progression-Free Survival (INV Primary Censoring Rule)	**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]**
Age group									
< 65	182	53 (29.1)	Not reached [12.0; -]	187	92 (49.2)	8.4 [6.7; 10.9]	0.45 [0.32; 0.64]	< 0.001	0.488
≥65	222	71 (32.0)	15.1 [12.1; -]	219	106 (48.4)	8.7 [8.3; 11.2]	0.51 [0.38; 0.69]	< 0.001	
ECOG									
0	262	78 (29.8)	19.8 [13.6; -]	264	125 (47.3)	8.7 [8.3; 11.3]	0.47 [0.35; 0.62]	< 0.001	0.643
1 or 2	142	46 (32.4)	13.1 [10.6; -]	142	73 (51.4)	8.3 [6.5; 10.9]	0.52 [0.36; 0.76]	< 0.001	
Region									
WHO Stratum A	400	122 (30.5)	n.c.	402	198 (49.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	4	0 (0.0)	n.c.	n.c.	n.c.	
Age group									
< 65	182	53 (29.1)	Not reached [12.0; -]	187	92 (49.2)	8.4 [6.7; 10.9]	0.45 [0.32; 0.64]	< 0.001	0.626
≥65 to <75	162	53 (32.7)	15.1 [11.5; -]	164	75 (45.7)	8.7 [8.0; 11.3]	0.54 [0.38; 0.77]	< 0.001	
≥75	60	18 (30.0)	13.1 [10.7; -]	55	31 (56.4)	8.7 [6.3; 11.3]	0.43 [0.24; 0.78]	0.005	
Race									
White	303	94 (31.0)	19.5 [13.4; -]	297	146 (49.2)	8.7 [8.3; 11.0]	0.50 [0.39; 0.65]	< 0.001	0.264
All Others	80	21 (26.3)	Not reached [11.1; -]	85	39 (45.9)	8.3 [6.5; 11.5]	0.38 [0.22; 0.65]	< 0.001	
Histology									
Endometrioid	246	70 (28.5)	30.7 [13.5; -]	239	114 (47.7)	8.7 [8.0; 11.3]	0.44 [0.33; 0.60]	< 0.001	0.298
Other	158	54 (34.2)	13.1 [8.6; -]	166	83 (50.0)	8.5 [6.6; 10.9]	0.56 [0.40; 0.80]	0.001	

Analysis of Progression-Free Survival Based on Investigator Assessment per RECIST 1.1 (Protocol Censoring Rule) for Subgroups With P-Value for Interaction test ≥ 0.05 or not Calculated in All-comers Participants (Intention-to-Treat Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
Progression-Free Survival (INV Primary Censoring Rule)	**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]**
Measurable disease at baseline									
Yes	315	101 (32.1)	15.6 [12.1; -]	330	173 (52.4)	8.3 [6.6; 8.7]	0.44 [0.34; 0.56]	< 0.001	0.063
No	89	23 (25.8)	19.8 [15.1; -]	76	25 (32.9)	14.3 [10.6; -]	0.80 [0.45; 1.41]	0.441	
Status of Disease									
Primary	164	43 (26.2)	Not reached [15.6; -]	173	87 (50.3)	8.5 [6.5; 11.3]	0.39 [0.27; 0.56]	< 0.001	0.098
Recurrent/Persistent	240	81 (33.8)	13.5 [11.1; -]	233	111 (47.6)	8.7 [8.3; 11.1]	0.56 [0.42; 0.75]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: confidence interval; dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; INV: Investigator; 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); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.2-32
Analysis of Time to Subsequent Therapy or Death
for Subgroups With P-Value for Interaction test ≥ 0.05 or not Calculated
in All-comers Participants
(Intention-to-Treat Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
Time to Subsequent Therapy or Death	N[b]	Participants with Event n (%)	Median Time[c] in Months [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Months [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	p-Value for Interaction Test[f]
Age group									
< 65	182	52 (28.6)	Not reached [13.2; -]	187	91 (48.7)	9.4 [7.6; 10.6]	0.46 [0.33; 0.65]	< 0.001	0.721
≥65	222	69 (31.1)	16.8 [12.3; -]	219	109 (49.8)	9.0 [8.0; 10.3]	0.49 [0.36; 0.66]	< 0.001	
ECOG									
0	262	75 (28.6)	20.9 [14.6; -]	264	121 (45.8)	9.8 [8.3; 11.2]	0.47 [0.35; 0.63]	< 0.001	0.953
1 or 2	142	46 (32.4)	13.6 [11.7; -]	142	79 (55.6)	8.5 [7.0; 9.6]	0.49 [0.34; 0.71]	< 0.001	
Region									
WHO Stratum A	400	119 (29.8)	n.c.	402	200 (49.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	2 (50.0)	n.c.	4	0 (0.0)	n.c.	n.c.	n.c.	
Prior Chemotherapy									
Yes	80	36 (45.0)	10.9 [9.1; 15.7]	81	38 (46.9)	9.4 [6.9; 11.2]	0.68 [0.43; 1.09]	0.107	0.051
No	324	85 (26.2)	31.6 [17.7; -]	325	162 (49.8)	9.1 [8.0; 10.3]	0.42 [0.32; 0.54]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: intention-to-treat population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: confidence interval; dMMR: deficient mismatch repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: proficient mismatch repair; WHO: World Health Organization

Table 4.6-33
Analyses of Time to Adverse Events for Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
Age group									
< 65	172	169 (98.3)	0.3 [-; -]	174	173 (99.4)	0.3 [0.3; 0.4]	1.11 [0.90; 1.37]	0.342	0.346
≥65	210	207 (98.6)	0.3 [0.3; 0.4]	203	202 (99.5)	0.3 [-; -]	0.97 [0.80; 1.18]	0.759	
ECOG									
0	252	248 (98.4)	0.3 [0.3; 0.4]	247	246 (99.6)	0.3 [0.3; 0.4]	1.01 [0.84; 1.20]	0.950	0.581
1 or 2	130	128 (98.5)	0.3 [0.1; 0.3]	130	129 (99.2)	0.3 [0.1; 0.3]	1.09 [0.85; 1.40]	0.483	
Region									
WHO Stratum A	378	372 (98.4)	n.c.	374	372 (99.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	4 (100.0)	n.c.	3	3 (100.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	106 (99.1)	0.3 [0.1; 0.3]	105	105 (100.0)	0.3 [0.3; 0.4]	1.16 [0.89; 1.53]	0.273	0.352
No	275	270 (98.2)	0.3 [0.3; 0.4]	272	270 (99.3)	0.3 [-; -]	0.99 [0.84; 1.17]	0.921	
Prior Chemotherapy									
Yes	77	73 (94.8)	0.4 [0.3; 0.4]	72	72 (100.0)	0.3 [0.1; 0.4]	0.78 [0.56; 1.08]	0.140	0.054
No	305	303 (99.3)	0.3 [-; -]	305	303 (99.3)	0.3 [0.3; 0.4]	1.11 [0.95; 1.30]	0.193	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants
b: Number of participants: all-participants-as-treated population
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
e: Two-sided p-value using Wald test
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CI: Confidence Interval; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; WHO: World Health Organization

Table 4.6-34
Analyses of Time to Serious Adverse Events for Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		p-Value for Interaction Test[f]
Serious Adverse Events	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	N[b]	Participants with Event n (%)	Median Time[c] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][d]	p-Value[d,e]	
Age group									
< 65	172	54 (31.4)	80.9 [63.0; -]	174	33 (19.0)	Not reached [-; -]	1.68 [1.09; 2.59]	0.019	0.571
≥65	210	78 (37.1)	Not reached [47.9; -]	203	40 (19.7)	Not reached [74.0; -]	1.96 [1.34; 2.88]	< 0.001	
ECOG									
0	252	77 (30.6)	Not reached [63.0; -]	247	39 (15.8)	Not reached [-; -]	1.93 [1.32; 2.85]	< 0.001	0.746
1 or 2	130	55 (42.3)	80.9 [21.1; -]	130	34 (26.2)	Not reached [-; -]	1.74 [1.13; 2.67]	0.011	
Region									
WHO Stratum A	378	132 (34.9)	n.c.	374	72 (19.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	1 (33.3)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	39 (36.4)	Not reached [47.9; -]	105	22 (21.0)	Not reached [-; -]	1.77 [1.05; 2.98]	0.033	0.770
No	275	93 (33.8)	80.9 [57.9; -]	272	51 (18.8)	Not reached [74.0; -]	1.88 [1.34; 2.65]	< 0.001	
Prior Chemotherapy									
Yes	77	30 (39.0)	60.6 [29.7; -]	72	15 (20.8)	Not reached [-; -]	1.95 [1.05; 3.63]	0.036	0.794
No	305	102 (33.4)	Not reached [80.9; -]	305	58 (19.0)	Not reached [-; -]	1.80 [1.30; 2.49]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; WHO: World Health Organization

Table 4.6-35
Analyses of Time to Severe Adverse Events (CTCAE-Grade 3-5) for Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
Age group									
< 65	172	97 (56.4)	19.9 [15.1; 31.6]	174	82 (47.1)	23.0 [15.0; -]	1.17 [0.87; 1.57]	0.297	0.291
≥65	210	128 (61.0)	15.1 [11.0; 19.0]	203	92 (45.3)	50.6 [17.7; -]	1.46 [1.11; 1.90]	0.006	
ECOG									
0	252	142 (56.3)	19.9 [15.1; 28.7]	247	100 (40.5)	74.0 [23.7; -]	1.45 [1.13; 1.88]	0.004	0.241
1 or 2	130	83 (63.8)	12.6 [9.0; 18.0]	130	74 (56.9)	15.0 [9.3; 20.9]	1.13 [0.82; 1.55]	0.453	
Region									
WHO Stratum A	378	224 (59.3)	n.c.	374	171 (45.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	3	3 (100.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	66 (61.7)	18.6 [15.4; 35.3]	105	50 (47.6)	28.1 [17.1; -]	1.22 [0.84; 1.77]	0.287	0.607
No	275	159 (57.8)	15.1 [12.0; 19.9]	272	124 (45.6)	23.0 [15.6; -]	1.37 [1.08; 1.73]	0.009	
Prior Chemotherapy									
Yes	77	51 (66.2)	10.6 [6.7; 18.0]	72	31 (43.1)	Not reached [10.7; -]	1.84 [1.18; 2.89]	0.008	0.113
No	305	174 (57.0)	18.6 [15.1; 24.1]	305	143 (46.9)	23.7 [17.7; -]	1.22 [0.97; 1.52]	0.083	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; WHO: World Health Organization

Table 4.7-36
Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]: Cardiac disorders									
Age group									
< 65	172	22 (12.8)	Not reached [-; -]	174	8 (4.6)	Not reached [-; -]	2.74 [1.21; 6.16]	0.015	0.139
≥65	210	28 (13.3)	Not reached [-; -]	203	20 (9.9)	Not reached [-; -]	1.31 [0.74; 2.33]	0.353	
ECOG									
0	252	34 (13.5)	Not reached [-; -]	247	16 (6.5)	Not reached [-; -]	2.02 [1.11; 3.66]	0.021	0.357
1 or 2	130	16 (12.3)	Not reached [-; -]	130	12 (9.2)	Not reached [-; -]	1.34 [0.63; 2.84]	0.442	
Region									
WHO Stratum A	378	50 (13.2)	n.c.	374	28 (7.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	20 (18.7)	Not reached [-; -]	105	6 (5.7)	Not reached [-; -]	3.26 [1.31; 8.14]	0.011	0.089
No	275	30 (10.9)	Not reached [-; -]	272	22 (8.1)	Not reached [-; -]	1.32 [0.76; 2.28]	0.329	
Prior Chemotherapy									
Yes	77	7 (9.1)	Not reached [-; -]	72	8 (11.1)	Not reached [-; -]	0.79 [0.29; 2.20]	0.656	0.093
No	305	43 (14.1)	Not reached [-; -]	305	20 (6.6)	Not reached [-; -]	2.11 [1.24; 3.59]	0.006	
SOC[g]: Endocrine disorders									

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	172	32 (18.6)	Not reached [-; -]	174	10 (5.7)	Not reached [79.0; -]	3.31 [1.62; 6.75]	< 0.001	0.279
≥65	210	32 (15.2)	Not reached [-; -]	203	15 (7.4)	Not reached [-; -]	1.98 [1.07; 3.66]	0.029	
ECOG									
0	252	47 (18.7)	Not reached [-; -]	247	20 (8.1)	Not reached [79.0; -]	2.30 [1.36; 3.89]	0.002	0.519
1 or 2	130	17 (13.1)	Not reached [-; -]	130	5 (3.8)	Not reached [-; -]	3.34 [1.23; 9.09]	0.018	
Region									
WHO Stratum A	378	64 (16.9)	n.c.	374	25 (6.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	17 (15.9)	Not reached [-; -]	105	11 (10.5)	Not reached [79.0; -]	1.40 [0.65; 3.02]	0.392	0.069
No	275	47 (17.1)	Not reached [78.7; -]	272	14 (5.1)	Not reached [-; -]	3.39 [1.87; 6.16]	< 0.001	
Prior Chemotherapy									
Yes	77	15 (19.5)	Not reached [-; -]	72	3 (4.2)	Not reached [-; -]	4.89 [1.41; 16.92]	0.012	0.213
No	305	49 (16.1)	Not reached [-; -]	305	22 (7.2)	Not reached [79.0; -]	2.17 [1.31; 3.59]	0.003	
SOC[g]: General disorders and administration site conditions									
Age group									
< 65	172	132 (76.7)	4.1 [3.1; 6.1]	174	124 (71.3)	6.1 [3.1; 9.1]	1.15 [0.90; 1.46]	0.276	0.477
≥65	210	169 (80.5)	3.7 [3.1; 5.7]	203	141 (69.5)	5.9 [3.3; 8.9]	1.28 [1.03; 1.61]	0.029	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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									
0	252	200 (79.4)	3.4 [3.1; 5.1]	247	168 (68.0)	4.4 [3.1; 9.1]	1.24 [1.01; 1.52]	0.040	0.797
1 or 2	130	101 (77.7)	5.0 [3.1; 6.3]	130	97 (74.6)	6.1 [3.4; 9.0]	1.21 [0.91; 1.60]	0.182	
Region									
WHO Stratum A	378	300 (79.4)	n.c.	374	263 (70.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	3	2 (66.7)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	88 (82.2)	3.9 [3.0; 6.1]	105	72 (68.6)	9.1 [4.3; 12.7]	1.47 [1.08; 2.01]	0.015	0.193
No	275	213 (77.5)	4.0 [3.3; 5.7]	272	193 (71.0)	4.3 [3.1; 6.1]	1.14 [0.94; 1.38]	0.196	
Prior Chemotherapy									
Yes	77	66 (85.7)	3.4 [3.0; 7.1]	72	48 (66.7)	6.1 [2.0; 9.6]	1.34 [0.93; 1.95]	0.121	0.578
No	305	235 (77.0)	4.1 [3.3; 5.9]	305	217 (71.1)	6.1 [3.4; 8.4]	1.20 [0.99; 1.44]	0.057	
SOC[g]: Skin and subcutaneous tissue disorders									
ECOG									
0	252	192 (76.2)	3.1 [2.9; 3.4]	247	164 (66.4)	3.1 [3.1; 5.7]	1.24 [1.00; 1.52]	0.046	0.575
1 or 2	130	88 (67.7)	3.1 [2.9; 6.1]	130	87 (66.9)	3.3 [3.1; 6.1]	1.12 [0.83; 1.50]	0.464	
Region									
WHO Stratum A	378	277 (73.3)	n.c.	374	249 (66.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	3 (75.0)	n.c.	3	2 (66.7)	n.c.	n.c.	n.c.	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Mismatch repair deficient (dMMR)									
Yes	107	88 (82.2)	3.1 [2.7; 5.4]	105	72 (68.6)	3.1 [3.0; 6.1]	1.34 [0.98; 1.82]	0.068	0.443
No	275	192 (69.8)	3.1 [3.0; 3.6]	272	179 (65.8)	3.3 [3.1; 5.9]	1.15 [0.93; 1.40]	0.192	
Prior Chemotherapy									
Yes	77	54 (70.1)	3.9 [3.1; 6.1]	72	48 (66.7)	3.9 [3.0; 12.1]	1.06 [0.72; 1.56]	0.781	0.480
No	305	226 (74.1)	3.1 [2.9; 3.3]	305	203 (66.6)	3.1 [3.1; 4.3]	1.24 [1.02; 1.49]	0.028	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

CI: Confidence Interval; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-37
Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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: Cardiac disorders - PT[g]: Palpitations									
Age group									
< 65	172	4 (2.3)	n.c.	174	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥65	210	6 (2.9)	n.c.	203	2 (1.0)	n.c.	n.c.	n.c.	
ECOG									
0	252	10 (4.0)	Not reached [-; -]	247	2 (0.8)	Not reached [-; -]	4.79 [1.05; 21.86]	0.043	0.997
1 or 2	130	0 (0.0)	Not reached [-; -]	130	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
Region									
WHO Stratum A	378	10 (2.6)	n.c.	374	2 (0.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	n.c.	105	0 (0.0)	n.c.	n.c.	n.c.	n.c.
No	275	6 (2.2)	n.c.	272	2 (0.7)	n.c.	n.c.	n.c.	
SOC: Endocrine disorders - PT[g]: Hyperthyroidism									
Age group									
< 65	172	14 (8.1)	Not reached [-; -]	174	3 (1.7)	Not reached [-; -]	4.74 [1.36; 16.53]	0.015	0.120
≥65	210	11 (5.2)	Not reached [-; -]	203	7 (3.4)	Not reached [-; -]	1.43 [0.55; 3.69]	0.465	
ECOG									
0	252	20 (7.9)	Not reached [-; -]	247	7 (2.8)	Not reached [-; -]	2.78 [1.17; 6.57]	0.020	0.539
1 or 2	130	5 (3.8)	Not reached [-; -]	130	3 (2.3)	Not reached [57.1; -]	1.52 [0.36; 6.39]	0.571	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Region									
WHO Stratum A	378	25 (6.6)	n.c.	374	10 (2.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	9 (8.4)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	4.15 [0.89; 19.38]	0.070	0.363
No	275	16 (5.8)	Not reached [-; -]	272	8 (2.9)	Not reached [-; -]	1.91 [0.82; 4.48]	0.134	
Prior Chemotherapy									
Yes	77	4 (5.2)	Not reached [-; -]	72	2 (2.8)	Not reached [-; -]	1.85 [0.34; 10.10]	0.478	0.704
No	305	21 (6.9)	Not reached [-; -]	305	8 (2.6)	Not reached [-; -]	2.53 [1.12; 5.72]	0.026	
SOC: Endocrine disorders - PT[g]: Hypothyroidism									
Age group									
< 65	172	22 (12.8)	Not reached [-; -]	174	7 (4.0)	Not reached [79.0; -]	3.11 [1.32; 7.29]	0.009	0.899
≥65	210	25 (11.9)	Not reached [-; -]	203	7 (3.4)	Not reached [-; -]	3.38 [1.46; 7.83]	0.004	
Region									
WHO Stratum A	378	47 (12.4)	n.c.	374	14 (3.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Gastrointestinal disorders - PT[g]: Dry mouth									
Age group									
< 65	172	12 (7.0)	Not reached [-; -]	174	1 (0.6)	Not reached [-; -]	11.28 [1.46; 86.99]	0.020	0.064
≥65	210	12 (5.7)	Not reached [-; -]	203	6 (3.0)	Not reached [-; -]	1.81 [0.68; 4.84]	0.235	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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									
0	252	19 (7.5)	Not reached [-; -]	247	5 (2.0)	Not reached [-; -]	3.53 [1.32; 9.48]	0.012	0.672
1 or 2	130	5 (3.8)	Not reached [-; -]	130	2 (1.5)	Not reached [-; -]	2.21 [0.43; 11.50]	0.344	
Region									
WHO Stratum A	378	24 (6.3)	n.c.	374	7 (1.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Prior Chemotherapy									
Yes	77	4 (5.2)	Not reached [-; -]	72	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.064	0.149
No	305	20 (6.6)	Not reached [-; -]	305	7 (2.3)	Not reached [-; -]	2.67 [1.13; 6.32]	0.026	
SOC: Gastrointestinal disorders - PT[g]: Vomiting									
Age group									
< 65	172	39 (22.7)	Not reached [-; -]	174	24 (13.8)	Not reached [-; -]	1.66 [1.00; 2.76]	0.052	0.791
≥65	210	37 (17.6)	Not reached [-; -]	203	24 (11.8)	Not reached [-; -]	1.50 [0.90; 2.50]	0.124	
ECOG									
0	252	54 (21.4)	Not reached [-; -]	247	32 (13.0)	Not reached [-; -]	1.67 [1.08; 2.58]	0.022	0.642
1 or 2	130	22 (16.9)	Not reached [-; -]	130	16 (12.3)	Not reached [-; -]	1.38 [0.72; 2.63]	0.327	
Region									
WHO Stratum A	378	75 (19.8)	n.c.	374	46 (12.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	3	2 (66.7)	n.c.	n.c.	n.c.	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Mismatch repair deficient (dMMR)									
Yes	107	22 (20.6)	Not reached [-; -]	105	9 (8.6)	Not reached [-; -]	2.51 [1.16; 5.47]	0.020	0.166
No	275	54 (19.6)	Not reached [-; -]	272	39 (14.3)	Not reached [-; -]	1.36 [0.90; 2.05]	0.143	
SOC: General disorders and administration site conditions - PT[g]: Chills									
Age group									
< 65	172	6 (3.5)	Not reached [-; -]	174	4 (2.3)	Not reached [-; -]	1.48 [0.42; 5.27]	0.541	0.112
≥65	210	14 (6.7)	Not reached [-; -]	203	2 (1.0)	Not reached [-; -]	6.51 [1.48; 28.66]	0.013	
ECOG									
0	252	10 (4.0)	Not reached [-; -]	247	3 (1.2)	Not reached [-; -]	3.16 [0.87; 11.48]	0.081	0.991
1 or 2	130	10 (7.7)	Not reached [-; -]	130	3 (2.3)	Not reached [-; -]	3.11 [0.85; 11.41]	0.088	
Region									
WHO Stratum A	378	20 (5.3)	n.c.	374	6 (1.6)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	6 (5.6)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	2.51 [0.50; 12.61]	0.265	0.803
No	275	14 (5.1)	Not reached [-; -]	272	4 (1.5)	Not reached [-; -]	3.42 [1.12; 10.38]	0.030	
Prior Chemotherapy									
Yes	77	4 (5.2)	Not reached [-; -]	72	2 (2.8)	Not reached [-; -]	1.94 [0.35; 10.57]	0.446	0.508
No	305	16 (5.2)	Not reached [-; -]	305	4 (1.3)	Not reached [-; -]	3.75 [1.25; 11.24]	0.018	
SOC: General disorders and administration site conditions - PT[g]: Pyrexia									

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	172	16 (9.3)	Not reached [-; -]	174	4 (2.3)	Not reached [-; -]	3.81 [1.27; 11.43]	0.017	0.402
≥65	210	14 (6.7)	Not reached [-; -]	203	6 (3.0)	Not reached [-; -]	2.11 [0.81; 5.50]	0.127	
ECOG									
0	252	20 (7.9)	Not reached [-; -]	247	5 (2.0)	Not reached [-; -]	3.64 [1.36; 9.72]	0.010	0.369
1 or 2	130	10 (7.7)	Not reached [-; -]	130	5 (3.8)	Not reached [-; -]	1.94 [0.66; 5.70]	0.226	
Region									
WHO Stratum A	378	30 (7.9)	n.c.	374	10 (2.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	12 (11.2)	Not reached [-; -]	105	3 (2.9)	Not reached [-; -]	3.59 [1.01; 12.79]	0.049	0.628
No	275	18 (6.5)	Not reached [-; -]	272	7 (2.6)	Not reached [-; -]	2.44 [1.02; 5.85]	0.046	
Prior Chemotherapy									
Yes	77	5 (6.5)	Not reached [-; -]	72	2 (2.8)	Not reached [-; -]	2.23 [0.43; 11.56]	0.340	0.741
No	305	25 (8.2)	Not reached [-; -]	305	8 (2.6)	Not reached [-; -]	2.94 [1.33; 6.54]	0.008	
SOC: Investigations - PT[g]: Aspartate aminotransferase increased									
Age group									
< 65	172	25 (14.5)	Not reached [-; -]	174	17 (9.8)	Not reached [-; -]	1.46 [0.79; 2.70]	0.233	0.260
≥65	210	24 (11.4)	92.0 [92.0; -]	203	9 (4.4)	Not reached [-; -]	2.48 [1.15; 5.35]	0.020	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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									
0	252	36 (14.3)	Not reached [92.0; -]	247	21 (8.5)	Not reached [-; -]	1.58 [0.92; 2.72]	0.095	0.433
1 or 2	130	13 (10.0)	Not reached [-; -]	130	5 (3.8)	Not reached [-; -]	2.64 [0.94; 7.40]	0.066	
Region									
WHO Stratum A	378	49 (13.0)	n.c.	374	26 (7.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	13 (12.1)	Not reached [-; -]	105	5 (4.8)	Not reached [-; -]	2.43 [0.86; 6.83]	0.093	0.574
No	275	36 (13.1)	Not reached [92.0; -]	272	21 (7.7)	Not reached [-; -]	1.66 [0.97; 2.84]	0.065	
Prior Chemotherapy									
Yes	77	5 (6.5)	Not reached [-; -]	72	6 (8.3)	Not reached [-; -]	0.74 [0.23; 2.42]	0.618	0.108
No	305	44 (14.4)	Not reached [92.0; -]	305	20 (6.6)	Not reached [-; -]	2.13 [1.25; 3.62]	0.005	
SOC: Investigations - PT[g]: Blood creatinine increased									
Age group									
< 65	172	29 (16.9)	Not reached [-; -]	174	12 (6.9)	Not reached [-; -]	2.33 [1.19; 4.58]	0.014	0.700
≥65	210	39 (18.6)	Not reached [-; -]	203	18 (8.9)	Not reached [-; -]	1.99 [1.14; 3.49]	0.016	
ECOG									
0	252	40 (15.9)	Not reached [-; -]	247	19 (7.7)	Not reached [-; -]	1.97 [1.14; 3.41]	0.015	0.582
1 or 2	130	28 (21.5)	Not reached [59.7; -]	130	11 (8.5)	Not reached [-; -]	2.40 [1.19; 4.84]	0.014	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Region									
WHO Stratum A	378	67 (17.7)	n.c.	374	30 (8.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	22 (20.6)	Not reached [72.9; -]	105	9 (8.6)	Not reached [-; -]	2.09 [0.96; 4.58]	0.064	0.991
No	275	46 (16.7)	Not reached [-; -]	272	21 (7.7)	Not reached [-; -]	2.14 [1.28; 3.58]	0.004	
Prior Chemotherapy									
Yes	77	18 (23.4)	Not reached [-; -]	72	6 (8.3)	Not reached [-; -]	3.01 [1.19; 7.60]	0.019	0.431
No	305	50 (16.4)	Not reached [-; -]	305	24 (7.9)	Not reached [-; -]	1.92 [1.18; 3.13]	0.009	
SOC: Metabolism and nutrition disorders - PT[g]: Hypokalaemia									
Age group									
< 65	172	18 (10.5)	Not reached [-; -]	174	31 (17.8)	Not reached [-; -]	0.55 [0.31; 0.99]	0.045	0.402
≥65	210	31 (14.8)	Not reached [-; -]	203	38 (18.7)	Not reached [-; -]	0.74 [0.46; 1.18]	0.207	
ECOG									
0	252	33 (13.1)	Not reached [-; -]	247	39 (15.8)	Not reached [-; -]	0.80 [0.50; 1.27]	0.339	0.183
1 or 2	130	16 (12.3)	Not reached [-; -]	130	30 (23.1)	Not reached [-; -]	0.48 [0.26; 0.87]	0.017	
Region									
WHO Stratum A	378	49 (13.0)	n.c.	374	69 (18.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	

Analyses of Time to Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Mismatch repair deficient (dMMR)									
Yes	107	16 (15.0)	Not reached [-; -]	105	20 (19.0)	Not reached [-; -]	0.71 [0.36; 1.37]	0.305	0.755
No	275	33 (12.0)	Not reached [-; -]	272	49 (18.0)	Not reached [-; -]	0.63 [0.40; 0.98]	0.039	
Prior Chemotherapy									
Yes	77	12 (15.6)	Not reached [-; -]	72	18 (25.0)	Not reached [-; -]	0.62 [0.30; 1.28]	0.193	0.767
No	305	37 (12.1)	Not reached [-; -]	305	51 (16.7)	Not reached [-; -]	0.67 [0.44; 1.03]	0.065	
SOC: Musculoskeletal and connective tissue disorders - PT[g]: Arthralgia									
Age group									
< 65	172	55 (32.0)	Not reached [81.0; -]	174	58 (33.3)	Not reached [45.4; -]	0.92 [0.63; 1.33]	0.649	0.193
≥65	210	59 (28.1)	Not reached [-; -]	203	75 (36.9)	Not reached [-; -]	0.65 [0.46; 0.92]	0.014	
ECOG									
0	252	79 (31.3)	Not reached [-; -]	247	88 (35.6)	Not reached [-; -]	0.83 [0.61; 1.12]	0.222	0.493
1 or 2	130	35 (26.9)	Not reached [55.0; -]	130	45 (34.6)	Not reached [23.0; -]	0.62 [0.40; 0.98]	0.039	
Region									
WHO Stratum A	378	113 (29.9)	n.c.	374	130 (34.8)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	1 (25.0)	n.c.	3	3 (100.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	36 (33.6)	Not reached [51.9; -]	105	39 (37.1)	Not reached [30.9; -]	0.79 [0.50; 1.24]	0.303	0.888
No	275	78 (28.4)	Not reached [81.0; -]	272	94 (34.6)	Not reached [45.4; -]	0.75 [0.56; 1.02]	0.063	

Analyses of Time to Adverse Event by Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated (Incidence ≥ 10 % or (Incidence ≥ 1 % and in at least 10 Participants) in One or More Treatment Groups) For Preferred Terms in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Prior Chemotherapy									
Yes	77	20 (26.0)	Not reached [41.7; -]	72	27 (37.5)	Not reached [18.0; -]	0.56 [0.31; 1.00]	0.050[h]	0.258
No	305	94 (30.8)	Not reached [81.0; -]	305	106 (34.8)	Not reached [-; -]	0.82 [0.62; 1.08]	0.164	
SOC: Skin and subcutaneous tissue disorders - PT[g]: Rash maculo-papular									
ECOG									
0	252	35 (13.9)	Not reached [-; -]	247	13 (5.3)	Not reached [-; -]	2.64 [1.39; 4.99]	0.003	0.898
1 or 2	130	15 (11.5)	Not reached [-; -]	130	6 (4.6)	Not reached [-; -]	2.52 [0.98; 6.49]	0.056	
Region									
WHO Stratum A	378	50 (13.2)	n.c.	374	19 (5.1)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	18 (16.8)	Not reached [-; -]	105	9 (8.6)	Not reached [-; -]	1.86 [0.83; 4.16]	0.130	0.302
No	275	32 (11.6)	Not reached [-; -]	272	10 (3.7)	Not reached [-; -]	3.24 [1.59; 6.60]	0.001	
Prior Chemotherapy									
Yes	77	4 (5.2)	Not reached [-; -]	72	3 (4.2)	Not reached [-; -]	1.26 [0.28; 5.64]	0.761	0.290
No	305	46 (15.1)	Not reached [-; -]	305	16 (5.2)	Not reached [-; -]	2.90 [1.64; 5.12]	< 0.001	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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

h: Unrounded p-value > 0.050

CI: Confidence Interval; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; PT: Preferred Term; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-38
Analyses of Time to Serious Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
SOC[g]: Investigations									
Age group									
< 65	172	7 (4.1)	Not reached [-; -]	174	3 (1.7)	Not reached [-; -]	2.36 [0.61; 9.13]	0.213	0.903
≥65	210	19 (9.0)	Not reached [-; -]	203	7 (3.4)	Not reached [-; -]	2.58 [1.08; 6.14]	0.032	
ECOG									
0	252	16 (6.3)	Not reached [-; -]	247	7 (2.8)	Not reached [-; -]	2.24 [0.92; 5.44]	0.075	0.594
1 or 2	130	10 (7.7)	Not reached [-; -]	130	3 (2.3)	Not reached [-; -]	3.21 [0.88; 11.68]	0.077	
Region									
WHO Stratum A	378	26 (6.9)	n.c.	374	10 (2.7)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	11 (10.3)	Not reached [-; -]	105	6 (5.7)	Not reached [-; -]	1.70 [0.63; 4.61]	0.299	0.317
No	275	15 (5.5)	Not reached [-; -]	272	4 (1.5)	Not reached [-; -]	3.70 [1.23; 11.16]	0.020	
Prior Chemotherapy									
Yes	77	3 (3.9)	Not reached [-; -]	72	3 (4.2)	Not reached [-; -]	0.77 [0.15; 3.91]	0.757	0.164
No	305	23 (7.5)	Not reached [-; -]	305	7 (2.3)	Not reached [-; -]	3.30 [1.42; 7.69]	0.006	
SOC[g]: Nervous system disorders									

Analyses of Time to Serious Adverse Event by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1 % and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	172	3 (1.7)	Not reached [-; -]	174	2 (1.1)	Not reached [-; -]	1.54 [0.26; 9.24]	0.634	0.500
≥65	210	19 (9.0)	Not reached [-; -]	203	6 (3.0)	Not reached [-; -]	3.10 [1.24; 7.76]	0.016	
ECOG									
0	252	11 (4.4)	Not reached [-; -]	247	3 (1.2)	Not reached [-; -]	3.58 [1.00; 12.84]	0.050[h]	0.585
1 or 2	130	11 (8.5)	Not reached [-; -]	130	5 (3.8)	Not reached [-; -]	2.28 [0.79; 6.57]	0.126	
Region									
WHO Stratum A	378	22 (5.8)	n.c.	374	8 (2.1)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	8 (7.5)	Not reached [-; -]	105	4 (3.8)	Not reached [-; -]	2.00 [0.60; 6.63]	0.259	0.502
No	275	14 (5.1)	Not reached [-; -]	272	4 (1.5)	Not reached [-; -]	3.49 [1.15; 10.61]	0.027	
Prior Chemotherapy									
Yes	77	3 (3.9)	Not reached [-; -]	72	1 (1.4)	Not reached [-; -]	2.90 [0.30; 27.88]	0.356	0.972
No	305	19 (6.2)	Not reached [-; -]	305	7 (2.3)	Not reached [-; -]	2.74 [1.15; 6.52]	0.023	
SOC[g]: Respiratory, thoracic and mediastinal disorders									
Age group									
< 65	172	10 (5.8)	Not reached [-; -]	174	4 (2.3)	Not reached [-; -]	2.59 [0.81; 8.24]	0.108	0.876
≥65	210	12 (5.7)	Not reached [-; -]	203	5 (2.5)	Not reached [-; -]	2.13 [0.75; 6.07]	0.155	

Analyses of Time to Serious Adverse Event by Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated (Incidence ≥ 5% or (Incidence ≥ 1 % and in at least 10 Participants) in One or More Treatment Groups) For System Organ Classes in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
ECOG									
0	252	9 (3.6)	Not reached [-; -]	247	4 (1.6)	Not reached [-; -]	2.05 [0.63; 6.68]	0.233	0.809
1 or 2	130	13 (10.0)	Not reached [-; -]	130	5 (3.8)	Not reached [-; -]	2.57 [0.91; 7.21]	0.074	
Region									
WHO Stratum A	378	22 (5.8)	n.c.	374	9 (2.4)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	7 (6.5)	Not reached [-; -]	105	2 (1.9)	Not reached [-; -]	3.20 [0.66; 15.51]	0.148	0.653
No	275	15 (5.5)	Not reached [-; -]	272	7 (2.6)	Not reached [-; -]	2.07 [0.84; 5.09]	0.111	
Prior Chemotherapy									
Yes	77	7 (9.1)	Not reached [-; -]	72	3 (4.2)	Not reached [-; -]	2.11 [0.54; 8.21]	0.279	0.891
No	305	15 (4.9)	Not reached [-; -]	305	6 (2.0)	Not reached [-; -]	2.40 [0.93; 6.20]	0.070	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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 ≥5% 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

h: Unrounded p-value > 0.050

CI: Confidence Interval; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-39
Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated (Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups) For System Organ Classes in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
SOC[g]: Blood and lymphatic system disorders									
Age group									
< 65	172	34 (19.8)	Not reached [-; -]	174	21 (12.1)	Not reached [-; -]	1.69 [0.98; 2.92]	0.058	0.907
≥65	210	43 (20.5)	Not reached [-; -]	203	26 (12.8)	Not reached [-; -]	1.62 [1.00; 2.64]	0.052	
ECOG									
0	252	46 (18.3)	Not reached [-; -]	247	25 (10.1)	Not reached [-; -]	1.79 [1.10; 2.92]	0.019	0.586
1 or 2	130	31 (23.8)	Not reached [-; -]	130	22 (16.9)	Not reached [-; -]	1.54 [0.89; 2.66]	0.121	
Region									
WHO Stratum A	378	77 (20.4)	n.c.	374	45 (12.0)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	2 (66.7)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	23 (21.5)	Not reached [-; -]	105	14 (13.3)	Not reached [-; -]	1.63 [0.84; 3.17]	0.150	0.892
No	275	54 (19.6)	Not reached [-; -]	272	33 (12.1)	Not reached [-; -]	1.68 [1.09; 2.59]	0.019	
Prior Chemotherapy									
Yes	77	17 (22.1)	Not reached [-; -]	72	8 (11.1)	Not reached [-; -]	2.07 [0.89; 4.82]	0.092	0.508
No	305	60 (19.7)	Not reached [-; -]	305	39 (12.8)	Not reached [-; -]	1.57 [1.05; 2.34]	0.029	
SOC[g]: Infections and infestations									

Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Age group									
< 65	172	16 (9.3)	Not reached [-; -]	174	11 (6.3)	Not reached [-; -]	1.34 [0.62; 2.89]	0.460	0.251
≥65	210	29 (13.8)	Not reached [-; -]	203	11 (5.4)	Not reached [-; -]	2.36 [1.18; 4.73]	0.016	
ECOG									
0	252	19 (7.5)	Not reached [-; -]	247	10 (4.0)	Not reached [-; -]	1.69 [0.78; 3.65]	0.181	0.781
1 or 2	130	26 (20.0)	Not reached [66.0; -]	130	12 (9.2)	Not reached [-; -]	1.90 [0.95; 3.79]	0.070	
Region									
WHO Stratum A	378	45 (11.9)	n.c.	374	22 (5.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	18 (16.8)	Not reached [-; -]	105	8 (7.6)	Not reached [-; -]	1.81 [0.78; 4.21]	0.166	0.964
No	275	27 (9.8)	Not reached [-; -]	272	14 (5.1)	Not reached [-; -]	1.82 [0.96; 3.48]	0.068	
Prior Chemotherapy									
Yes	77	8 (10.4)	Not reached [53.6; -]	72	6 (8.3)	Not reached [-; -]	0.97 [0.33; 2.85]	0.953	0.305
No	305	37 (12.1)	Not reached [-; -]	305	16 (5.2)	Not reached [-; -]	2.13 [1.18; 3.83]	0.012	
SOC[g]: Respiratory, thoracic and mediastinal disorders									
Age group									
< 65	172	11 (6.4)	Not reached [-; -]	174	5 (2.9)	Not reached [-; -]	2.21 [0.77; 6.38]	0.141	0.817
≥65	210	16 (7.6)	Not reached [-; -]	203	8 (3.9)	Not reached [-; -]	1.81 [0.77; 4.24]	0.172	

Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
ECOG									
0	252	10 (4.0)	Not reached [-; -]	247	5 (2.0)	Not reached [-; -]	1.85 [0.63; 5.43]	0.263	0.855
1 or 2	130	17 (13.1)	Not reached [-; -]	130	8 (6.2)	Not reached [-; -]	2.09 [0.90; 4.85]	0.086	
Region									
WHO Stratum A	378	27 (7.1)	n.c.	374	13 (3.5)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	11 (10.3)	Not reached [-; -]	105	3 (2.9)	Not reached [-; -]	3.53 [0.98; 12.69]	0.053	0.300
No	275	16 (5.8)	Not reached [-; -]	272	10 (3.7)	Not reached [-; -]	1.52 [0.69; 3.36]	0.297	
Prior Chemotherapy									
Yes	77	5 (6.5)	Not reached [-; -]	72	2 (2.8)	Not reached [-; -]	2.12 [0.40; 11.13]	0.374	0.860
No	305	22 (7.2)	Not reached [-; -]	305	11 (3.6)	Not reached [-; -]	1.92 [0.93; 3.96]	0.079	
SOC[g]: Skin and subcutaneous tissue disorders									
Age group									
< 65	172	6 (3.5)	Not reached [-; -]	174	2 (1.1)	Not reached [-; -]	2.88 [0.58; 14.34]	0.197	0.967
≥65	210	9 (4.3)	Not reached [-; -]	203	3 (1.5)	Not reached [-; -]	2.70 [0.73; 10.00]	0.137	
ECOG									
0	252	12 (4.8)	Not reached [-; -]	247	3 (1.2)	Not reached [-; -]	3.61 [1.01; 12.84]	0.047	0.396
1 or 2	130	3 (2.3)	Not reached [-; -]	130	2 (1.5)	Not reached [-; -]	1.49 [0.25; 8.91]	0.663	

Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups
with p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
in All-comers Participants
(All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
Region									
WHO Stratum A	378	15 (4.0)	n.c.	374	5 (1.3)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	1 (1.0)	Not reached [-; -]	2.98 [0.32; 27.40]	0.335	0.827
No	275	11 (4.0)	Not reached [-; -]	272	4 (1.5)	Not reached [-; -]	2.68 [0.85; 8.43]	0.091	
Prior Chemotherapy									
Yes	77	2 (2.6)	Not reached [-; -]	72	1 (1.4)	Not reached [-; -]	1.88 [0.17; 20.75]	0.606	0.685
No	305	13 (4.3)	Not reached [-; -]	305	4 (1.3)	Not reached [-; -]	3.03 [0.98; 9.31]	0.053	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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 ≥5% 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

CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; SOC: System Organ Class; WHO: World Health Organization

Table 4.7-40
Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated (Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups) For Preferred Terms in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	Paclitaxel + Carboplatin + Pembrolizumab			Paclitaxel + Carboplatin + Placebo			Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo		
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]
SOC: Blood and lymphatic system disorders - PT[g]: Anaemia									
Age group									
< 65	172	25 (14.5)	Not reached [-; -]	174	14 (8.0)	Not reached [-; -]	1.84 [0.96; 3.55]	0.067	0.473
≥65	210	34 (16.2)	Not reached [-; -]	203	24 (11.8)	Not reached [-; -]	1.36 [0.81; 2.30]	0.250	
ECOG									
0	252	33 (13.1)	Not reached [-; -]	247	18 (7.3)	Not reached [-; -]	1.73 [0.97; 3.08]	0.061	0.529
1 or 2	130	26 (20.0)	Not reached [-; -]	130	20 (15.4)	Not reached [-; -]	1.41 [0.79; 2.53]	0.248	
Region									
WHO Stratum A	378	59 (15.6)	n.c.	374	37 (9.9)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	1 (33.3)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	20 (18.7)	Not reached [-; -]	105	11 (10.5)	Not reached [-; -]	1.77 [0.85; 3.71]	0.128	0.704
No	275	39 (14.2)	Not reached [-; -]	272	27 (9.9)	Not reached [-; -]	1.45 [0.89; 2.37]	0.136	
Prior Chemotherapy									
Yes	77	13 (16.9)	Not reached [-; -]	72	8 (11.1)	Not reached [-; -]	1.52 [0.63; 3.70]	0.352	0.952
No	305	46 (15.1)	Not reached [-; -]	305	30 (9.8)	Not reached [-; -]	1.54 [0.97; 2.44]	0.067	
SOC: Blood and lymphatic system disorders - PT[g]: Febrile neutropenia									
Age group									
< 65	172	5 (2.9)	Not reached [-; -]	174	2 (1.1)	Not reached [-; -]	2.62 [0.51; 13.49]	0.250	0.720
≥65	210	8 (3.8)	Not reached [-; -]	203	2 (1.0)	Not reached [-; -]	3.91 [0.83; 18.41]	0.085	

Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups with p-Value for Interaction Test ≥ 0.05 or not Calculated (Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants) in One or More Treatment Groups) For Preferred Terms in All-comers Participants (All-Participants-as-Treated Population)

Study: KEYNOTE 868[a]	**Paclitaxel + Carboplatin + Pembrolizumab**			**Paclitaxel + Carboplatin + Placebo**			**Paclitaxel + Carboplatin + Pembrolizumab vs. Paclitaxel + Carboplatin + Placebo**		
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]**
ECOG									
0	252	7 (2.8)	Not reached [-; -]	247	3 (1.2)	Not reached [-; -]	2.31 [0.60; 8.94]	0.225	0.425
1 or 2	130	6 (4.6)	Not reached [-; -]	130	1 (0.8)	Not reached [-; -]	6.12 [0.74; 50.81]	0.093	
Region									
WHO Stratum A	378	13 (3.4)	n.c.	374	4 (1.1)	n.c.	n.c.	n.c.	n.c.
Rest of World	4	0 (0.0)	n.c.	3	0 (0.0)	n.c.	n.c.	n.c.	
Mismatch repair deficient (dMMR)									
Yes	107	4 (3.7)	Not reached [-; -]	105	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.044	0.112
No	275	9 (3.3)	Not reached [-; -]	272	4 (1.5)	Not reached [-; -]	2.25 [0.69; 7.29]	0.178	
Prior Chemotherapy									
Yes	77	1 (1.3)	Not reached [-; -]	72	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.326	0.469
No	305	12 (3.9)	Not reached [-; -]	305	4 (1.3)	Not reached [-; -]	3.05 [0.98; 9.45]	0.054	

a: Database Cutoff Date: 16DEC2022 for dMMR participants; 06DEC2022 for pMMR participants

b: Number of participants: all-participants-as-treated population

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

d: Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method

e: Two-sided p-value using Wald test

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 ≥5% 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

CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; dMMR: Deficient Mismatch Repair; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); pMMR: Proficient Mismatch Repair; PT: Preferred Term; SOC: System Organ Class; WHO: World Health Organization